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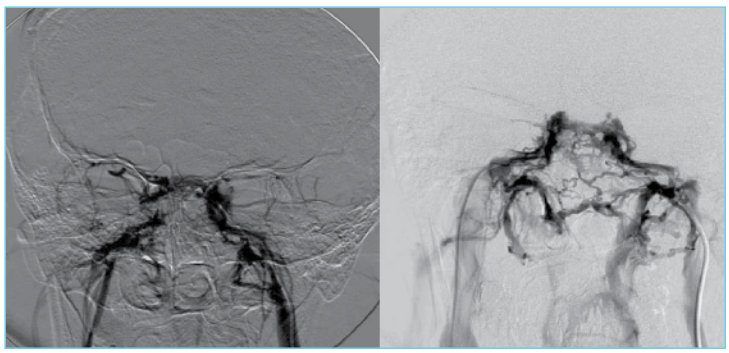

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Erciyes Medical Journal is an independent, unbiased, international, double-blind peer-reviewed, open access journal published in English. The journal, which has been in continuous publication since 1978, is published four times per year in March, June, September and December.

The journal accepts clinical and experimental research articles in different fields of medicine, original case reports, letters to the editor and invited reviews for publication. Research articles and case reports on regionally frequent and specific medical topics are prioritized. Manuscripts on national and international scientific meetings and symposiums and manuscripts sharing scientific correspondence and scientific knowledge between authors and their readers are also published.

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Information for the Authors

Erciyes Medical Journal is published by Erciyes University Medical Faculty which implements the double-blind peer review process. The journal publishes research articles on clinical and experimental subjects from all fields of medicine, review articles on up-to-date topics, letters to the editor, manuscripts on historical progress of general medicine and diseases and content on scientific research and ethical problems. Only online article submissions are accepted (www.erciyesmedj.com).

The basic qualities expected from a manuscript during evaluation processes for the acceptance to publication are; the originality and the contribution to the international scientific literature and to the continuing medical education.

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It is essential for a submitted article to be non-previously published in any other printed or electronic media. Submission of previous reviewer reports is mandatory for articles which have previously been submitted for publication in another journal and rejected. This practice will shorten the evaluation process of the article. If a submitted manuscript has previously been presented at any meeting, the name, date and city in which the meeting was held should be stated or it should be mentioned whether a submitted manuscript is preliminary study or part of a thesis.

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CONSORT guidelines for randomized studies, STROBE guidelines for observational studies, STARD for diagnostic studies, PRISMA for systematic reviews and meta-analysis, ARRIVE for animal experimental studies and TREND for non-randomized behavioral and public health intervention studies, should be taken into consideration.

In order to clarify the subjects of scientific contributions, responsibilities and conflicts of interest on the article, all authors should sign and send the Authorship Contribution Form and ICMJE Form for Disclosure of Potential Conflicts of Interest to the Editorial Office. Practices of the journal on this subject are in accordance with the rules of the International Committee of Medical Journal Editors (ICMJE) and Council of Science Editors (CSE).

The Editorial Office inspects all submitted manuscripts concerning plagiarism and duplication. If an ethical problem is detected, the editorial office will act according to the Committee on Publication Ethics (COPE) guidelines.

The authors should acknowledge and provide information on grants or other financial interests or affiliations with institutions, organizations, or companies relevant to the manuscript.

An Ethics Committee Report, prepared in accordance with "Guide for the Care and Use of Laboratory Animals" of the Helsinki Declaration prepared by the World Medical Association (WMA), is required for experimental, clinical and drug studies and some case reports. The Editorial Office may request the report of the ethics committee or an equivalent official document from the authors if found necessary. Manuscripts reporting results of experimental studies practiced on volunteers and patients should include a patient and volunteer consent statement after explaining the procedure(s) thoroughly. For animal experimental studies, measures taken to reduce pain and discomfort should be clearly stated.

Manuscripts submitted for publication should be written in English. Manuscripts submitted in other languages will be rejected.

Editors inspect whether a submitted manuscript is prepared in accordance with the journal's manuscript preparation rules before assigning the manuscript to reviewers. Manuscripts which are not written in accordance with the journal's manuscript preparation rules will not be evaluated. 21 days are allocated for reviewer evaluations and, if any corrections are required, 28 days are allocated for the author to implement the requested corrections.

All manuscripts will pass through a pre-evaluation process by the Editors and Associate Editors in the first stage of submission. Subsequently, manuscripts are assigned to at least two reviewers for evaluation. Reviewers are selected among external and independent specialists who also have publications in international literature in the same field. Research articles, systematic review articles and meta-analysis manuscripts will be checked by the statistical editor in addition to the assigned reviewers. All manuscripts are also checked for English grammatical and manuscript preparation rules.

Any retraction requests of manuscripts close to the final decision, without reasonable explanation, will be rejected. All authors of a manuscript accepted for publication should consent that editors could make corrections without changing the basic meaning of the text of the manuscript written.

The written files should be prepared in the Microsoft Word program. The Online Paper Acceptance and Evaluation System will be transferred to the authors at all stages and sending of the paper will be accomplished as rapidly and safely as possible. The paper files should be structured according to their types as follows:

Research article
The manuscript title should be stated first. A structured abstract of the article including Objective, Materials and Methods, Results and Conclusion sub-headings should be given below the title. Maximum total word count of the abstracts should be 250 (Turkish abstract is not mandatory for authors submitting outside Turkey). At least 3, at most 6, keywords concordant with MeSH vocabulary terms prepared by the National Library of Medicine (NLM) should be included in each research article. Title, abstract and keywords should be written in both Turkish and English languages (Turkish is not mandatory for authors submitting from outside Turkey). The main text should include Introduction, Materials and Methods (with sub-headings), Results, Discussion, Study Limitations, Conclusion, References, Tables-Figures-Images sections and it should not exceed 5000 words. A maximum of 50 references is sufficient regarding acceptability.

Statistical analysis should be performed in accordance with guidelines on reporting statistics in Medical journals (Altman DG, Gore SM, Gardner MJ, Pocock SJ. Statistical guidelines for contributors to medical journals. Br Med J 1983; 7(6376): 1489-93.). The software used for statistical analysis should be described. When parametric tests are used for comparison of continuous variables, they should be presented as Mean±Standard Deviation or Mean±Standard Error, while for nonparametric tests, data should be presented as Median and range (Minimum- Maximum) or Median and interquartile range (25th and 75th percentiles). Whenever complex analyses are used, the relative risk (RR, relative risk) odds (OR, odds ratio) and hazard ratios values (HR, hazard ratio) should be supported by providing confidence intervals and p values.

Review article
Review articles are accepted by invitation only. Manuscripts prepared by experts who have extensive knowledge in the field and whose knowledge has been projected to the literature as publications and citations will be evaluated. Review articles should be prepared concerning the latest clinical progress on a piece of information or a subject in a format which explains, discusses, evaluates and guides future studies. Review articles should include a title and an unstructured abstract of a maximum 250 words (Turkish abstract is not mandatory for authors submitting outside Turkey). At least 3, at most 6 keywords, concordant with MeSH vocabulary terms prepared by the National Library of Medicine (NLM) should be included. Title, abstract and keywords should be written in both Turkish and English languages (Turkish is not mandatory for authors submitting outside Turkey). With regard to the content of the manuscript, sub-headed main-text, references and tables-figures-images should be included. Total word count of a review article should not exceed 5000.

Case Report
Our journal reserves a limited space for case reports. Only interesting and informative case reports which are about rare diseases which are difficult to diagnose and treat or which suggest a new method, or include new information which cannot be found in the literature, will be published. A title and an unstructured abstract of maximum 200 words should be included in each case report. At least 3, at most 6, keywords concordant with MeSH vocabulary terms prepared by the National Library of Medicine (NLM) should be included. Title, abstract and keywords should be written in both Turkish and English languages (Turkish abstract is not mandatory for authors submitting outside Turkey). The main text should include Introduction, Case Report, Discussion, Conclusion, References and Tables-Figures-Images sections. Total word count should not exceed 1500. Case reports should not include more than 10 references.

Editorial Comment
Editorial Comments should include short discussion and presentation of a research article published in the journal. Editorials are written by the distinguished authors in the field who is invited by the editors. Editorials should be written in English with a maximum of 1500 words and 25 references.

Letter to the Editor
This type of manuscript discusses the importance, missing parts or an overlooked structure of a previously published article. Authors can also submit their comments to the editor on a subject which may be in the reader's field of interest especially on educational cases, in the Letter to the Editor form. Maximum reference number is 10 and no titles of sub-headings are required. A Letter to the Editor should not exceed 1000 words. Volume, year, issue, page numbers, title and author names of the article mentioned in a Letter to the Editor should be stated clearly.

Scientific Letter
Manuscripts with prior notification characteristics announcing new, clinically important scientific developments or information are accepted as Scientific Letters. Scientific Letters should not include sub-headings and should

not exceed 1500 words. The number of references should be limited to 15 and number of tables or figures should be limited to 2.

Education: Results of recently concluded research and conclusive information used in academic education and clinical practice are presented in detail in this type of manuscripts. Title should be given in both Turkish and English languages (Turkish is not mandatory for authors submitting outside Turkey). With regard to the content of the manuscript, sub-headed main-text, references and tables-figures-images should be included. Total word count should not exceed 5000 and total reference number should be limited to 50.

Author names, institution details and contact details, should not be included in the submitted document. These details should be filled in the relevant sections in the online manuscript submission system. All tables, figures, graphs and images should be visibly numbered within the article text and patient, physicians and institution names should be blinded. For microscopic figures, in addition to explanatory information, zoom levels and coloring techniques should also be stated. Line drawings should be done in a professional manner and, in pictures showing a patient's face, patient name and eyes should be covered so that the identity of the patient is not revealed. All images should be in high resolution at minimum 300 dpi. Lines with sufficient thickness should be used in graphs, thus preventing possible losses if resizing is necessary. Widths of images should be either 9 or 18 cm. Line drawings prepared by professionals are more appropriate. Gray tones should not be used in figures. Used abbreviations should be explained below each image in alphabetical order. Roman numerals should not be used in table and figure headings and sub-texts. Roman numerals should be avoided while numbering the Tables and Figures, or while identifying the tables in the text. Decimal fractions in the text, tables and figures should be separated by decimals points in sections in English and commas in sections in Turkish. In particular, tables should be explanatory for the text and should not duplicate the data given in the text.

References should be numbered in the order of citation in the main text (Vancouver style). Only published studies or studies accepted for publication should be cited. Abbreviations of journal titles should be done in accordance with journal abbreviations used in Index Medicus. For publications with 6 or fewer authors, a list of all authors is required, for publications with 7 or more authors, the first 6 authors should be listed, followed by "et al". Reference styles and punctuations should be in accordance with the examples below.

Periodicals: Mackness MI, Mackness B, Durrington PN, Fogelman AM, Berliner J, Lusis AJ, et al. Paraoxonase and coronary heart disease. Curr Opin Lipidol 1998; 9(2): 319-24.

Book chapters: Gary B. Green Peter M. Hill Approach To Chest Pain. In Judith E. Tintinally, MD, MS, Editor. Emergency Medicine. 6th ed. New York: McGraw-Hill; 2004.p.333-43.

Personal author(s): Cohn PF. Silent myocardial ischemia and infarction. 3rd ed. New York: Marcel Dekker; 1993. Editor(s) as author(s): Norman IJ, Redfern SJ, editors. Mental health care for elderly people. New York: Churchill Livingstone; 1996.

Article presented in a meeting: Bengisson S. Sothemin BG. Enforcement of data protection, privacy and security in medical informatics. In: Lun KC, Degoulet P, Piemme TE, Rienhoff O, editors. MEDINFO 92. Proceedings of the 7th World Congress on Medical Informatics; 1992 Sept 6-10; Geneva, Switzerland. Amsterdam: North-Holland; 1992.p.1561-5.

Scientific or technical reports: Smith P. Golladay K. Payment for durable medical equipment billed during skilled nursing facility stays. Final report. Dallas (TX) Dept. of Health and Human Services (US). Office of Evaluation and

Inspections: 1994 Oct. Report No: HHSIGOE 169200860.

Dissertation: Kaplan SI. Post-hospital home health care: the elderly access and utilization (dissertation). St. Louis (MO): Washington Univ. 1995.

Articles in electronic formats: Morse SS. Factors in the emergence of infectious diseases. Emerg Infect Dis (serial online) 1995 Jan-Mar (cited 1996 June 5): 1(1): (24 screens). Available from: URL: http:/ www.cdc.gov/ncidodlEID/cid.htm.

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ERCİYES MEDICAL JOURNAL

Contents

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How to Write a Thesis and Turn It into Publication

EDITORIAL

Cem Evereklioğlu

As a fellow or a researcher, we should completely be clear why we want to begin a thesis and to be published? Science progresses through writing a thesis that begins with brainstorming about novel ideas, iterative nature of drafting, soliciting feedback from the professors, and revising. The main finality of a thesis is to reach to a reader by publication of it in a prestigious peer-reviewed scientific or medical (inter)national journal. Therefore, learning of writing a thesis is central to science progress and writing skills are critical for this. In other words, a thesis is the first writing experience and opportunities of you to learn scientific writing, which should motivate you as you make the journey, for instance, to the front page of the "Survey of Ophthalmology" (1).

My aim is to give you some strategies to assist in the preperation of a thesis and to encourage you to disseminate your thesis through an international journal publication with practical ideas. Therefore, the primary audience for this "Editorial" is not only the fellows who are conducting a thesis at present, but also the assistant or associated professors of faculties who completed a thesis with their fellows in the last few years which remain unpublished. So, if you don't care about "finishing the thesis" or "being published", I immediately suggest you doing another useful job instead of reading the remaining of the present "Editorial".

When the hard part of a thesis (the completion of it) is over, you will soon realize that it is only just the beginning as it has to be written-up. However, it is obvious that the writing process of a thesis is frightening. Indeed, busy clinical training or work and lack of time make it difficult for you, the novice fellows, to turn your work into written thesis and then into peer-reviewed (inter)national publications. However, you must consider early publication of your thesis in journals before the examination of it by a selected jury will be completed. In other words, new data you found in your thesis have a limited shelf life and so get your thesis publish, when available, before it perishes.

Writing an international article from your thesis is always much more difficult than you anticipate. The authors who have discovered the tricks and the secrets of writing and publication are generally unwilling to pass it on to younger rivals, that is you in this circumstance, and this can be understandable (2). Therefore, you will face many frustrations along the way and you should be prepared for the consequences of writing a thesis as it is actually a stressful event. Indeed, it has scientifically been demonstrated that episodic stress associated with "writing a thesis" causes increased cortisol levels after awakening as a sign of psychosocial stress in undergraduate students (3). Additionally, you will soon realize that nobody pays any attention to what you did or published. Moreover, nobody will mention your thesis and nobody will respond it as well. Furthermore, it is extremely clear that most of you, as the readers of the present "Editorial", will never win the Nobel or even TUBİTAK prize as many theses are poor and will neither be read nor cited, unfortunately. But still, please do not drop out during the course, take others less seriously, do not let them discourage you and stop being scared by co-workers in your department who appear to be more successful at finding a new idea or tricks than you (2). For this, I will give you some realistic tips and tricks that may make the "writing" and "publishing" process as easy as possible. Please do not forget that you cannot learn to paint by visiting only the art galleries and looking at pictures hanged on the walls.

A fellow who begins a thesis and writes it is engaged in scientific ways of *thinking*, *questioning* and *synthesizing*. In other words, writing skills are not acquired automatically and one of the best opportunities to write like internationally published authors is to finish a thesis first and then write it. However, the skills that fellows are least likely to develop are "writing skills" and the hardest aspect of any thesis is the "thinking" part. Therefore, although a thesis

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supervisor, who is generally a faculty professor, works one-on-one with a fellow, the most important component of a thesis is not the data or the tables and figures, it is only you as the "thinking" and "writing" is extremely personal processes. Please do also not forget that writing a scientific journal article differs from writing a thesis. Moreover, you should understand that you can win the publication game at the end by only working very hard and becoming an international author. For this, you should finish and get your thesis published not only for intrinsic and extrinsic motives including employment opportunities, career advancement, academic pressure and personal satisfaction, but also to keep the journal editors in a job. Indeed, without you (the fellows, researchers and nationally or internationally published authors), there would be no editors and co-editors, like me. In other words, researching and writing a thesis play a major role in the acquisition of knowledge and writing skills that may consequently be transferred into scientific international articles. Therefore, we need you more than you need us and it is still worth learning how to begin and write theses (2).

About two decades ago, we would visit libraries to search the literature, leafing through thick editions and taking small notes on blank papers. We would then take a pencil to write the first draft. In today's fast moving scientific world, you are very lucky as you can search the needed databases from your own chairs, downloading articles that interest you in seconds. Your labour-saving personal computers produce a range of tables and graphs within minutes and warn you when you make errors of grammar and/or spelling (2).

Theses must contribute not only for knowledge enlargements, but also to solve problems, offering background for further investigations. The aim of a thesis must focus on or address a single research question. In other words, a hypothesis should clarify only one simple message per thesis (4), though it is not the case in general and in Turkey. But still, please do not come up with enormous questions and tasks at the beginning, but generate new knowledge or apply existing knowledge to an important problem. Otherwise, your writing will possibly fail as the reader is unable to come away with a clear message and generally he or she blame himself or herself for not being clever enough to understand your message, though the fault, in fact, lies with you (2).

Every thesis must obey to some rules and most faculties have their own guide to writing a thesis with some limited minor variations (5). Therefore, headings and subheadings should be formatted consistently, which generally uses a standard structure of Title Page with a "Title", Special Thanks, Table of Contents, Abbreviations, list of Graphs/Figures and Tables, Abstract with Key Words, Acknowledgements, Introduction and Aim, Background, Materials and Methods including Statistical Analysis, Results and Discussion with Summary, plus the final list of References. As a starting point, some criteria should first be fulfilled in a novel thesis as the basic building blocks of science are "original articles"; ***(1)*** is the idea new? *(original)*, ***(2)*** is there any important advance? *(significant)*, ***(3)*** has it been first demonstrated by the researcher? *(first disclosure)* and finally ***(4)*** can the investigation be repeated by independent other researchers? *(reproducible)* (2, 5-7).Then, put a realistic time limit on the whole writing process, such as 20 minutes a day and five days a week in a six-month period.

Now, you, as a researcher, know what and why need to write (2). So, please spend the necessary time deciding what you have to do to get there, that is, to get the final destination. Think first about what to write on the way to hospital or department. A good hypothesis is rooted in good thought, which is vital. Then, do a literature search in PubMed and set yourself a brief title. Keep the title as clear as possible and express it as one sentence of 10-20 words, with a verb. For example, imagine that you have started a prospective, controlled trial to see whether non-steroidal anti-inflammatory drugs are effective for preventing posterior capsule opacification after cataract surgery in pediatric cases. Finally, you will come up with a number of alternative titles:

1. *The effect of non-steroidal anti-inflammatory drugs on posterior capsule opacification in children with cataract surgery;*

2. *Non-steroidal anti-inflammatory drugs delay posterior capsule opacification after pediatric cataract surgery;*

3. *Do non-steroidal anti-inflammatory drugs delay posterior capsule opacification after phacoemulsification in children? A randomized, prospective controlled trial (8).*

Note that the first title gives the subject whereas the second and the third titles give the message, both of which have verbs. All might be plausible. However, the first title is generally preferred for the cover of theses whereas the remaining two for the journal publications. I personally preferred, for instance, the final third message, which was in "question style" (8).When writing a thesis or an article, such a message may narrow the field and should be a useful starting point for you. However, a thesis may also give the same title of subject during its (inter)national publication process *(The effect of reading and near-work on the development of myopia in emmetropic boys: A prospective, controlled, three year follow-up study)* (9).

How long should your thesis be? In general, a fellow think that the longer the thesis, the better it will be. It is completely wrong and the answer is quite simple. The problem is not the total number of words and the references, but how you order the thesis with clear messages. All theses can be shortened. This process will make life harder for you, but easier for the responsible university professors as well as for other readers.

Until present, you set an initial title of your work. Write the sections in the order in which they will be read in the thesis. Do not try to impress your professor. So, use your natural language. Therefore, please set a brief first and expand it appropriately. Then, try sketching in some of the "**INTRODUCTION**" (2).This section is the hardest part of anything you write and should answer the question "why did we start to the thesis?" In this section, state the aim of the thesis and summarize the rationale for the investigation. Write down the first opening sentence. If you do not like this sentence, start with the second one. Therefore, please do cite a small number of strictly pertinent papers with references in this section and do not include any data or conclusions being studied.

The first paragraph(s) should give the *background* to the thesis and the gap in knowledge that your thesis is about to answer. You may

spend days thinking of a good first sentence for the *Introduction* section that may give a brief lesson on the subject (the **seminar** approach) (2): *Cataract in children require surgical removal of the crystalline lenses*. A second technique is to refer to a controversy (Much Discussion Recently - **MDR** - approach): *There has recently been much discussion about how to treat posterior capsules in children who have cataract surgery.* An alternative is to emphasize the gravity of the condition (**alarmist** approach) (2), which I prefer in general: *Children with cataract obscuring the visual axis **promptly** require surgical removal with or without posterior chamber intraocular lens implantation to avoid **severe amblyopia**.* The last sentence of the *Introduction* should describe what the researcher of the thesis did *(The purpose of the present thesis was ...)*.

Afterwards, it is very easy for a fellow to collect traditional information to put in "**BACKGROUND**", but much harder to decide what to leave out. Please do not exaggerate this section and collect only the relevant references.

The "**MATERIALS** and **METHODS**" (2) section of a thesis answers the question "what did you do in a logical framework of time?" It expands on the information just given in the final paragraph of the *Introduction*. Information in this section should be sufficient enough for readers to enable them to evaluate and to replicate the work, when necessary, with relevant statistical analysis. For this, describe your selection of the observational or experimental subjects. Identify the age, sex, methods and procedures in sufficient detail to allow other investigators to replicate the results. Give appropriate references to establish both statistical and non-statistical methods with brief descriptions. Information on all major study elements including the protocol, assignment of interventions and the method of marking (blinding) should be included. Describe statistical methods with enough detail at the end.

The "**RESULTS**" (2) section answers the question "what did you find?" For most of the theses, the heart of this section is the data, mostly presented as tables and graphs/figures, which should be as simple as possible and be augment information given in the text. Otherwise, the reader will not thank you. Fellow often find it difficult to decide what goes in a table and what in the text. The text should emphasize or summarize only the important findings and observations to tell the main elements of the story and to draw the readers' attention to some of the main features of the tables and figures. So, present your results in logical sequence. Otherwise, the text in this section should not repeat the knowledge that was given in tables in detail or illustrations. Similarly, do not duplicate data in graphs and tables.

The "**DISCUSSION**" (2) section answers the question "what does it mean and why is it important to you and to readers?" Compare your findings with previous works. The first sentence should be clear and summarize the main finding(s) of the thesis: *"In the present study, we found that ... "*. The most alarming and intriguing sentence the (co-)editors interested in is: *"This study has demonstrated for the first time that ... "*. Therefore, the novel and important aspects of the investigation and the conclusion that follow from them have to be emphasized clearly to the readers and the editors. Do not repeat here the information and data given in the *Introduction* and/or *Results* sections. Include the implications of the findings and their limitations, and make a discussion on the other observations to relevant studies. Avoid statements and conclusions not completely supported by your data. State new hypotheses when warranted. Appropriate recommendations may be included. Please find the answers for the questions; are the findings reliable and what do they mean and where do we go from here? The limitations of the study, if present, should be discussed in this section.

The most important message should appear in the last sentence of the thesis. Some examples may be as follows: *"We conclude that non-steroidal anti-inflammatory drugs are effective for preventing posterior capsule opacification after cataract surgery in pediatric cases"*. Two other types of ending ("More Research is indicated" or "Perhaps Possibly" last sentences) may also be preferred in some instances: *"Further investigations are needed to support our preliminary results"*.

The "**REFERENCES**" (2) are an integral part of the text and should be numbered consecutively in the order in which they are first mentioned in the text. Avoid using abstracts as references. References to articles accepted but not yet published should be designed as "in press". All the references must be verified by you against the original document. In other words, you should have read all the papers you cite and be ensure that the article you cite say what you say they do. Make sure that the numbers of each reference in the text are the same as the numbers in the "reference list".

The "**SUMMARY**" (2) section should reflect the text accurately and briefly. It should briefly summarize the purpose, basic procedures, main findings and principal conclusions. This section must be short. So, try to avoid repetition here. If you have only one objective in your thesis, you should have one clear conclusion. So, do not add a new material to the summary. If you, on the other hand, have more than one objective, you may have more than one conclusion. But still, it should emphasize new and the most important aspects of your work, not every single finding. In addition, do not speculate or overestimate your conclusions those were not verified by your finding.

Fellows should write their thesis themselves, possibly with some help from their supervisors. Today, there are various unimaginable commercial services that provide help for writing a fellow thesis. This condition is called ghostwriters and is stated to be totally unacceptable (10).

Once you have finished your writing with the rules stated above, you possibly submitted a poorly written draft. So, walk away from the thesis and put some distance between you and it. Leave it for a few days or weeks on the shelf. Finally, read the print out of the drafted thesis/paper carefully for grammar, style and consistency. Otherwise, how can a professor in the jury or an editor rely on the accuracy and consistency of your work if you show no accuracy in your use of language, grammar and style? Check the consecutive page numbering as well as the consistency of the numbering of tables and figures or graphs. Check the tables and figures for their accuracy. Check the margins of the pages whether they are in accordance with the rules of your faculty. The right margins must also be justified throughout the thesis (2).

Many theses are not being submitted for professional publication, perhaps due to a combination of various factors including time constraints and lack of mentoring (10). In addition, a recently graduated fellow is now engaged in searching for a new position and moving to another city. However, please do not forget again that the longer you wait, the greater the risk that your data will grow stale (11).

One of the big problems a fellow confronted with is the order of the responsible researcher and the co-authors when a thesis will be published in a journal. You have carried out an outstanding work for your thesis and it has finally finished. Now you think that you deserve to be the first author due to your contributions and time allotted to your thesis. However, when the time came to write your thesis, you did not demonstrate any attempt to write it even though your supervisor warned you again and again (11). The reason of this may be that you do not have sufficient knowledge or skills to think and conduct a thesis and prepare a publishable article without substantial support from your supervisor (12).

Please do not forget that writing is a personal activity and you should know that first authorship is equated with substantial contribution to writing the manuscript, so it is important you understand this is part of the responsibilities of being first author (11). In peer-reviewed international scientific publications, the first and the last (senior/corresponding) authors are typically the researchers who made the most valuable contributions to the article (13). Doctoral students or fellows are usually authorized as the first authors of theses based on their dissertation research (14). It has been recommended that when there is any question as to who made the primary contribution, the student should receive higher authorship (11). The reason of this is to protect the student who has less power in such a situation (11).

Who would be the first author if the supervisor wrote the thesis for international publication instead of you? Although this kind of controversial situation may be familiar for you and your supervisor, there are no guidelines that might be implemented in advance to handle this kind of problem (11). But still, the supervisor and fellow should discuss the reasons for changing authorship order, when necessary. In general, authorship should be negotiated in the context of following questions; ***(1)*** who is the owner of original idea? ***(2)*** who planned and designed the study? ***(3)*** who carried out the work that created the data? ***(4)*** who wrote the first draft and the final article? Therefore, as intellectual contribution is more important than actual time and effort expended when determining the order of authorship (11), my personal opinion is that if you, as a fellow (not your responsible professor), is the person who is *thinking* the original idea, *writing* and *rewriting*, it means that you are the team leader and you can be the "first author". We know that the supervisor will revise your first draft. However, this activity does not warrant a change in authorship order (11).

If, on the other hand, the thinking and managing responsibility of the project belongs to your university professor and if you do not write even the first draft of your thesis, the paper will likely get written completely by your professor. In that case, he or she will have a sound of moral case to be the "first author" even if you seem to be the owner of the thesis (2, 3). But still, it will be the managing professor's responsibility to solicit you individually and make decisions. That is, the professor may prefer you as the first author and him/herself as the corresponding author.

We, editors and co-editors, have sometimes encountered by clear cases of "ghost authorship" when authors who had no right to share the credit have insisted that their names be included on the final authorship list during its publication process. However, only individuals who have made important substantial scientific or professional contributions to your thesis should be listed in the final authorship list, regardless of their status (12). At least one of the following criteria must be met; *conception*, *design*, *analysis* and *interpretation* of data, *drafting* or critical *revising* of the article, or *final approval* of the version to be published. That is, general supervision by, for instance, the head of the department is not sufficient for the authorship, which is sometimes the case in Turkey, unfortunately. If you do not want your thesis starts to look ridiculous, please avoid listing, for instance, eight or ten authors during the national or international publication process of your hypothesis reporting only a single test on a group of subjects, which will obviously jeopardize your chances of publication. Therefore, the order of remaining authorship should be negotiated between you and your supervisor in the initial stages of your thesis and its writing. If you do not perform all the statistical evaluation and analysis yourself, please do not forget that you involve a statistician in acknowledgements. If, on the other hand, you have consulted one who performed a significant contribution to the thesis with a numerous statistical analyses, please consider his or her name in your final authorship list, whenever relevant.

Start asking yourself the following difficult and critical questions (2); ***(1)*** is there a clear message in your thesis, ***(2)*** do you prove the message, and finally ***(3)*** is the structure and the length of the thesis appropriate and reader-friendly? Do micro-editing for omissions and errors. Be obsesive at this stage. Most computers have a spell check. Please use it. It will take only minutes. You will almost pick up many misspellings that you will probably never spot (Did you notice the missing "s" in "obsessive" above?). Please do not forget that long sentences are not reader-friendly or understandable. In addition, long sentences and words are not a sign of cleverness of you. In fact, new ideas must be conveyed in the fewest words. Therefore, be vigilant, use clear English and avoid pompous polysyllabic words. Finally, always ask someone else to read your thesis to check for its readability or use voluntary internal reviewers as good advice from your experienced co-workers will be essential (2).

Now, choose the appropriate journal for your article, as a paper delivered to an inappropriate audience will possibly be rejected directly by the editors. In other words, decide whether the journal you submitted your thesis is interested in the type of research you conducted, which can easily be find from the "Instructions to authors" of the journal (11).

Plagiarism, a familiar concept to most researchers and authors, should strictly be avoided, though many of it are unintentional as the authors are unaware of some of the nuances regarding plagiarism (11). However, there are two generally accepted categories (11, 15); ***(1)*** *cryptamnesia*, in which you think your idea is original when it in fact was reported previously by another person,

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Publishing in multiple sources should also be avoided. Although it is appropriate to submit some part of your work for presentation at a conference prior to its publication in a journal, an article should not be under review by more than one journal at a time.

Sometimes, a thesis may include various researching points. So, you can publish the different parts of your work in different journals provided that two papers differ substantially and you are citing this situation in your latter paper or disclose this situation appropriately in your cover letter. However, please strictly avoid from salami science.

Your thesis should generate transferable knowledge and skills that must be used in daily work. You are now familiar with how to search for and evaluate information in a scientific manner and required these attributes during your thesis process. In other words, writing a thesis is a way of learning how to write a scientific article. Therefore, you now won the publication game. Congratulations.

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REFERENCES

1. Evereklioğlu C. Current concepts in the etiology and treatment of Behçet disease (Major Review). Surv Ophthalmol 2005; 50(4): 297-350. [CrossRef]
2. Albert T. Winning the publications game. How to write a scientific paper without neglecting your patients. Redcliffe Medical Press, Oxon, 2000.
3. Izawa S, Sugaya N, Ogawa N, et al. Episodic stress associated with writing a graduation thesis and free cortisol secretion after awakening. Int J Psychophysiol 2007; 64(2): 141-5. [CrossRef]
4. Liebano RE, Dias SL, Ferreira LM. Number of objectives and conclusions in dissertations and thesis. Acta Cir Bras 2005; 20(4): 272-4. [CrossRef]
5. Cunningham SJ. How to write a thesis. J Orthod 2004; 31(2): 144-8. [CrossRef]
6. Whimster WF. Biomedical Research: how to plan, publish and present it. Springer-Verlag, London, 1997. [CrossRef]
7. Mathews JR, Bowen JM, Matthews RW. Successful Scientific Writing. Cambridge University press, Cambridge, 1996.
8. Evereklioğlu C, İlhan O. Do non-steroidal anti-inflammatory drugs delay posterior capsule opacification after phacoemulsification in children? A randomized, prospective controlled trial *(My fellow's thesis)*. Curr Eye Res 2011; 36(12): 1-9. [CrossRef]
9. Hepsen IF, Evereklioğlu C, Bayramlar H. The effect of reading and near-work on the development of myopia in emmetropic boys: A prospective, controlled, three year follow-up study *(My own thesis)*. Vision Res 2001; 41(19): 2511-20. [CrossRef]
10. Roberts PJ. Ghostwriters for doctoral thesis. Scand J Surg 2004; 93(1): 3.
11. Resta RG, McCarthy Veach P, Charles S, Vogel K, Blase T, Palmer CG. Publishing a master's thesis: a guide for novice authors. J Genet Couns 2010; 19(3): 217-27. [CrossRef]
12. Shadish W. APA ethics and student authorship on master's theses. Am Psychol 1994; 49(4): 1096. [CrossRef]
13. Laflin MT, Glover ED, McDermott RJ. Publication ethics: an examination of authorship practices. Am J Health Behav 2005; 29(6): 579-87. [CrossRef]
14. Nguyen T, Nguyen TD. Authorship ethics: issues and suggested guidelines for the helping professions. Couns Val 2006; 50(2): 208-16. [CrossRef]
15. Roig M. Plagiarism and paraphrasing criteria of college and university professors. Ethics Behav 2001; 11(7): 307-23. [CrossRef]
16. East J. The problem of plagiarism in academic culture. Int J Educ Integr 2006; 2: 16-28.
17. Lambie GW, Sias SM, Davis KM, Lawson G, Akos P. A scholarly writing resource for counselor educators and their students. J Couns Dev 2008; 86: 18-25. [CrossRef]

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Do Inferior Petrosal Sinus Drainage Variations Affect the Sampling Lateralization Results?

ORIGINAL INVESTIGATION

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ABSTRACT

Objective: To evaluate the relationship between adenoma lateralization and the variations in petrosal sinus drainage.

Materials and Methods: A total of 24 patients diagnosed as ACTH dependent Cushing Syndrome (CS) in the Department of Endocrinology and Metabolism Disorders between May 2006 and May 2012 were evaluated. The patient files for data, including laboratory results and imaging records, were analyzed retrospectively. MRI was performed using a 1.5-T scanner. The femoral vein was cannulated using the Seldinger technique and bilateral venous sheaths were inserted for bileteral inferior petrosal sinus sampling (BIPSS).

Results: Microadenomas were detected with MRI in 12 patients. Right lateralization has been determined in 12 patients (54.5%), left lateralization in 5 patients (22.7%) and central gradient in 2 patients (22.8%). No peripheral/central gradient was obtained by BIPSS in 3 patients compatible with an ectopic source of ACTH. Pituitary surgery was performed in 19 patients.

Conclusion: BIPSS may avoid unnecessary pituitary surgery. Asymmetric drainage may affect the results of lateralization. This study suggest that drainage variations may have subgroups.

Key words: Pituitary adenoma, BIPSS, Cushing's syndrome

INTRODUCTION

Cushing syndrome (CS) is associated with high rates of morbidity and mortality. ACTH-dependent CS is a heterogeneous disorder and requires a multidisciplinary and individualized approach to patient management (1). Early diagnosis, determination of the exact etiology and prompt management are essential for patients with CS. Endocrine tests may not always be sufficient in differentiating between ectopic and pituitary origins of ACTH dependent CS (2, 3). Even if endocrine tests show the pituitary as the origin of CS, Magnetic Resonance Imaging (MRI) may not reveal any abnormality in about 40-50% of patients with Cushing Disease (CD) (4, 5). For ACTH dependent CS, if MRI is negative or if the lesion is smaller, regardless of the endocrine test results, venous sampling is recommended (6). Bilateral Inferior Petrosal Sinus Sampling (BIPSS) may play an important role in lateralization of the site of ACTH hypersecretion.

There is a limited number of data concerning whether petrosal sinus drainage variations might cause false negative results (7, 8). This study aimed to investigate the relationship between adenoma lateralization and the variations in petrosal sinus drainage.

MATERIAL and METHODS

A total of 24 patients diagnosed as ACTH dependent CS in the Department of Endocrinology and Metabolism Disorders between May 2006 and May 2012 were evaluated. Microadenomas were detected with MRI in 12 patients. The patient files for data including laboratory results and imaging records were analyzed retrospectively. The Erciyes University School of Medicine Ethics Committee approved the study protocol and written informed consent was obtained from patients who participiated in this study.

MRI was performed using a 1.5-T scanner. Imaging interpretation was made independently by two experienced radiologists with knowledge of all associated clinical and biochemical information but blinded to surgical and histopathologic results. Radiographic interpretations of the pituitary MRI were recorded and classified according to the literature (9). A pituitary source of ACTH was established by histologic confirmation of an ACTH-secreting pituitary adenoma (pathologic criterion) or cure or significant remission of the hypercortisolism after pituitary microsurgery even if no tumor was found (clinical criterion). The diagnosis of ectopic ACTH- dependent CS was made if MRI was negative for a pituitary adenoma and succesful catheterization and BIPSS did not reveal a gradi-

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ent in favour of central localization. The patient was placed in the supine position on the fluoroscopy table for BIPSS. (Philips Integris Angio Netherlands). Each groin was prepared in sterile fashion for intravenous access. The femoral vein was cannulated using the Seldinger technique and bilateral venous sheaths were inserted.

Two 4-French glidecath hydrophilic-coated catheters, tip angle of 45 degrees (terumo interventional Systems, Japan) were introduced into the right and left femoral veins. Catheters were then advanced from the bilateral internal jugular vein to each inferior petrosal sinus.

Microguide wire (0.014 inch) (Rapid Transit microcatheters) (Cordis, Miami, FL, USA, Transend 0.014 Guidewires, Boston Scientific Corp.) and microcatheter have been used for patients who have not been selectively catheterized with 4-French diagnostic catheter. 5000 IU heparin as a bolus was given immediately before the process. Sinography was performed from the catheter that had been unilaterally replaced into the inferior sinus petrosus and guidance screenings were reported to screen the other sinus petrosus. The drainage variations and types were determined. After the correct replacement of catheters, simultaneous blood samplings of 3cc were obtained from each of the three ports (peripheral, left inferior petrosal sinus, and right inferior petrosal sinus). After collecting the baseline samples, long-acting analogue of AVP, desmopressin (DDAVP) or CRH was injected as IV bolus peripherally and post-DDAVP samples were obtained from each part at 3, 5, 8, 10, 13 and 15 minutes. Blood samples were immediately placed into lavender-top EDTA-containing tubes and placed on ice. Processing of the blood, including centrifugation and plasma decantation were done and samples were analyzed immediately. After blood sampling, catheters and sheaths were removed and compression of the groin was performed until venous hemostasis. Threshold criteria for pituitary source is defined as an inferior petrosal sinus to peripheral (IPS:P) basal ratio of 2:1 or greater without CRH or an IPS:P ratio 3:1 or greater after the administration of CRH.

The Shiu classification has been used in the determinations of inferior petrosal sinus drainage variations (10). Type I is the shedding of the inferior petrosal sinus with hypoplasic image anterior condylary vein just before integrating the jugular vein. If the shedding is after integrating the jugular vein this is type II drainage pattern. Type III is the shedding of the inferior petrosal sinus to the jugular vein like a plexus but not like a unique vein and type IV is the drainage of the inferior petrosal sinus to the vertebral venous plexus by the anterior condylar vein before assocaiaton with the jugular vein.

Statistical analysis

SPSS 15.0 software (Windows, SPSS, Inc, Chicago, Illinois, USA) was used to statistical analysis and data in the study was given as descriptive statistics, number, percent and the median (range).

RESULTS

This study included 24 consecutive patients with ACTH dependent CS (20 females (83%), 4 males (17%); mean age 49, age range, 19-69 years). BIPSS was performed with selective catheterization in 22 patients. Two patients have been exluded from the study as selective catheterization could not be performed. Of the 22 patients, the selective catheterization of inferior petrosal sinuses were performed from 35 localization with 4F diagnostic catheter (79.5%), while microcatheters were used from 9 localization (20.5%). The catheterization success rate was 91.6%.

Inferior petrosal sinus drainage variations are shown in Table 1. Right lateralization has been determined in 12 patients (54.5%), left lateralization in 5 patients (22.7%) and central gradient in 2 patients (22.8%). No peripheral/central gradient was obtained by BIPSS in 3 patients compatible with an ectopic source of ACTH. Of 3 patients, one patient had bilateral Type III and two patients had bilateral Type I variations. The distribution of types and lateralization results are shown in Table 2.

All 19 patients who were detected to have a central gradient of ACTH secretion underwent pituitary surgery and an adenoma was detected in all during surgery. Only one case showed BIPSS lateralization to the opposite site of the adenoma which was detected on pituitary MRI. During pituitary surgery the adenoma was found to be localized on the site detected with MRI. Secondary adrenal insufficiency detected after surgery confirmed that the adenoma found during surgery and MRI was the origin of ACTH secretion. So BIPSS was able to localize the pituitary origin of ACTH secretion, but resulted in false lateralization (7). Asymmetric type III drainage was present in 4 patients. Among such patients BIPSS resulted in false lateralization to the side with type III drainage in only one patient. According to these results, both the specificity and sensitivity of BIPSS was found to be 100% in differentiating ectopic and pituitary origins of ACTH secretion, but correct lateralization could be achieved in 95% of the patients.

Pituitary MRI revealed images; microadenomas were detected in 12 patients (55%) and suspicious results for adenoma in 2 patients (9%). No adenoma was detected on MRI in 8 patients (36%). The specificity and sensitivity of MRI were determined as 100% and 54.5%, respectively.

Two (66%) of 3 patients who had no peripheral/central gradient on BIPSS, had suspicious results for adenoma on MRI and no adenoma was reported on MRI in one patient (33%). No hypophyseal surgery was performed in these patients but bilateral adrenalectomy was done. There was no patient with Nelson's syndrome. Patients were diagnosed as Cushing's Disease in 86% of cases and ectopic CS in 14% of cases. Other imaging methods were done in all cases who had ectopic CS and there were no sources of ACTH.

Table 1. Variations of inferior petrosal sinus drainage

Drainage type	Type I	Type II	Type III	Type IV
N	17	17	10	0
%	39	39	22	0

Table 2. The distribution of drainage types and lateralization results

	Type I	Type II	Type III	Total
Right	2 (17%)	7 (58%)	3 (25%)	12 (63%)
Left	3 (60%)	1 (20%)	1 (20%)	5 (26%)
Central	1 (50%)	1 (50%)	-	2 (11%)
Total	6 (32%)	9 (47%)	4 (21%)	19 (100%)

Bilateral symmetric drainage was found in 12 (55%) of 22 patients and asymmetric drainage was found in 10 patients (45%). The patients who had asymmetric drainage are shown in Table 3. No complication due to operational process has been observed.

DISCUSSION

Cushing's syndrome (CS) may be caused by cortisol or ACTH secreting tumors especially pituitary adenoma (11-13). Plasma ACTH levels are the first-line testing in the differential diagnosis of CS (14). Non-supressed plasma levels of ACTH in a hypercortisolemic patient indicates ACTH-dependent CS, which may be pituitary or ectopic in origin (15). BIPSS is used to confirm a central source of ACTH, and it also plays a role in lateralization of ACTH hypersecretion from the pituitary. In patients with ACTH-dependent CS presenting with a clear adenoma on pituitary MRI, the BIPSS does not need to be carried out. However if clinical and laboratory features suggest ectopic ACTH secretion or a clear adenoma cannot be seen on pituitary MRI, BIPSS is required (9). In this study; 2 suspicious pituitary microadenomas were detected in 2 (67%) of 3 patients with ACTH-dependent CS. In these 3 patients; central CS was not diagnosed with BIPSS so unnecessary pituitary surgery has been avoided.

The BIPSS procedure was technically successful in 22 of 24 (91.6%) patients. The success rate of the BIPSS procedure is reported as 71.6%-98.9% in the literature (9, 16-19). This is similar to our study. We suggest that sinography that has been performed with contrast liquid through the first catheterized sinus led the physicians to achieve techniqual success. This may be explained by the occasions that sinography serves for choosing diagnostic or micro catheters.

The most common drainage pattern is type I (45%) according to Shiu et all, (10). Type II, type III, andtype IV are observed with a frequency of 24%, 24% and 7% respectively (10). In our study, type I, II and III drainage patterns were obseved as 39%, 39% and 22% respectively. Pituitary surgery was performed on 19 (86%) patients. Adenomas were found to be in the correct site during surgery according to BIPSS lateralization results in 18 of 19 patients. The specificity and sensitivity of BIPSS in defining a pituitary or ectopic ACTH secretion was found to be 100%, but among patients with a pituitary origin of ACTH secretion, BIPSS failed to correctly lateralize the ACTH-secreting adenoma. Correct lateralization rate was found to be 95%. These findings are similiar to previously reported data (9, 16-19). BIPSS and surgery were not correlated in one patient. (Case 6, Figure 1). In this patient, type III drainage was present on the right and type I was present on the left. However, the same drainage pattern was also present in another patient whom (type III in the right and type II in the left) BIPSS and surgery findings were correlated (Case 5, Figure 2). The different results obtained in these two patients suggest that Type III drainage may have subgroups.

Table 3. The distribution of patients with asymmetric drainage

	Right	Left	BIPSS	MRI	Surgery
Case 1	Type II	TypeIII	right	right	right
Case 2	Type III	Type II	left	left	left
Case 3	Type II	Type I	right	right	right
Case 4	Type I	Type II	right	right	right
Case 5	TypeIII	TypeII	right	right	right
Case 6	Tip III	Type I	left	right	right
Case 7	Type I	Type II	right	left	left
Case 8	Type II	Type I	right	right	right
Case 9	Type II	Type I	right	right	right
Case 10	Type I	Type II	left	left	left

BIPSS: Bileteral inferior petrosal sinus sampling, MRI: Magnetic resonance imaging

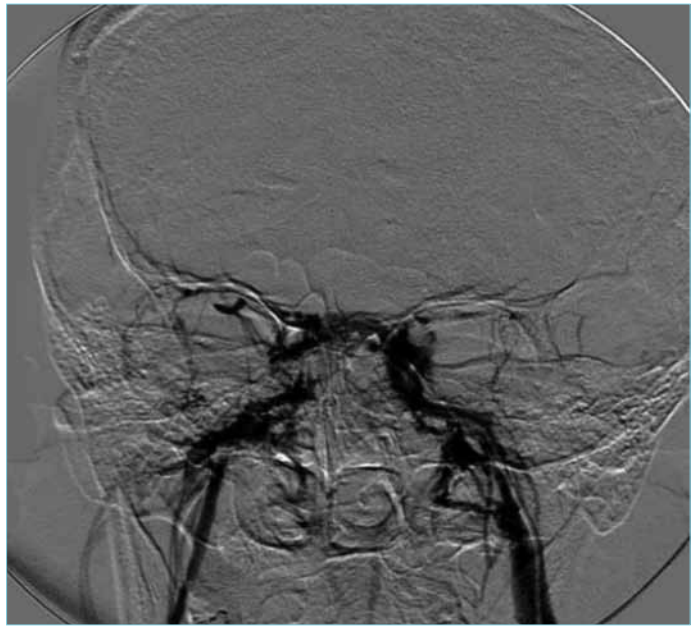

Figure 1. **Drainage variation in the patient 6, type III drainage was present on in the right and type I was present the left**

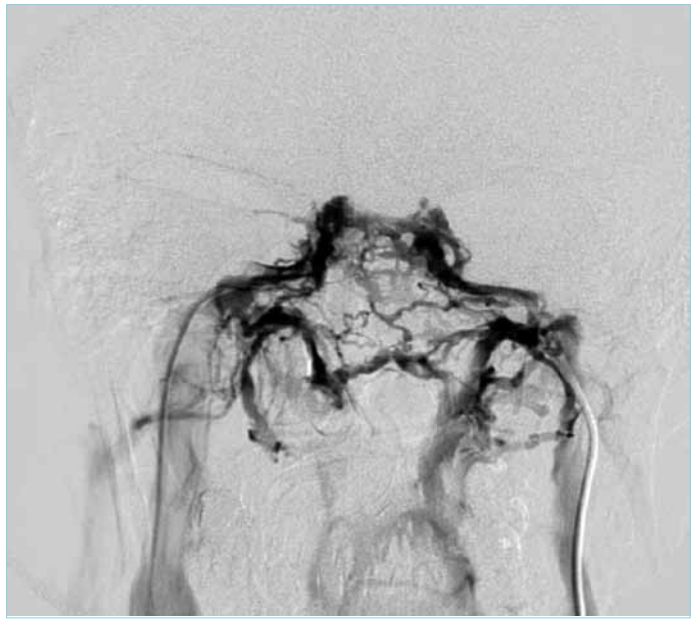

Figure 2. **Drainage variation in the patient 5, type III in the right and type II in the left**

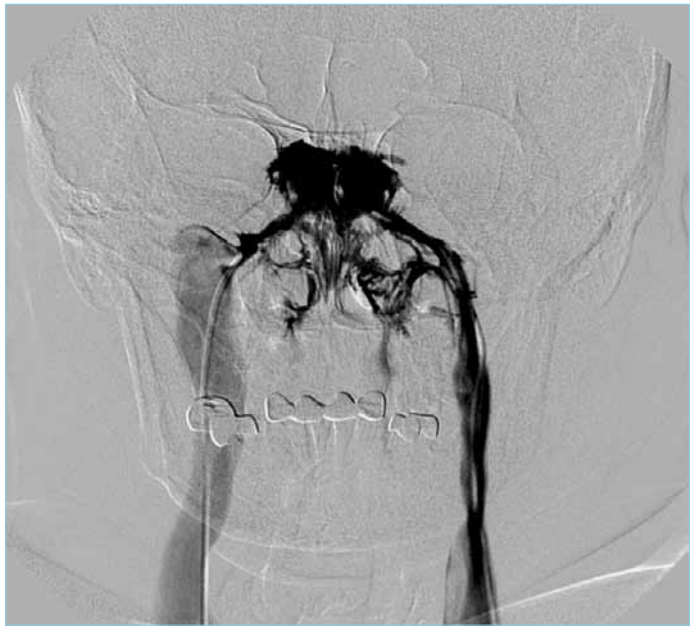

Figure 3. Drainage pattern which is symmetrical, type I

Mamelak et al. (21) have found symmetric drainage (55%) that was consistent with our results (55%). The specificity and sensitivity of the MRI technique in the diagnosis of pituitary adenomas in our study was; 100% and 54.5% respectively. The data for specificity and sensitivity is reported as 62.5% -100 and 45%- 67%, respectively in previous studies (9, 22, 23).

In our series, BIPSS procedure was performed safely in all patients. Risks of BIPSS are uncommon; however, there are potential adverse events. The most common complication is groin hematoma, occurring in 3-4% of the patients (24). The complication of insert area was less common, which could be suggested as a result of femoral catheterization with guidance of USG. Complications such as; deep venous thrombosis, pulmonary thromboembolism (25, 26), pontocerebellar junction stroke (27), brain stem injury (28), cranial nerve palsy (29), venous subarachnoid hemorrhage and obstructive hydrocephalus (30) are observed rare complications. None of these were seen in our study during the operation. Contrast liquid was given from the catheterized site that led to formation of road maps. As a result, the use of these road maps allowed catheterization of the opposite site that resulted in less complications.

In order to avoid the thrombosis of cavernous sinus and coaxial catheter system, intravenous heparin (70U/kg/h wasgiven intravenously. During operation, the coaxial catheter system has been irrigated with saline solutions. The most common complaints were; headache and discomfort that did not require treatment. These problems have been reported in previous data (24) that could be avoided by obtaining informed consent forms. This may be regarded as an alternative method for patients having problems in bilateral catheterization by arterial puncture serving venous phase screenings. No complication due to the operational process has been observed in this study.

In 2 patients, no lateralization could be done (Figure 3) there was a central (pituitary) source of CS. However, drainage patterns were found to be symmetrical. There were no cases in the literature similar to our results.

The effect of drainage variations to the results of BIPSS could be verified with large studies including patients who have more central lesions like our two patient and other patients who have an asymmetric drainage.

CONCLUSION

Although laboratory data and MRI techniques suggest the diagnosis of ACTH-dependent CS; BIPSS may avoid unnecessary pituitary surgery. Asymmetric drainage may affect the results of lateralization. This study suggests that drainage variations may have subgroups.

Ethics Committee Approval: Ethics committee approval was obtained for this study from the ethics committee of Erciyes University School of Medicine.

Informed Consent: Written informed consent was obtained from patients who participiated in this study.

Peer-review: Externally peer-reviewed.

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REFERENCES

1. Biller BMK, Grossman AB, Stewart PM, Melmed S, Bertagna X, Bertherat J, et al. Treatment of adrenocorticotropin-dependent Cushing's syndrome: a consensus statement. J Clin Endocrinol Metab 2008; 93(7): 2454-62. [CrossRef]
2. Dichek HL, Nieman LK, Oldfield EH, Pass HI, Malley JD, Cutler GB. A comparison of the standard high dose dexamethasone suppression test for the differential diagnosis of adrenocorticotropin-dependent Cushing's syndrome. J Clin Endocrinol Metab 1994; 78(2): 418-22.
3. Avgerinos PC, Yanovski JA, Oldfield EH, Nieman LK, Cutler GB. The metyrapone and dexamethasone suppression tests for the differential diagnosis of the adrenocorticotropin-dependent Cushing's syndrome: a comparison. Ann Intern Med 1994; 121(5): 318-27. [CrossRef]
4. Hall WA, Luciano MG, Doppman JL, Patronas NP, Oldfield EH. Pituitary magnetic resonance imaging for normal human volunteers: occult adenomas in the general population. Ann Intern Med 1994; 120(10): 817-20. [CrossRef]
5. Landolt AM, Schubiger O, Maurer R, Girard J. The value of inferior petrosal sinus sampling in diagnosis and treatment of Cushing's disease. Clin Endocrinol 1994; 40(4): 485-92. [CrossRef]
6. Colao A, Faggiano A, Pivonello R, Pecori Giraldi F, Cavagnini F, Lombardi G. Study Group of the Italian Endocrinology Society on the Pathophsiology of the Hypothalamic-Pituitary-Adrenal Axis. Inferior petrosal sinus sampling in the differential diagnosis of Cushing's syndrome: results of an Italian multicenter study. Eur J Endocrinol 2001; 144(5): 499-507. [CrossRef]

7. Elbüken G, Karaca Z, Çakır İ, Dönmez H, Selçuklu A, Çolak R, et al. Anatomical variations may ınterfere with bilateral ınferior petrosal sinus sampling results. Turk Jem 2010; 14: 95-9.
8. Doppman JL, Chang R, Oldfield EH, Chrousos G, Stratakis CA, Nieman LK. The hypoplastic inferior petrosal sinus: a potential source of false-negative results in petrosal sampling for Cushing's disease. J Clin Endocrinol Metab 1999; 84(2): 533-40.
9. Kaskarelis IS, Tsatalou EG, Benakis SV, Malagari K, Komninos I, Vassiliadi D, et al. Bilateral inferior petrosal sinuses sampling in the routine investigation of Cushing's syndrome: a comparison with MRI. AJR Am J Roentgenol 2006; 187(2): 562-70. [CrossRef]
10. Shiu PC, Hanafee WN, Wilson GH, Rand RW. Cavernous sinus venography. AJR 1968; 104(1): 57-62. [CrossRef]
11. Boscaro M, Arnaldi G. Approach to the patient with possible Cushing's syndrome. J Clin Endocrinol Metab 2009; 94(9): 3121-31. [CrossRef]
12. Nieman L. Causes and pathophysiology of Cushing's syndrome. In: DS Basow, ed. UpToDate. Waltham, MA; 2011.
13. Nieman L, Lacroix A, Martin K. Establishing the case of Cushing's syndrome. In: DS Basow, ed. Waltham, MA: UpToDate; 2011.
14. Gross BA, Mindea SA, Pick AJ, Chandler JP, Batjer HH. Diagnostic approach to Cushing disease. Neurosurg Focus 2007; 23: E1. [CrossRef]
15. Tomycz ND, Horowitz MB. Inferior Petrosal sinus sampling in the diagnosis of sellar neuropathology. Neurosurg Clin N Am 2009; 20(3): 361-7. [CrossRef]
16. Kaltsas GA, Giannulis MG, Newell-Price JD, Dacie JE, Thakkar C, Afshar F, et al. A critical analysis of the value of simultaneous inferior petrosal sinus sampling in Cushing's disease and the occult ectopic adrenocorticotropin syndrome. J Clin Endocrinol Metab 1999; 84(2): 487-92.
17. Oldfield EH, Doppman JL, Nieman LK, Chrousos GP, Miller DL, Katz DA, et al. Petrosal sinus sampling with and without corticotropin-releasing hormone for the differential diagnosis of Cushing's syndrome. N Engl J Med 1991; 325(13): 897-905. [CrossRef]
18. Wiggam MI, Heaney AP, McIlrath EM, McCance DR, Sheridan B, Hadden DR, et al. Bilateral inferior petrosal sinus sampling in the differential diagnosis of adrenocorticotropin-dependent Cushing's syndrome: a comparison with other diagnostic tests. J Clin Endocrinol Metab 2000; 85(4): 1525-32.
19. Swearingen B, Katznelson L, Miller K, Grinspoon S, Waltman A, Dorer DJ, et al. Diagnostic errors after inferior petrosal sinus sampling. J Clin Endocrinol Metab 2004; 89(8): 3752-63. [CrossRef]
20. Castinetti F, Morange I, Dufour H, Jaquet P, Conte-Devolx B, Girard N, et al. Desmopressin test during petrosal sinus sampling: a valuable tool to discriminate pituitary or ectopic ACTH- dependent Cushing's syndrome. Eur J Endocrinol 2007; 157(3): 271-7. [CrossRef]
21. Mamelak A, Dowd C, Tyrrell J, McDonald J, Wilson C. Venous angiography is needed to interpret inferior petrosal sinus and cavernous sinus sampling data for lateralizing adrenocorticotropin-secreting adenomas. J Clin Endocrinol Metab 1996; 81(2): 475-81.
22. Graham KE, Samuels MH, Nesbit GM, Cook DM, O'Neill OR, Barnwell SL, et al. Cavernous sinus sampling is highly accurate in distinguishing Cushing's disease from the ectopic adrenocorticotropin syndrome and in predicting intrapituitary tumor location. J Clin Endocrinol Metab 1999; 84(5): 1602-10.
23. Tabarin A, Laurent F, Catargi B, Olivier-Puel F, Lescene R, Berge J, et al. Comparative evaluation of conventional and dynamic magnetic resonance imaging of the pituitary gland for the diagnosis of Cushing's disease. Clin Endocrinol (Oxf) 1998; 49(3): 293-300. [CrossRef]
24. Miller D, Doppman J. Petrosal sinus sampling: Technique and rationale. Radiology 1991; 178(1): 37-47.
25. Diez J, Iglesias P. Pulmonary thromboembolism after inferior petrosal sinus sampling in Cushing's syndrome. Clin Endocrinol 1997; 46(6): 777.
26. Obuobie K, Davies J, Ogunko A, Scanlon M. Venous thrombo- embolism following inferior petrosal sinus sampling in Cushing's disease. J Endocrinol Invest 2000; 23(8): 542-4. [CrossRef]
27. Sturrock N, Jeffcoate W. A neurological complication of inferior petrosal sinus sampling during investigation for Cushing's disease: A case report. J Neurol Neurosurg Psychiatry 1997; 62(5): 527-8. [CrossRef]
28. Miller D, Doppman J, Peterman S, Nieman L, Oldfield E, Chang R. Neurologic complications of petrosal sinus sampling. Radiology 1992; 185(1): 143-7.
29. Lefournier V, Gatta B, Martinie M, Vasdev A, Tabarin A, Bessou P, et al. One transient neurological complication (sixth nerve palsy) in 166 consecutive inferior petrosal sinus samplings for the etiological diagnosis of Cushing's syndrome. J Clin Endocrinol Metab 1999; 84(9): 3401-2.
30. Bonelli FS, Huston III J, Meyer FB, Carpenter PC. Venous subarachnoid hemorrhage after inferior petrosal sinus sampling for adrenocorticotropic hormone. AJNR Am J Neuroradiol 1999; 20(2): 306-7.

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Comparison of the Efficacy of Phonophoresis and Conventional Ultrasound Therapy in Patients with Primary Knee Osteoarthritis

ORIGINAL INVESTIGATION

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ABSTRACT

Objective: To compare the efficacy of phonophoresis (PH) versus ultrasound (US) in patients with primary knee osteoarthritis (OA).

Materials and Methods: Forty patients were divided into two groups as PH and US. Acoustic gel containing no pharmacological agent was applied in the US group, whereas a gel containing 1.16% diclofenac diethylamonium was applied in the PH group for 10 sessions. The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain subscale and Visual Analogue Scale (VAS) were used for the assessment of pain. The WOMAC physical function subscale, Lequesne functional index and Stanford Health Assessment Questionnaire (HAQ) were used for the assessment of physical activities. Patients were assessed for a 3 month follow-up period.

Results: In the PH group, painless walking duration improved at all follow-up times except for week 2 ($p<0.05$). Painless walking distance and VAS scores also improved at all follow-up times ($p<0.05$). In the US group, VAS scores during walking and flexion of the knee, WOMAC pain and physical function scores and total WOMAC scores improved significantly at all follow-up times ($p<0.05$).

Conclusion: Both therapeutic modalities were found effective. We suggest neither therapy is superior to the other but PH can improve painless walking duration more successfully than US.

Key words: Knee osteoarthritis, phonophoresis, ultrasound

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INTRODUCTION

Osteoarthritis (OA) is a degenerative disease that causes osteophytic formations, subchondral sclerosis and erosions in the joint cartilage. It can also be associated with biochemical and morphologic changes in the joint capsule. The knee is one of joints most affected by osteoarthritic effects in the human skeleton. Patients with knee OA may have progressive functional disability while walking, standing and climbing. OA principally affects the elderly and causes significant morbidity (1, 2).

Clinicians initially aim at protecting the joint's functions and reducing the pain caused by joint OA. Another important aim is to improve the quality of life, which is affected by this degenerative disease. Although there is no exact cure for OA, recommended approaches for the medical management of knee OA include non-pharmacologic modalities and drug therapy (3). Non steroidal anti-inflammatory drugs (NSAIDs) are generally used for the treatment of OA, but they also have some potential risks for the elderly due to their renal, cardiac and gastrointestinal side effects (4-9). Physical therapy modalities are other methods that can be used in the treatment of OA (3, 10). They are very important in improving physical functions, reducing pain and producing a desired effect in the treatment of edema and inflammation (3, 10-13).

Ultrasound is one of the physical therapy modalities generally used for many musculoskeletal disorders. US converts electrical energy to an acoustic waveform that is converted to heat as it passes through tissues with different resistance compositions (14).

Phonophoresis is the use of ultrasound to enhance percutaneous absorption of a drug (15-18). Phonophoresis provides an advantage as it bypasses the hepatic first-pass metabolism and avoids the side effects in absorption that occur with oral administration (18-20).

The number of clinical trials which compare PH to the other physical therapies is quite limited, which may be explained by the absence of optimizing frequency and the duration of therapy. In some clinical trials, ibuprofen and dexamethasone were used by investigators for phonophoresis in patients with knee OA (21-23). However, we found no trial in our "pubmed" search regarding diclofenac phonophoresis in patients with knee OA.

Cardero et al. (24) indicated the highest transdermal penetration of diclofenac among NSAIDs such as indomethacin, piroxicam, tenoxicam, ketorolac and aceclofenac. Rosim et al. (25) also showed that therapeutic ultrasound administration enhanced the percutaneous absorption of the topical diclofenac gel. According to this, diclofenac seems to be a good candidate for phonophoresis administration.

In this prospective randomised controlled trial, we aimed to compare the efficacy of diclofenac phonophoresis with conventional ultrasound therapy in patients with knee OA at the three-month-follow-up.

MATERIAL and METHODS

Forty patients were randomly assigned to two treatment groups by one of the non-treating authors by drawing an envelope among 40 for each participant which were labeled 'A' (Group I: phonophoresis; 13 woman, 7 men) and 'B' (Group II: ultrasound; 17 women, 3 men). All the patients fulfilled the American College of Rheumatology criteria for knee OA (26) and had Kellgreen and Lawrence (27) scores between II-IV. Patients who had a Visual Analogue Scale (VAS) score over 50 in one of three parameters-i.e walking, flexion of the knee and resting- were included in the trial. On the other hand, patients who had a secondary OA, had received intraarticular or intramuscular corticosteroids or received intaarticular hyaluronic acid injections in the past 3 months, had been on any physical therapy program in the past 6 months and had any systemic disease or abnormal laboratory test results, dermatological problems, skin allergy to NSAIDs and malignant diseases were excluded from the trial.

The Western Ontario and McMasters Universities Osteoarthritis Index (WOMAC) was used to assess pain, stiffness and physical functions (28, 29). WOMAC scores were evaluated on a Likert scale of 0-4, where 0 stood for no pain/limitation, 1 for mild pain/limitation, 2 for moderate pain/limitation and 4 for severe pain/limitation. The patients' WOMAC scores were evaluated at the beginning and end of the trial as well as in the first, second and third months. For the normalization of values among each other, the scores were multiplied by 0.5, 1.25 and 0.147 for pain, stiffness and physical functions, respectively. HAQ scores were also used for the assessment of functional activities. This scale is used for assessing daily activities. Activities are marked between 0-3, where 0 stands for no limitation, 1 for mild limitation, 2 for severe limitation and 3 for complete limitation. All the patients were evaluated according to their HAQ scores, which were recorded.

Pain the patients felt during walking, resting and flexion of the knee was assessed by VAS (VAS 0: No pain, VAS 10: most severe pain). Painless walking duration was measured in minutes whereas painless walking distance was measured in meters and range of flexion by goniometers at the beginning and end of the therapy as well as all the follow-up times.

The State/Trait Anxiety Inventory was used for the assessment of anxiety whereas the Beck Depression Inventory was used for the assessment of depression symptoms.

The patients were asked to rate the treatment efficacy by one of the following: ineffective, poorly effective, effective and very effective. All assessments were repeated at the first, second and third months after the therapy.

A total of 60 patients had been referred to US or PH therapies initially. However, 10 patients refused to participate in the trial for various reasons. In addition, a total of 10 patients were excluded from the trial-3 due to diabetes mellitus, 2 due to a history of intraarticular corticosteroid injection in the past 3 months and 5 due to high sedimentation rates.

The patients were asked about their age, weight, height, level of education, duration of disease, sporting activities and location of the pain in the knee. All the patients underwent physical examination. The patients were also evaluated with their laboratory findings. Complete blood count (CBC), erythrocyte sedimentation rate, C- reactive protein, rheumatoid factor (RF) and routine biochemical tests were performed to rule out other diseases. The patients who were included in the trial had normal laboratory findings.

The use of NSAIDs or other analgesic drugs was not permitted during the study period.

The trial was performed in accordance with the principles stated in the declaration of Helsinki. All the patients were informed about the study design both in verbal and written forms. Each participant gave their written informed consent to the study prior to participation. Patients who fulfilled the ACR knee OA criteria were included in this trial which was conducted in our Clinic of Physical Therapy and Rehabilitation.

Intervention

A physiotherapy program was administrated five times a week for a total of two weeks in 10 sessions. In the US group, an acoustic gel which did not contain any pharmacologic agent was applied to the skin of the knee. In the PH group, gel containing 1.16% diclofenac diethylamonium was applied by an US device to the superomedial, inferomedial and lateral sides of the knee in circular movements. Continuous ultrasonic waves with a frequency of 1 MHz and power of 1.5 W/cm^2 were used in the two groups. US and PH therapies were administered for 10 minutes per session for each knee.

Statistical analysis

We determined the sample size according to the recommendations available at the time of planning the study. To provide 83% capacity for detecting 30% improvement in WOMAC scores at a significance level of 5%, a minimum of 20 patients would be required in each group. Consequently, 40 patients were randomized in the study in order to form diclofenac phonophoresis (PH) and conventional ultrasound (US) groups, each consisting of 20 patients. Data collected were analyzed by using the Statistical Package for the Social Sciences (SPSS 10.0). Results were expressed as mean±standard deviation. Statistical significance was tested using the Two-way analysis of variance for repeated measures of the same group, and student-t test was used for comparisons between the two groups. In addition, the Chi-square test or Fisher's exact test was used for categorical variables when the cell number was small. The level of statistical significance was set at a two-tailed p-value of 0.05.

RESULTS

Characteristics of the patients

A total of 40 patients with primary knee OA (10 men and 30 women) were included in this study. There were 13 women and 7 men at the mean age of 54.55±8.65 in the PH group. On the other hand, there were 17 women and 3 men at a mean age of 55.05±10.08 in the US group. There was no significant difference between the two study groups with respect to demographic data including age, sex, level of education, duration of disease, X-ray scores, location of pain and body mass index (p>0.05) (Table 1). There was also no significant difference between the two groups with respect to clinical parameters at the beginning of the trial (p>0.05) (Table 2).

Clinical changes in the PH group

All the parameters were checked at the beginning of the therapy, in the second week and in the first, second and third months of the therapy.

Fifteen days after the initiation of the therapy (first follow-up), painless walking distance (p=0.033), walking VAS scores (p=0.002), resting VAS scores (p=0.001), flexion of the knee VAS scores (p=0.004), WOMAC physical function scores (p=0.020), total WOMAC scores (p=0.019) and Lequesne Index (p=0.027) scores all improved in relation to the baseline values.

Improvements continued in the first month in painless walking distance (p=0.027), walking VAS scores (p=0.001), resting VAS scores (p=0.001), flexion of the knee VAS scores (p=0.001), WOMAC physical function scores (p=0.005), total WOMAC scores (p=0.008) and Lequesne Index scores (p=0.01). Improvements started to occur in the painless walking duration in the first month (p=0.006). On the other hand, improvements in the WOMAC physical function scores, total WOMAC scores and Lequesne Index scores were not sustained in the second and third months.

Improvements in the painless walking duration (p=0.035), painless walking distance (p=0.02), walking VAS scores (p=0.002), resting VAS scores (p=0.002) and flexion of the knee VAS scores (p=0.005) continued in the PH group in the second month.

In the third month, improvements in the painless walking duration (p=0.034), painless walking distance (p=0.017), walking VAS scores (p=0.03), resting VAS scores (p=0.007) and flexion of the knee VAS scores (p=0.007) were found to be permanent (Table 3).

Table 1. Demographic features of the patients (mean±standard deviation)

		Phonophoresis group	Ultrasound group
Age (year)		54.55±8.65	55.05±10.08
Sex	Woman	13 (65%)	17 (85%)
	Man	7 (35%)	3 (15%)
BMI* (kg/m^2)		29.67±4.21	30.20±3.29
Smoking (year)	Non-smoker	15 (75%)	17 (85)
	0-5 year	0 (0%)	0 (0%)
	5-10 year	0 (0%)	0 (0%)
	10-20 year	0 (0%)	1 (5%)
	>20 year	5 (25%)	2 (10%)
Education	Illiterate	9 (45%)	12 (60%)
	Primary school	5 (25%)	5 (25%)
	Secondary School	3 (15%)	1 (5%)
	High school	1(5%)	1 (5%)
	University	2 (10%)	1 (5%)
Duration of disease (year)		4.50±4.77	4.70±5.31
Location of pain	Lateral	0 (0%)	0 (0%)
	Medial	5 (25%)	0 (0%)
	Patellofemoral	2 (10%)	2 (10%)
	Mixed	13 (65%)	18 (90%)
Radiologic Grade	Right Knee		
	Grade 2	12 (60%)	10 (50%)
	Grade 3	7 (35%)	6 (30%)
	Grade 4	1(5%)	4 (20%)
Radiologic Grade	Left Knee		
	Grade 2	12 (60%)	10 (50%)
	Grade 3	6 (30%)	7 (35%)
	Grade 4	2 (10%)	3 (15%)

*BMI: Body mass index

Table 2. Baseline clinical parameters before administration of US and PH therapies

Clinical parameters	Phonophoresis n=20	Ultrasound n=20
Maximum flexion of knee right	123.1±7.18	122.55±6.29
Maximum flexion of knee left	123.1±6.8	122.35±3.89
Painless walking duration (min)	9.9±7.98	6.75±5.19
Painless walking distance (m)	195±174.64	155±187.71
Walking VAS	64.5±14.68	61±13.72
Resting VAS	49.25±26.66	48±22.14
Flexion movement VAS	53.25±30.18	61±22.45
WOMAC pain	6.37±1.70	7.05±1.83
WOMAC stiffness	1.8±2.19	1.17±1.60
WOMAC physical function	6.55±2.45	7.73±1.39
WOMAC total	14.73±5.14	15.95±3.95
Lequesne Index	11.8±4.33	12.5±2.25
HAQ	0.83±0.66	0.66±0.30
STAI TX-1	44.45±9.20	43.35±8.05
STAI TX-2	50.3±5.71	49.4±5.59
Beck Depression Inventory	6.7±6.56	10.15±8.43

min: minute, m: meter, VAS: Visual analog scale, WOMAC: Western Ontario and McMasters Universities Osteoarthritis Index, HAQ: Health Assessment Questionnaire, STAI TX: State/Trait Anxiety Inventory

There was no improvement in either State-Trait Anxiety Inventory or Beck Depression Inventory scores. Changes in the goniometric measurements were not statistically significant when compared to the baseline values.

Clinical changes in the US group

All the patients in the US group were evaluated at the same intervals as the PH group. Fifteen days after the initiation of the therapy statistically significant changes occurred in almost the same parameters where the PH group showed improvements. Painless walking distance (p=0.011), walking VAS scores (p=0.001), resting VAS scores (p=0.008), flexing of the knee VAS scores (p=0.005), WOMAC pain scores (p=0.001), WOMAC physical function scores (p=0.001) and total WOMAC scores (p=0.001) significantly improved in relation to the baseline values.

Improvements in the above mentioned parameters continued in the first month.

In the second month, statistically significant improvements continued in walking VAS scores (p=0.007), flexion of the knee VAS scores (p=0.001), WOMAC pain scores (p=0.001), WOMAC physical function scores (p=0.003) and total WOMAC scores (p=0.003); however, there was no improvement at this time in painless walking distance and resting VAS scores.

Improvements in walking VAS scores (p=0.024), flexion of the knee VAS scores (p=0.003) and total WOMAC scores (p=0.004) were sustained for 3 months after initiation of the therapy. On the other hand, unlike the 15th day and the first month, painless walking distance (p=0.644) and resting VAS scores (p=0.096) showed no significant improvement in the second month (Table 4).

Clinical differences between the treatment groups

In the comparison of parameters between the two groups, it was observed that painless walking duration improved more significantly in the PH group in all follow-ups except for the 15th day (p<0.05).

On the 15th day, 5% of the patients rated the therapy ineffective in the PH group versus 15% in the US group. In the first month, only 10% of the patients in the PH group rated the therapy ineffective versus 25% in the US group. Those who rated the therapy ineffective in the second month constituted 25% and 35 % of the patients in the PH and US groups, respectively. In the third month of the therapy, only 30% of the patients rated the therapy ineffective in both the groups.

We suggest that the US and PH groups are similar to each other in most of the parameters; however, PH therapy is superior to the US in improving painless walking duration (p<0.05).

DISCUSSION

In this randomized controlled study, there were significant improvements in most of the clinical parameters in both of the groups. Neither modality was found to be superior to the other in most of the clinical parameters except for painless walking duration where PH therapy was more successful in improving the patient's condition than US therapy.

Ultrasound is one of the deep heating modalities used in the clinics of physical therapy. Therapeutic ultrasound is generated by a transducer that converts electrical energy to ultrasound by utilizing the piezoelectric principle (30).

Although the exact mechanism of action is unknown, one of the important effects is heating. It increases regional blood flow and connective tissue extensibility. Non-thermal effects may be related with molecular vibration that increases cell membrane permeability and enhances metabolic product transport (31).

In our trial, we used diclofenac diethylamonium gel. Diclofenac is a NSAID that is derived from phenyl acetic acid. It inhibits both COX 1 and COX 2. It has been in use for more than 30 years (32, 33). It has a poor acidic structure which allows it to pass through most of the tissues more easily than many other NSAIDs (24, 32, 33).

Therapeutic ultrasound administration enhances percutaneous penetration of topical diclofenac gel (25). Therefore, diclofenac seems to be a good candidate for phonophoresis administration.

We suggest that deeper penetration of diclofenac results in clinical benefits due to sonographic administration, but still both treatment modalities were found effective.

We made a search in the literature regarding ultrasound and phonophoresis in knee OA and found only a limited number of articles about these modalities.

Table 3. Changes in the clinical outcomes after administration of therapy in the PH group

Clinical parameters	Baseline	15th Day	1st month	2nd month	3rd month
Maximum flexion of knee (right)	123.1±7.18	123.75±6.85 p=0.263	123.15±6.32 p=0.934	122.50±7.34 p=0.586	123.50±6.90 p=0.701
Maximum flexion of knee (left)	123.1±6.8	123.65±6.79 p=0.547	123.30±5.93 p=0.799	123.90±6.40 p=0.500	124±5.75 p=0.299
Painless walking duration (min)	9.9±7.98	11.2±8.88 p=0.086	13.9±9.77§ p=0.006	15.25±14.34¶ p=0.035	15.5±14.38β p=0.034
Painless walking distance (m)	195±174.64	245±205.77 p=0.033	285±218.90 p=0.027	293.5±275.01 p=0.023	298.5±271.72 p=0.017
Walking VAS	64.5±14.68	52±12.81 p=0.002	41.5±19.80 p=0.001	47±22.73 p=0.002	47.75±19.89 p=0.003
Resting VAS	49.25±26.66	33.5±22.77 p=0.001	31±23.37 p=0.001	32±21.17 p=0.002	32.5±23.59 p=0.007
Flexion movement VAS	53.25±30.18	39±25.73 p=0.004	33.5±25.39 p=0.001	37±29.39 p=0.005	35.5±31.03 p=0.007
WOMAC pain	6.37±1.70	5.85±1.77 p=0.153	5.7±2.51 p=0.199	5.57±2.78 p=0.115	5.85±2.76 p=0.309
WOMAC stiffness	1.8±2.19	1.56±2.10 p=0.467	1.18±1.43 p=0.107	1.35±2.09 p=0.261	1.70±2.35 p=0.852
WOMAC physical function	6.55±2.45	5.65±2.14 p=0.020	5.08±2.65 p=0.005	6.06±2.57 p=0.316	6.32±2.69 p=0.670
WOMAC total	14.73±5.14	13.14±4.85 p=0.019	11.96±5.25 p=0.008	12.97±6.03 p=0.071	13.88±6.84 p=0.480
Lequesne Index	11.8±4.33	10.8±4.25 p=0.027	10.65±4.59 p=0.010	11.35±4.72 p=0.342	11.05±5.38 p=0.276
HAQ	0.83±0.66	0.75±0.53 p=0.299	0.66±0.50 p=0.017	0.76±0.55 p=0.361	0.77±0.61 p=0.321
STAI TX-1	44.45±9.20	43.85±6.63 p=0.666	42.8±7.25 p=0.256	43.8±5.88 p=0.689	45.75±5.30 p=0.526
STAI TX-2	50.3±5.71	49.65±4.38 p=0.352	49.95±5.15 p=0.702	50.1±4.59 p=0.763	49.75±5.67 p=0.516
Beck Depression Inventory	6.7±6.56	5.45±7.79 p=0.154	5.95±6.70 p=0.231	7±7.19 p=0.781	7.5±7.94 p=0.269

§First month values significantly different from US group $p<0.05$
¶Second month values significantly different from US group $p<0.05$
βThird month values significantly different from US group $p<0.05$
min: minute, m: meter, VAS: Visual analog scale, WOMAC: Western Ontario and McMasters Universities Osteoarthritis Index, HAQ: Health Assessment Questionnaire, STAI TX: State/Trait Anxiety Inventory

Welch et al. (34) researched the literature about knee OA and found only 3 randomized controlled trials which suggested that ultrasound was not superior to placebo, short wave diathermy or galvanic current (21). Bansil et al. (35) compared short wave diathermy to ultrasound therapy in patients with primary knee OA and suggested that US therapy was superior to short wave diathermy.

In an interesting study, it was shown that low intensity ultrasound therapy could affect human cartilage explants by stimulating expression of proteoglycans and type II collagen in 200 mV/cm^2 dosage (36).

Kozanoglu et al. (21) compared the effectiveness of ibuprofen phonophoresis versus conventional ultrasound therapy in knee OA. They noted 30% improvement in WOMAC scores in both of the groups. They also found improvements in pain scores, range of knee motion and walking distance in the two groups. They suggested that both the US and PH were effective and ibuprofen phonophoresis was not superior to conventional US therapy in patients with knee OA.

In a study, diclofenac diethylamonium was used in the painful shoulder syndrome. A total of 64 patients were divided into two groups to receive either US or diclofenac PH therapy. It was sug-

Table 4. Changes in the clinical outcomes after administration of therapy in the US group

Clinical Parameters	Baseline	15th day	1st month	2nd month	3rd month
Maximum flexion of knee (right)	122.55±6.29	123.4±5.34 p=0.047	124.3±4.97 p=0.017	124.35±4.79 p=0.011	124±4.53 p=0.096
Maximum flexion of knee (left)	122.35±3.89	122.8±3.94 p=0.407	123.35±4.05 p=0.135	123.35±3.84 p=0.084	123.8±4.02 p=0.025
Painless walking duration (min)	6.75±5.19	7.75±6.58 p=0.163	8±6.76 p=0.135	6.5±5.64 p=0.666	7.5±6.97 p=0.419
Painless walking distance (m)	155±187.71	178.75±194.88 p=0.011	181.25±185.11 p=0.029	160.75±191.06 p=0.074	163.50±192.66 p=0.644
Walking VAS	61±13.72	50±11.23 p=0.001	51±11.19 p=0.003	52.5±7.86 p=0.007	53.5±9.33 p=0.024
Resting VAS	48±22.14	40±17.16 p=0.008	41.5±13.08 p=0.033	43.5±13.08 p=0.234	40±13.76 p=0.096
Flexion movement VAS	61±22.45	49.5±15.71 p=0.005	45.5±18.77 p=0.001	47±18.66 p=0.001	46±19.02 p=0.001
WOMAC pain	7.05±1.83	5.3±1.16 p=0.001	5.45±1.59 p=0.001	5.32±1.19 p=0.001	5.6±1.20 p=0.005
WOMAC stiffness	1.17±1.60	0.93±1.20 p=0.301	0.93±1.27 p=0.268	0.93±1.06 p=0.441	0.93±1.13 p=0.419
WOMAC physical function	7.73±1.39	6.39±0.86 p=0.001	6.20±1.11 p=0.001	6.45±0.94 p=0.003	6.35±0.87 p=0.003
WOMAC total	15.95±3.95	12.63±2.02 p=0.001	12.56±2.61 p=0.001	12.71±2.03 p=0.003	12.85±2.03 p=0.004
Lequesne Index	12.5±2.25	12.05±2.35 p=0.058	12.1±2.38 p=0.189	13.15±2.03 p=0.073	12.85±1.72 p=0.367
HAQ	0.66±0.30	0.67±0.35 p=0.899	0.58±0.27 p=0.095	0.68±0.30 p=0.766	0.71±0.26 p=0.399
STAI TX-1	43.35±8.05	42.3±6.79 p=0.378	40.8±6.32 p=0.07	40.9±7.49 p=0.257	40.80±5.15 p=0.156
STAI TX-2	49.4±5.59	49.55±5.23 p=0.769	47.4±3.80 p=0.039	48.45±4.80 p=0.138	49.55±5.06 p=0.842
Beck Depression Inventory	10.15±8.43	8.25±5.55 p=0.034	8.8±6.5 p=0.139	8.75±5.73 p=0.116	8.85±6.13 p=0.174

min: minute, m: meter, VAS: Visual analog scale, WOMAC: Western Ontario and McMasters Universities Osteoarthritis Index, HAQ: Health Assessment Questionnaire, STAI TX: State/Trait Anxiety Inventory

gested that both the modalities were successful in improving pain and increasing the range of joint motion in relation to the baseline values. It was also stated that PH was superior to conventional US in increasing the range of joint motion (13).

Shin and Choi (12) evaluated the effects of indomethacin phonophoresis on the relief of temporomandibular joint pain. They suggested that indomethacin phonophoresis decreased the pain and increased the pressure pain threshold in the phonophoresis group versus the placebo group which was given placebo cream.

Recently, Luksurapan (37) suggested that piroxicam phonophoresis was more effective than US therapy in reducingpain and improving knee functioning in patients with knee OA.

When searched the literature reviews, we found contradictions between clinical trials. Such contradictions may have originated from non-standardized administration of US regarding frequency and power (21, 34, 35, 38-40).

Our trial is one of the few studies which compares US and PH in patients with knee OA, and diclofenac diethylamonium is one of the rare agents used in PH trials.

Our trial indicated improvements in the VAS scores during walking, resting and flexion of the knee in both of the groups. In this respect, there are similarities between our trial and ibuprofen phonophoresis trial by Kozanoglu et al.

In our trial, these improvements continued in the first, second and third months in both of the groups. However, improvements in resting VAS scores lasted only until the second month in the US group. When we compared the PH and US groups, we found therapeutic modalities effective and generally well tolerated, but diclofenac phonophoresis was superior to conventional US therapy in improving painless walking duration.

Our study differs from many other studies because it compares PH and US in a 3-month-follow-up period. Such a follow-up period may give us some clues about whether the effects of PH and US are permanent.

In this trial, we did not administer any physical therapy modality besides US and PH therapies. This approach helps to evaluate the solitary effects of the two modalities in each group and compare the effects between the groups.

Study limitations

One of the most important limitations of this study is the absence of SHAM US therapy. Addition of a SHAM US group might allow us to comment on the additional effects of US and PH alone.

CONCLUSION

We suggest that both of the therapeutic modalities are effective and safe for patients with primary knee OA. However, PH may be particularly helpful in patients with gastric problems and hypertension who are sensitive to any systemic form of NSAIDs as well as the elderly population in whom the use of NSAIDs is considered to increase the risk of gastric, renal and cardiac events (6-9).

Large and long term studies are needed for more data on the use of PH and conventional US therapies.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Authors' Contributions: Conceived and designed the experiments or case: PO, AG. Performed the experiments or case: PO, İY, MC. Analyzed the data: AG, KN, FC. Wrote the paper: MB, SE, DU. All authors have read and approved the final manuscript.

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REFERENCES

1. Mow VC, Setton LA, Fuilak F, Ratcliffe A. Mechanical factors in articular cartilage and their role in osteoarthritis. In: Kuettner KE, Goldberg VM, editors. Osteoarthritic disorders. American Academy of Orthopaedic Surgeons. Resomont; 1995.p.147-72.
2. Poole AR. Imbalances of anabolism and catabolism of cartilage matrix components in osteoarthritis. In: Kuettner KE, Goldberg VM, editors. Osteoarthritic disorders. American Academy of Orthopaedic Surgeons; Rosemont; 1995.p.247-60.
3. Recommendations for the medical management of osteoarthritis of the hip and knee. American College of Rheumatology subcommittee on osteoarthritis guidelines. 2000 update. Arthritis Rheum 2000; 43(9): 1905-15. [CrossRef]
4. Griffin MR, Ray WA, Schaffner W. Nonsteroidal antiinflammatory drug use and death from peptic ulcer in elderly persons. Ann Intern Med 1988; 109(5): 359-63. [CrossRef]
5. Griffin MR, Piper JM, Daugherty JR, Snowden M, Ray WA. Nonsteroidal anti-inflammatory drug use and increased risk for peptic ulcer disease in elderly persons. Ann Intern Med 1991; 114(4): 257-63. [CrossRef]
6. Turajene T, Wongbunnak R, Patcharatrakul T, Ratansumawong K, Poigampetch Y, Songpatanasilp T. Gastrointestinal and cardiovascular risk of non-selective NSAIDs and COX-2 inhibitors in elderly patients with knee osteoarthritis. J Med Assoc Thai 2009; 92(6): 19-26.
7. Nuki G. Pain control and the use of non-steroidal analgesic anti-inflammatory drugs. Br Med Bull 1990; 46(1): 262-78.
8. Laporte JR, Came X, Vidal X, Morena M, Juan J. Upper gastrointestinal bleeding in relation to previous use of analgesics and non-steroidal antiinflammatory drugs. Lancet 1991; 337(8733): 85-9. [CrossRef]
9. Bateman DN, Kennedy JG. Non-steroidal anti-inflammatory drugs and elderly patients. BMJ 1995; 310(6983): 817-8. [CrossRef]
10. Rutjes AW, Nüesch E, Sterchi R, Jüni P. Therapeutic ultrasound for osteoarthritis of the knee or hip. Cochrane Database Syst Rev 2010; 20(1): CD003132.
11. Ozgonenel L, Aytekin E, Durmuşoglu G. A double blind trial of clinical effects of therapeutic ultrasound in knee osteoarthritis. Ultrasound Med Biol 2009; 35(1): 44-9. [CrossRef]
12. Shin SM, Choi JK. Effect of indomethacin phonophoresis on the relief of temporomandibular joint pain. Cranio 1997; 15(4): 345-8.
13. Vlak T. Comparative study of the efficacy of ultrasound and sonophoresis in the treatment of painful shoulder syndrome. Reumatizam 1999; 46(1): 5-11.
14. Klaiman MD, Shrader JA, Danoff JV, Hicks JE, Pesce WJ, Ferland J. Phonophoresis versus ultrasound in the treatment of common musculoskeletal conditions. Med Sci Sports Exerc 1998; 30(9): 1349-55.
15. Brucks R, Nanavaty M, Jung D, Siegel F. The effect of ultrasound on ibuprofen through human epidermis. Pharm. Res 1989; 6(8): 697-701. [CrossRef]
16. Byl NB. The use of ultrasound as an enhancer for transcutaneous drug delivery: phonophoresis. Phys Ther 1995; 75(6): 539-53.
17. Tachibana K, Tachibana S. Transdermal delivery of insulin by ultrasonic vibration. J Pharm Pharmacol 1991; 43(4): 270-1. [CrossRef]
18. Mitragotri S, Blankschtein D, Langer R. Ultrasound mediated transdermal protein delivery. Science 1995; 269(5225): 850-3. [CrossRef]
19. Sinha VR, Kaur MP. Permeation enhancers for transdermal drug delivery. Drug Dev Ind Pharm 2000; 26(11): 1131-40. [CrossRef]
20. Asbill CS, El-Kattan AF, Michniak B. Enhancement of transdermal drug delivery: chemical and physical approaches. Crit Rev Ther Drug Carrier Syst 2000; 17(6): 621-58. [CrossRef]
21. Kozanoglu E, Basaran S, Guzel R, Uysal FG. Short term efficacy of ibuprofen phonophoresis versus continuous ultrasound therapy in knee osteoarthritis. Swiss Med Weekly 2003; 133(23-24): 333-8.
22. Akinbo SR, Aiyejusunle CB, Akinyemi OA, Adesegun SA, Danesi MA. Comparison of the therapeutic efficacy of phonophoresis and iontophoresis using dexamethasone sodium phosphate in the management of patients with knee osteoarthritis. Niger Postgrad Med J 2007; 14(3): 190-4.
23. Serikov NP. Efficacy of ibuprofen ultraphonophoresis for pain relief in osteoarthritis. Ter Arkh 2007; 79(5): 79-81.
24. Cordero JA, Alarcon L, Escribano E, Obach R, Domenech J. A comparative study of the transdermal penetration of series of nonsteroidal antiinflammatory drugs. J Pharm Sci 1997; 86(4): 503-8. [CrossRef]
25. Rosim GC, Barbieri CH, Lancas FM, Mazzer N. Diclofenac phonophoresis in human volunteers. Ultrasound Med Biol 2005; 31(3): 337-43. [CrossRef]
26. Altman R, Asch E, Bloch D, Bole G, Borenstein D, Brandt K, et al. Development of criteria for the lassification and reporting of osteoarthritis. Classification of osteoarthritis of the knee. Diagnostic and Therapeutic Criteria Committee of the American Rheumatism Association. Arthritis Rheum 1986; 29(8): 1039-49. [CrossRef]

27. Kellgren JH, Lawrence JS. Radiological assessment of osteo-arthrosis. Ann Rheum Dis 1957; 16(4): 494-501. [CrossRef]
28. Bellamy N, Buchanan W, Goldsmith CH, Campbell J, Stitt LW. Validation study of WOMAC: a health status instrument for measuring clinically important patient relevant outcomes to antirheumatic drug therapy in patients with osteoarthritis of the hip or knee. J Rhumatol 1988; 15(12): 1833-40.
29. Tüzün EH, Eker L, Aytar A, Daşkapan A, Bayramoğlu M. Acceptability, reliability, validity and responsiveness of the Turkish version of WOMAC osteoarthritis index. Osteoarthritis Cartilage 2005; 13(1): 28-33. [CrossRef]
30. Rao R, Nando S. Sonophoresis recent advancements and future trends. JPP 2009; 61(6): 689-705.
31. Basford JR. Physical Agents. In: DeLisa JA, Gans BM, eds. Rehabilitation Medicine: Principles and Practice. Philadelphia; 1998.p.483-503.
32. Mitchell JA, Warner TD. Cyclo-oksygenase 2 pharmacology, physiology, biochemistry and relevance to NSAID therapy. Br J Pharmacol 1999; 128(6): 1121-32. [CrossRef]
33. Brune K. Persistence of NSAIDs at effect sites and rapid disappearance from side effect compartments contributes to tolerability. Curr Med Res Opin 2007; 23(12): 2985-95. [CrossRef]
34. Welch V, Brosseau L, Peterson J, Shea B, Tugwell P, Wells G. Therapeutic ultrasound for osteoarthritis of the knee. Cochrane Database Syst Rev 2001; (3): CD003132.
35. Bansil CK, Joshi JB. Effectiveness of shortwave diathermy and ultrasound in the treatment of osteoarthritis of the knee joint. Med J Zambia 1975; 9(5): 138-9.
36. Min BH, Woo JH, Cho HS, Choi BH, Park SJ, Choi MJ, et al. Effects of low intensity ultrasound stimulation on human cartilage explants. Scand J Rheumatol 2006; 35(4): 305-11. [CrossRef]
37. Luksurapan W, Boonhong J. Effects of Phonophoresis of Piroxicam and Ultrasound on Symptomatic Knee Osteoarthritis. Arch Phys Med Rehabil 2013; 94(2): 250-5. [CrossRef]
38. Falconer J, Hayes KW, Chang RW. Effect of ultrasound on mobility in osteoarthritis of the knee. A randomized clinical trial. Arthritis Care Res 1992; 5(1): 29-35. [CrossRef]
39. Jan MH, Lai JS. The effects of physiotherapy on osteoarthritic knees of females. J Formos Med Assoc 1991; 90(10): 1008-13.
40. Robertson VJ, Baker KG. A review of therapeutic ultrasound: effectiveness studies. Phys Ther 2001; 81(7): 1339-50.

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A Retrospective Evaluation of the Patients with Rhabdomyoma

ORIGINAL INVESTIGATION

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ABSTRACT

Objective: To evaluate the location of rhabdomyomas in the heart, and the spontaneous regression, clinical and echocardiographic findings and association of rhabdomyomas with tuberous sclerosis.

Materials and Methods: The medical files of 12 rhabdomyoma cases diagnosed between 2005 and 2011 in the outpatient clinic of Paediatric Cardiology Department were retrospectively evaluated. Rhabdomyoma diagnosis was based on transthoracic echocardiography (TTE) and tuberous sclerosis was diagnosed according to clinical characteristics and imaging methods.

Results: The mean age at diagnosis of 12 cases, eight (66.6%) male, four (33.3%) female, male/female ratio 2, was 3.3+4.3 years (3 months-13 years). Seven cases (58.3%) were diagnosed to have definite tuberous sclerosis. Location of rhabdomyomas was as follows, seven cases (58.3%) in the left ventricle, two cases (16.6%) in the right ventricle, two cases (16.6%) in both ventricles and one case (8.3%) in the right atrium. The mass showed spontaneous regression in four of our cases (33.3%). Left ventricular size and systolic functions were normal in all cases. While the majority of the cases were asymptomatic, three cases had signs of congestive heart failure and one case had arrhythmia. The tumours of the cases with congestive heart failure were surgically excised.

Conclusion: Consistent with the literature, the frequency of definite tuberous sclerosis was 58.3%. While most of the rhabdomyomas were located in the left ventricle, 4 (33.3%) cases had spontaneous regression.

Key words: Echocardiography, rhabdomyoma, tuberous sclerosis

INTRODUCTION

Tuberous sclerosis complex (TSC) is an autosomal dominant genetic disorder, with an incidence ranging from 1/6000 to 1/30000. The disease is characterized by hamartomas in organs including brain, retina, skin, lungs, kidneys and heart. It frequently leads to cortical dysplasia, subependymal nodules, giant cell astrocytoma, retinal astrocytic hamartoma, facial angiofibroma, renal and lung angiomyolipoma and cardiac rhabdomyoma (1). Cardiac rhabdomyomas are generally associated with tuberous sclerosis. Rhabdomyomas are seen in approximately 43-60% of childhood tuberous sclerosis cases (2-4). Although primary cardiac tumours are rare, rhabdomyomas are common in infancy and childhood (2). While childhood rhabdomyomas can be asymptomatic, they may present with sudden death, fatigue, palpitations, chest pain, arrhythmia or congestive heart failure according to the number, location and size of the tumours. Echocardiography has an important place in the diagnosis and follow-up of rhabdomyomas (5-7). In this present article, we aimed to evaluate the location of rhabdomyomas in the heart, as well as the clinical and echocardiographic findings and the association with tuberous sclerosis.

MATERIAL and METHODS

The medical files of 12 rhabdomyoma cases diagnosed in the Paediatric Cardiology outpatient clinic between 2005 and 2011 were retrospectively evaluated. The written informed consents of the parents were obtained. The age at diagnosis, gender, neurological and systemic examination findings, transthoracic echocardiography (TTE), electrocardiography (EKG), electroencephalography, abdominal ultrasound, abdominal tomography, computed tomography (CT) of the brain), brain magnetic resonance imaging (MRI) and ocular findings of the cases were recorded. Rhabdomyoma diagnosis was based on echocardiographic examinations, and tuberous sclerosis was diagnosed based on clinical characteristics and imaging methods (Figure 1) (8).

Diagnostic criteria for tuberous sclerosis (8)

Primary characteristics

1. Cardiac rhabdomyoma (single or multiple)
2. Cortical tubers

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3. Facial angiofibromas or forehead plaque
4. Hypomelanotic macules (3 or more)
5. Lymphangioleiomyomatosis
6. Retinal nodular hamartomas (more than 1)
7. Non-traumatic ungula or periungual fibroma
8. Renal angiomyolipoma
9. Shagreen patch (connective tissue nevus)
10. Subependymal giant cell astrocytomas
11. Subependymal nodules

Secondary characteristics

1. Bone cysts
2. Cerebral white matter migration tracts
3. Confetti skin lesions
4. Gingival fibromas
5. Hamartomatous rectal polyps
6. Pitting of the dental enamel
7. Multiple renal cysts
8. Non-renal hamartoma
9. Retinal achromic patch

Definite tuberous sclerosis

2 primary or 1 primary+2 secondary characteristics

Probable TSC

1 primary +1 secondary characteristics

Possible TSC

1 primary characteristic or 2 or more secondary characteristics.

RESULTS

Of the twelve cases, eight were (66.6%) males, and four were (33.3%) females with a male to female ratio of 2. The mean age at diagnosis was 3.3±4.3 years (3 months-13 years), and eight (66.7%) of the cases were in the 0-3 years age group, and four (33.3%) of them was more than three years of age. One of the cases was diagnosed in the prenatal period by foetal TTE. According to the revised diagnostic criteria of tuberous sclerosis (8), seven cases (58.3%) were diagnosed as definite tuberous sclerosis. Apart from the three cases having dyspnoea, tachypnea, sinus tachycardia, or hepatomegaly, the physical examination findings of the cases were normal. A grade 3/6 systolic ejection murmur was present at the pulmonic area of a case (case 5) due to a mild obstruction in the right ventricular outlet that was caused by rhabdomyoma (Figure 2). Rhabdomyoma was located in the left ventricle in seven of the cases (58.3%) (Figure 3), in the right ventricle in two (25%) cases (Figure 4), in both ventricles in two (16.6%) cases (Figure 5) and in the right atrium in one (8.3%) case (Figure 6) (Table 1). Additionally, TTE showed one tumour mass in each seven cases (58.3%), two masses in each of the three cases (25%), five masses in one case (8.3%), and nine cardiac rhabdomyomas in one case (8.3%). Spontaneous regression of the mass was observed in four of our cases (33.3%). One of these cases, was the case with nine cardiac rhabdomyomas, while three of the tumours disappeared, there was a regression in the size of the biggest tumour. Left ven-

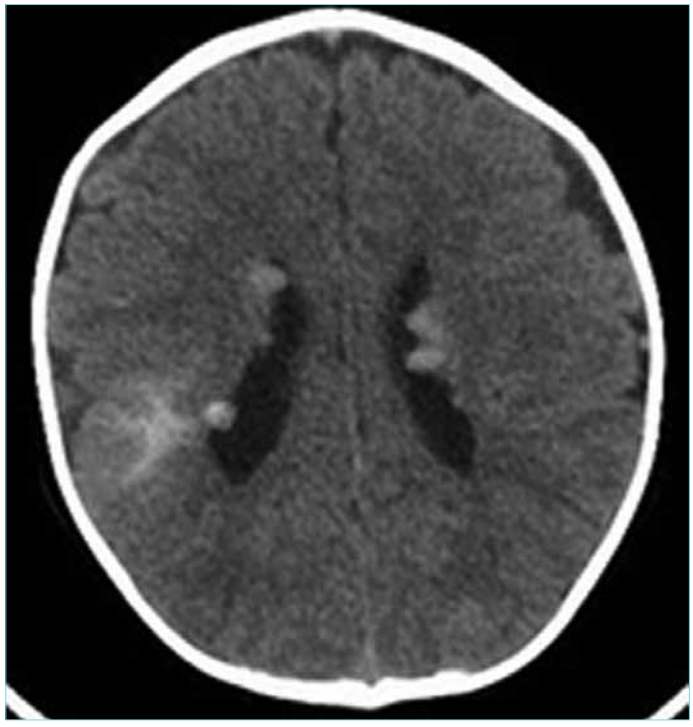

Figure 1. Brain CT scan of a case showing subependymal nodule, one of the primary characteristics of tuberous sclerosis

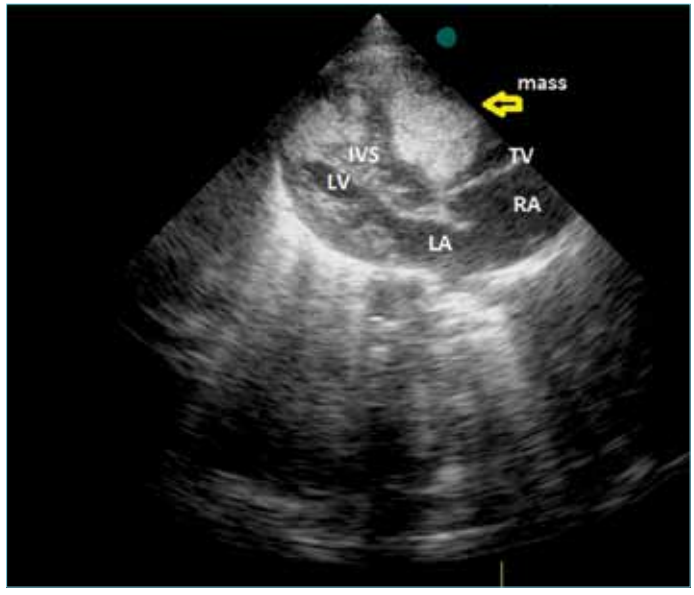

Figure 2. Echocardiographic image of case number 5

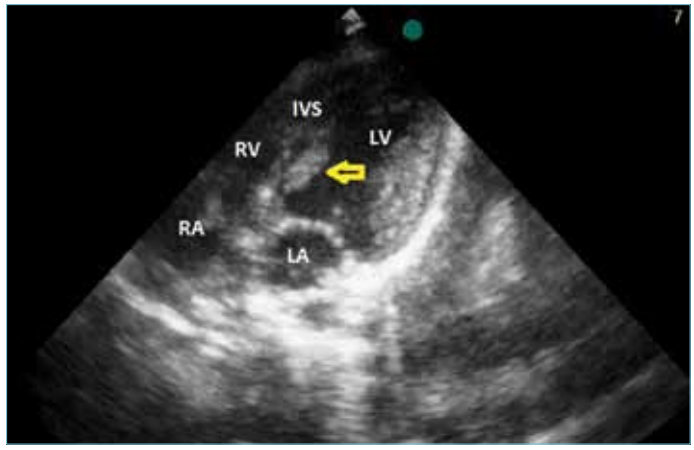

Figure 3. Echocardiographic image of case number 1

Figure 4. Echocardiographic image of case number 6

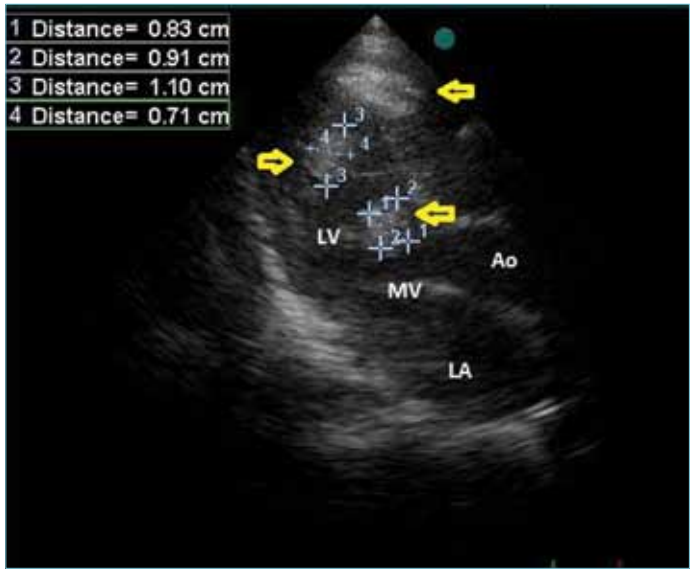

Figure 5. Echocardiographic image of case number 8

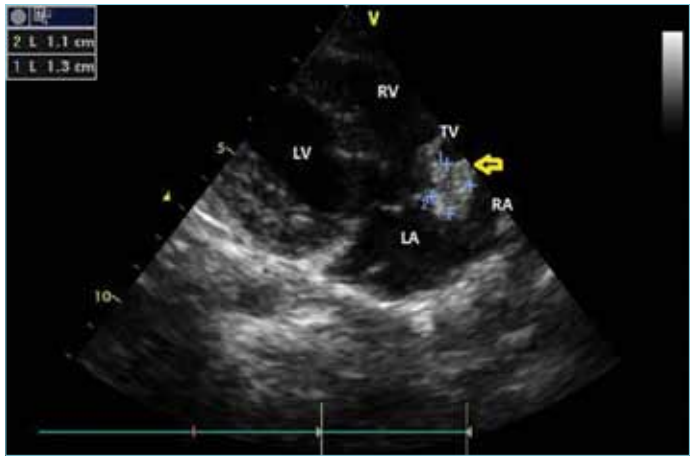

Figure 6. Echocardiographic image of case number 9

tricular size and systolic functions were normal in all cases. Holter monitoring showed a ventricular tachycardia attack (Figure 7) in the case (case 5) with mild obstruction in the right ventricular outlet (systolic pressure gradient 28 mmHg). The patient was started on beta blocker (propranolol, 3 mg/kg/day) therapy for arrhythmia. In 24-months follow-up, the mass reduced in size from 31x18mm to 15.6x9.4mm. Repeat Holter monitoring showed no ventricular tachycardia attacks, and the medical treatment of this asymptomatic case was discontinued. The tumours of the three cases were surgically excised as congestive heart failure developed. A 10 year-old tuberous sclerosis case with a rhabdomyoma located in the midseptal region of the left ventricle, additionally had an angiomyolipoma, approximately 20x10mm in size in the left kidney.

Statistical analysis

Frequencies, percentages and mean ± standard deviation values are given as descriptive statistics. SPSS for Windows version 11.5 software program was used for statistical analysis.

DISCUSSION

Rhabdomyomas are the most common benign cardiac tumours of the childhood (4, 7). Tuberous sclerosis complex is commonly associated with rhabdomyomas (9, 10). Rhabdomyomas observed in majority of the cases with tuberous sclerosis, are multiple, regular contoured, noncapsulated white or grey coloured benign intracavitary or intramural tumours that can be located in any part of the heart. The ventricles are involved in most cases. Histologically, it consists of large cells with glycogen-rich vacuoles. The size of the tumour varies between 1 mm and 10 cm. They generally originate from the left heart; left ventricle and interventricular septum (11-15). Atrial rhabdomyomas have also been reported, as seen in one of our cases (16). Spontaneous regression is among the important characteristics of rhabdomyomas.

Before transthoracic echocardiography was introduced for use, rhabdomyomas were generally diagnosed in autopsies. TTE has an important place in the diagnosis and follow-up of rhabdomyomas (17). Rhabdomyoma diagnosis can be made by foetal TTE in the prenatal period (5-7, 18). The frequency of rhabdomyomas in adult tuberous sclerosis cases decreasing to 20% also supports spontaneous regression (13, 14). After infancy, approximately more than 50% of the rhabdomyomas show a decrease in mass (17, 19-22). Spontaneous regression was observed in 4 (33.3%) of our cases. The prognosis is excellent in asymptomatic rhabdomyomas. Therefore, if life-threatening hemodynamic disturbances do not develop, regular clinical follow-up is recommended as is most of our cases.

Foetal echocardiography has an important place in the diagnosis of cases in the risk group in the prenatal period, and in the follow-up of the sizes and number of tumours in cases diagnosed. The evaluation of these cases with regards to tuberous sclerosis after birth leads to early diagnosis (9, 18, 21). In our case series, tuberous sclerosis was not identified in the postnatal examinations of the rhabdomyoma case diagnosed in the prenatal period.

Rhabdomyomas may lead to sudden cardiac death, or arrhythmias including ventricular tachycardia, supraventricular tachycardia and preexcitation syndrome, via compression of the cardiac conduction system. If these tumours lead to important clinical problems, surgical excision is recommended as the prognosis is bad (16, 17, 23-25). Miyake et al (24) determined a frequency of 6% for ventricular tachycardia and 10% for preexcitation syndrome in 106 rhabdo-

Table 1. Echocardiographic Findings of the rhabdomyomas

Case	Gender	Age	Echocardiographic findings	Duration of follow-up	Change in the size of the mass
Case 1	Male	4 years	A 11x4 mm mass in the LV, at the 1/3 superior aspect of the IVS (Figure 1)	2 years	Mass increased in size by 3x1 mm to 14x5 mm.
Case 2	Male	13 years	A 16x6 mm mass in the midventricular septum in the LV	2.5 years	Mass decreased in size to 11.5x3.5 mm.
Case 3	Male	6.5 years	A low density 35x31 mm mass adjacent to the posterior wall of the LV, 3 masses in the LV, the smallest being 5x5 mm (Figure 1)	6 months	Mass was surgically excised.
Case 4	Male	3 month	A 26x22 mm mass in the LV adjacent to the septum.	1 month	Mass was surgically excised
Case 5	Male	1 year	A large, regular contoured lobulated mass 31x18 mm in size, filling 2/3 of the RV cavity and leading to obstruction in the RVOT.	2 years	Mass 15.6x9.4 mm regressed in size.
Case 6	Female	1 year	An apical regular contoured homogenous mass, 22x20 mm in size attached to the free wall of the RV.	7 months	No changes in the size of the mass
Case 7	Male	1 year	A 14x12 mm apical mass in the LV, two masses 12x13 mm in size adjacent to the LVOT.	6.5 months	No changes in the size of the mass
Case 8	Male	7 months	A 11x7 mm apical mass in the LV, two masses 9x8 mm in size, adjacent to the mitral valve.	13 months	Apical mass was reduced to 4.5x 3.4 mm.
Case 9	Male	9 years	A hyperechogenic, regular contoured 13x11 mm mass adjacent to the anterior leaflet of the tricuspid valve in the RA.	8 months	No changes in the size of the mass
Case 10	Female	1 years	Nine regular contoured masses with homogenous density, mostly located in the apex of the RV, the largest being 13x7 mm.	9 months	The three small masses disappeared, the largest mass was reduced in size to 8x3 mm
Case 11	Male	10 years	Hyperechogenic image 12x5 mm in size in the midventricular septum.	2.5 years	No changes in the size of the mass
Case 12	Female	32 years	Foetal cardiac rhabdomyoma (Two masses leading to a reduction of LV and RV cavities, Grade 2 MF, mild aortic stenosis.	10 days	Mass was surgically excised

LV: left ventricle, LVOT: left ventricular outlet, MF: mitral failure, RV: right ventricle, RVOT: right ventricular outlet, IVS: interventricular septum

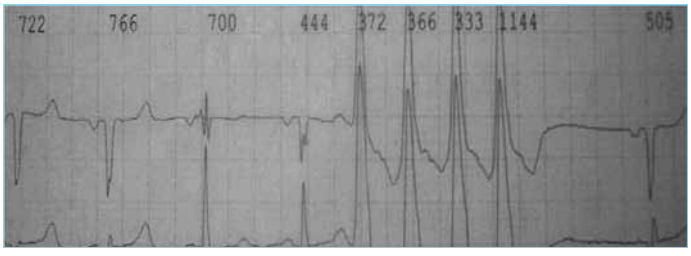

Figure 7. Short term ventricular tachycardia attack in the Holter ECG of case number 5

myoma cases. Di Liang et al (17) reported a mortality rate of 78% in symptomatic cases below one years of age. In our case series, ventricular extra-systoles and short term ventricular tachycardia attack due to compression of the cardiac conduction system was observed in a case with a tumour filling 2/3 of the right ventricular cavity. Arrhythmia was taken under control with medical treatment and regression of the tumour in time.

Rhabdomyomas may be surgically removed when they cause cardiac failure, obstruction and hemodynamic disturbances (26, 27). The tumours of the three cases were surgically excised as they caused congestive heart failure. In the post-operative follow-up, symptoms of congestive heart failure disappeared.

CONCLUSION

By multidisciplinary approach, we suggest that TTE, ECG and Holter monitoring have an important place in the follow-up and management of cardiac rhabdomyoma cases and complications in the follow-up period can be treated with appropriate and timely medical and surgical approaches.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Gaziantep University Clinical Research Ethics Committee.

Informed Consent: Written informed consent was obtained from patients' parents who participated in this study.

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Authors' contributions: Conceived and designed the experiments or case: Aİ, OB, MK, MK. Performed the experiments or case: Aİ, DAŞ. Analyzed the data: OB, MK, KY. Wrote the paper: Aİ, SI. All authors have read and approved the final manuscript.

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REFERENCES

1. Osborne JP, Fryer A, Webb D. Epidemiology of tuberous sclerosis. Ann N Y Acad Sci 1991; 615: 125-7. [CrossRef]
2. Silverman NA. Primary cardiac tumors. Ann Surg 1980; 191(2): 127-38. [CrossRef]
3. Weiss SW, Goldblum JR. Rhabdomyoma. In Soft Tissue Tumors, 4th Ed. St. Louis: Mosby; 2001 p.769-83.
4. Harding CO, Pagon RA. Incidence of tuberous sclerosis in patients with cardiac rhabdomyoma. Am J Med Genet 1990; 37(4): 443-6. [CrossRef]
5. Bader RS, Chitayat D, Kelly E, Ryan G, Smallhorn JF, Toi A, et al. Fetal rhabdomyoma: prenatal diagnosis, clinical outcome, and incidence of associated tuberous sclerosis complex. J Pediatr 2003; 143(5): 620-4. [CrossRef]
6. Butany J, Nair V, Naseemuddin A, Nair GM, Catton C, Yau T. Cardiac tumors: diagnosis and management. Lancet Oncol 2005; 6(4): 219-28. [CrossRef]
7. Gupta A, Narula N, Mahajan R, Rohit M. Sudden death of a young child due to cardiac rhabdomyoma. Pediatr Cardiol 2010; 31(6): 894-6. [CrossRef]
8. Roach ES, Gomez MR, Northrup H. Tuberous sclerosis complex consensus conference: revised clinical diagnostic criteria. J Child Neurol 1998; 13(12): 624-8. [CrossRef]
9. Baron Y, Barkovich AJ. MR Imaging of tuberosclerosis in neonates and young infants. AJNR Am J Neuroradiol 1999; 20(5): 907-16.
10. Quek SC, Yip W, Quek ST, Chang SK, Wong ML, Low PS. Cardiac manifestation in tuberous sclerosis: a 10-year review. J Pediatr Child Health 1998; 34(3): 283-7. [CrossRef]
11. Marx GR, Moran MA. Cardiac tumors. In Allen HD, Gutgesell HP, Clark EB, editors. Moss and Adams' Heart Disease in Infant, Children and Adolescents. 7th edition. Philadelphia: Lippincott Williams and Wilkins; 2008.p.1479-95.
12. Jóźwiak S, Kawalec W, Dłuzewska J, Daszkowska J, Mirkowicz-Małek M, Michałowicz R. Cardiac tumours in tuberous sclerosis: their incidence and course. Eur J Pediatr 1994; 153(3): 155-7. [CrossRef]
13. Webb DW, Thomas RD, Osborne JP. Cardiac rhabdomyoma and their association with tuberous sclerosis. Arch Dis Child 1993; 68(3): 367-70. [CrossRef]
14. Smith HC, Watson GH, Patel RG, Super M. Cardiac rhabdomyomata in tuberous sclerosis: their course and diagnostic value. Arch Dis Child 1989; 64(2): 196-200. [CrossRef]
15. Bass JL, Breningstall GN, Swaiman KF. Echocardiographic incidence of cardiac rhabdomyoma in tuberous sclerosis. Am J Cardiol 1985; 55(11): 1379-82. [CrossRef]
16. Tejero Hernández MA, Gómez Guzmán E, Tejero Mateos I, Pérez Navero JL, Suárez de Lezo Cruz Conde J. Right atrial rhabdomyoma and Wolff-Parkinson-White syndrome in an infant with tuberous sclerosis. An Pediatr (Barc) 2009; 70(5): 500-2. [CrossRef]
17. Di Liang C, Ko SF, Huang SC. Echocardiographic evaluation of cardiac rhabdomyoma in infants and children. J Clin Ultrasound 2000; 28(8): 381-6. [CrossRef]
18. Başpınar O, Celkan MA, Adlı M, Yılmaz K, Kervancıoğlu S. Fetal Rhabdomyoma: Prenatal diagonsis and postnatal outcome. Gaziantep Tıp Derg 2008; 14(02): 41-2.
19. Freedom RM, Lee KJ, MacDonald C, Taylor G. Selected aspects of cardiac tumors in infancy and childhood. Pediatr Cardiol 2000; 21(4): 299-316. [CrossRef]
20. Farooki ZQ, Ross RD, Paridon SM, Humes RA, Karpowich PP, Pinsky WW. Spontaneous regression of cardiac rhabdomyoma. Am J Cardiol 1991; 67(9): 897-9. [CrossRef]
21. Whiteside W, Saba Z, Kurio G. Postnatal growth of rhabdomyoma prior to tumor regression. Pediatr Cardiol 2010; 31(4): 541-4. [CrossRef]
22. Das BB, Sharma J. Cardiac rhabdomyoma and tuberous sclerosis: prenatal diagnosis and follow-up. Indian J Pediatr 2003; 70(1): 87-9. [CrossRef]
23. Krasuski RA, Hesselson AB, Landolfo KP, Ellington KJ, Bashore TM. Cardiac rhabdomyoma in an adult patient presenting with ventricular arrhythmia. Chest 2000; 118(4): 1217-21. [CrossRef]
24. Miyake CY, Del Nido PJ, Alexander ME, Cecchin F, Berul CI, Triedman JK, et al. Cardiac tumors and associated arrhythmias in pediatric patients, with observations on surgical therapy for ventricular tachycardia. J Am Coll Cardiol 2011; 58(18): 1903-9. [CrossRef]
25. Venugopalan P, Babu JS, Al-Bulushi A. Right atrial rhabdomyoma acting as the substrate for Wolff-Parkinson-White syndrome in a 3-month-old infant. Acta Cardiol 2005; 60(5): 543-5. [CrossRef]
26. De Rosa G, De Carolis MP, Pardeo M, Bersani I, Tempera A, De Nisco A, et al. Neonatal emergencies associated with cardiac rhabdomyomas: an 8-year experience. Fetal Diagn Ther 2011; 29(2): 169-77. [CrossRef]
27. Kohut J, Krzystolik-Ładzińska J, Szydłowski L, Smoleńska-Petelenz J, Giec-Fuglewicz G, Pajak J. The diagnosis, clinical course and follow-up of children with cardiac tumours - a single-centre experience. Kardiol Pol 2010; 68(3): 304-9.

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The Relationship of Hyperlactatemia Following Paediatric Open Heart Surgery with Mortality, Morbidity and Risk Factors

ORIGINAL INVESTIGATION

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ABSTRACT

Objective: In this present study, the association of hyperlactatemia frequency with probable risk factors, postoperative morbidity and mortality were investigated in patients undergoing paediatric open heart surgery.

Materials and Methods: The present study included 45 consecutive paediatric patients who had undergone open heart surgery with hypothermic cardiopulmonary bypass in the cardiovascular surgery clinic between January 2008 and July 2008. Four blood samples for lactate analysis were collected from each of the patients preoperatively, intraoperatively and at 1 and 12 hours postoperatively. The patients were divided into two groups according to blood lactate levels as the high lactate group (mean lactate level≥ 3 mmol/L) and the normal lactate group (mean lactate level <3 mmol/L). Hyperlactatemia frequency, associated risk factors, and the relationship with morbidity and mortality were statistically analysed.

Results: Of 45 cases, 33 (73.3%) were included in the normal lactate (NL) group, and 12 (26.7%) were included in the high lactate (HL) group. A borderline association was found between lactate levels and mortality in the HL group (p=0.052). Body surface area, age, low cardiac output syndrome, intraoperative and postoperative inotropic support requirement, duration of mechanical ventilation were determined as risk factors associated with mortality (p<0.05), and low cardiac output syndrome, urine output and metabolic acidosis were determined as risk factors associated with hyperlactatemia (p<0.05).

Conclusion: In patients followed up in the intensive care unit, lactate concentration is a good indicator for disease severity. Blood lactate levels seems to be a parameter that can be used in routine follow-up.

Key words: Pediatric open heart surgery, hyperlactatemia, congenital heart disease

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INTRODUCTION

Hyperlactatemia is a common metabolic abnormality after open heart surgery (1). As hyperlactatemia is the early indicator of hypoperfusion, which is fatal, monitoring blood lactate levels in critical patients may increase the chance of an early life-saving intervention (2). Metabolic acidosis with hyperlactatemia is the most important indicator of septic shock-related mortality (3). Hyperlactatemia can occur regardless of the presence of tissue hypoxia after cardiac surgery. It has been demonstrated that blood flow and oxygenation in the splanchnic region is decreased and there is a significant mucosal hypoperfusion during cardiopulmonary bypass (CPB). Due to the increased lactate production and decreased elimination in the splanchnic region, lactate levels are expected to increase in CPB; however, this increase normal and anlamlı kabul edilebilecek levels üzerinde yeterli çalışma yapılmamıştır (4). In patients undergoing paediatric open heart surgery, close follow-up of lactate levels in the preoperative, intraoperative and postoperative periods may be an early indicator of mortality (5, 6). In this present study, we aimed to evaluate hyperlactatemia frequency, risk factors that are probably related to hyperlactatemia and the relation between postoperative morbidity and mortality and hyperlactatemia in patients who had undergone paediatric cardiac surgery.

MATERIAL and METHODS

Consecutive 45 paediatric cases that had undergone elective open heart surgery with hypothermic cardiopulmonary bypass in the cardiovascular surgery clinic between January 2008 and July 2008 were included in the study. Before the surgery, the legal representatives of the patients were informed about the study and informed consents were obtained. Patients who underwent emergency surgery and re-surgery were excluded from the study. Characteristics of the patients are presented in Table 1. After preoperative routine examinations were performed, the patients were taken to the surgery. After anaesthetic monitoring was completed, the first arterial blood sample for lactate analysis (preoperative) was taken. Necessary cardiac repairs were accomplished through a median sternotomy under CPB. During CPB, the mean arterial blood pressure (MABP) was maintained at 60 mmHg (50-70 mmHg), and the mean body temperature was maintained at 30°C (28-31°C). After the intervention, cardiac output was decreased and the patient was weaned from CPB. Four blood samples for lactate analysis were col-

Table 1. Characteristics of the cases

	Total n=45 (100%) mean (min-max)	NL Group n=33 (73.3%) mean (min-max)	HL Group n=12 (26.7%) mean (min-max)	p value (p<0.05)
Age (years)	6.31 (0.4-15)	6.63 (0.4-15)	5.4 (0.5-14)	p= 0.008
Gender (M/F)	(20/25)	(15/18)	(5/7)	NS
BSA, (m^2)	0.88 (0.33-1.95)	0.93 (0.35-1.95)	0.74 (0.33-1.62)	p<0.001

NL: Normal lactate, HL: High lactate, BSA: Body surface area, NS: Not significant

Table 2. Surgical parameters

	Total Mean (min-max)	NL Group Mean (min-max)	HL Group Mean(min-max)	p value (p<0.05)
Duration of CPB, minutes	80.1 (25-175)	75.81 (25-150)	91.91 (43-176)	NS
XCL time, minutes	48.2 (14-100)	44.60 (14-90)	58.16 (18-100)	NS
BP, mmHg	66.5 (54-75)	66.48 (58-75)	65.75 (54-70)	NS
VP requirement	1 (2.2%)	0	1 (8.3%)	NS
ISR	15 (33.3%)	8 (24.2%)	7 (58.3%)	p= 0.009
Volume supplementation	1 (2.2%)	1 (3.0%)	0	NS

CPB: Cardiopulmonary bypass, XCL: Cross clamp, BP: Blood pressure, VP: Vasopressor, ISR: Inotropic support requirement, NS: Not significant

lected from each of the patients preoperatively, intraoperatively and at 1 and 12 hours postoperatively. Additionally, body surface area (BSA), duration of CPB, cross clamp (XCL) time, degree of hypothermia during CPB, MABP, requirement of volume supplementation, intraoperative vasopressor (VP) and inotropic support requirement (ISR), length of stay in the intensive care unit (ICU), mechanical ventilation duration (MVD), postoperative ISR, low cardiac output syndrome (LCOS), urine output, metabolic acidosis, amount of tube drainage, revision requirement, increased glucose levels, hepatic dysfunction, renal failure, infection, fever, increased white blood cell (WBC) count, gastrointestinal (GIS) complications, β-agonist requirement were recorded in the follow-up forms. Criteria for starting inotropic support were determined as difficulty in weaning from CPB, post-CPB acute left heart and/or right heart failure, and low cardiac output in the postoperative period. The values obtained in the intraoperative period are presented in Table 2. The UV-160A Shimadzu visible recording spectrophotometer in the metabolism laboratory was used to determine lactate levels. In order to increase the accuracy of testing, the collected samples were immediately transferred to the laboratory in ice batteries in accordance with cold chain requirements. According to the laboratory results, patients with an arterial lactate concentration <3 mmol/L were included in the normal lactate (NL) group (group 1) and those with an arterial lactate concentration≥ 3 mmol/L were included in the high lactate (HL) group (group 2). A blood glucose level >150 mg/dl was considered as a high glucose level, a WBC count>15000/mm^3 was considered as leucocytosis, and body temperature≥ 38.0°C (100.4 F) was considered as fever. A postoperative alanine aminotransferase (ALT) level >100 IU/L was accepted as hepatic dysfunction. Urine output was calculated in ml/kg/h and recorded. The patients were monitored until discharge and all clinical and laboratory changes were recorded.

Statistical analysis

Data were analysed using the Statistical Package for the Social Sciences (SPSS) 15.0 statistical package program. A chi square test was used in the comparison of qualitative variables. Normality testing of data was performed using the Kolmogorov-Smirnov test. The independent two sample t test was used in variables with normal distribution, and the Mann Whitney U test was used in non-normally distributed variables. A p value <0.05 was considered statistically significant.

RESULTS

A total of 45 paediatric patients (25 boys, 20 girls) were included in the study. The reasons for surgery were as follows, ventricular septal defect (VSD) in 16 (35.5%) patients, Tetralogy of Fallot (TOF) in 11 (24.4%) patients, atrial septal defect (ASD) in 9 (20%) patients, aortic valve replacement (AVR) in 2 (4.4%) patients, transposition of the great arteries (TGA) in 2 (4.4%) patients, atrioventricular septal defect (AVSD) in 2 (4.4%) patients, subvalvular aortic stenosis (SVAS) in 2 (4.4%) patients, and pulmonary stenosis (PS) in 1 (2.2%) patient. Of the patients, 12 (26.7%) of them had hyperlactatemia (≥3 mmol/L). Normal lactate group (NL) included 33 cases (15 boys, 18 girls), and high lactate group included 12 cases (5 boys, 7 girls). While all values, other than those obtained in the preoperative period, were>3 mmol/L in the HL group, lactate levels >3 mmol/L was not observed at any time point including the preoperative period in the NL group. Mean lactate levels measured at the four time points were 2.22, 3.16, 3.72 and 3.48 mmol/L, respectively in the HL group, whereas the corresponding values in the NL group were 1.79, 2.23, 2.19 and 2.01 mmol/L, respectively. The mean age was 6.31±3.1 years; 6.63±3.6 years in the NL group and 5.4±2.1 years in the HL group. There was a significant relation between mean age and mortality (p=0.008). Mean

BSA was 0.88±0.4m² (0.33-1.95); 0.93±0.5 m² (0.35-1.95) in the NL group and 0.74±0.3 m² (0.33-1.62) in the HL group. The relation between low BSA and mortality was significant (p<0.001). Mean cardiopulmonary bypass duration was 80.1±22.4 (25-176) minutes; 75.81±26.4 (25-150) minutes in the NL group, and 91.91±25.6 (43-176) minutes in the HL group. Mean cross clamp time was 48.2±26.6 (14 -100) minutes; 44.60±22.6 (14 -90) minutes in the NL group, and 58.16±28.6 (18-100) minutes in the HL group. Inotropic support was required in 8 cases (24.2%) in the NL group and 7 cases (58.3%) in the HL group in the intraoperative period. There was a significant relation between intraoperative ISR and mortality (p=0.009). Mechanical ventilation duration was 8.06±4.8 (4-23) hours in the NL group and 12.0±6.8 (6-24) hours in the HL group. There was a significant relation between increased MVD and mortality (p=0.006). Length of stay in the intensive care unit was 3.09±2.8 (2-10) days in the NL group and 3.08±1.8 (1-6) days in the HL group. Inotropic support was required in 9 cases (27.2%) in the NL group and in 7 cases (58.3%) in the HL group in the ICU. ISR in the ICU was significantly related with mortality (p=0.012). Low cardiac output syndrome occurred in 3 cases (25%) in the HL group, and none of the cases in the NL group. LCOS was significantly related with both mortality and hyperlactatemia (p<0.001, p=0.016). Mean urine output was 1.84±0.8 (0.3-3.1) ml/kg/h in the NL group and 1.41±0.9 (0.3-2.7) ml/kg/h in the HL group. Decreased urine output was significantly related with hyperlactatemia (p=0.015). Metabolic acidosis occurred in 4 patients (12.1%) in the NL group and 8 (66.6%) patients in the HL group. There was a significant relation between metabolic acidosis and hyperlactatemia (p= 0.001). Of the 45 cases, 4 (8.8%) of them died in the postoperative period, 3 (25%) from the HL group and 1 (3%) from the NL group. The patients who died in the HL group died due to low cardiac output syndrome at the postoperative 20, 24 and 30 hours. Two of them were operated because of TOF and one of them was operated with a diagnosis of ventricular septal defect (VSD). The patient who died in the NL group had a diagnosis of VSD; he/she was intubated at postoperative 4 days due to sudden onset unconsciousness and respiratory failure, and was planned to be transferred to the ward as he/she was clinically and hemodynamically stable. This situation was probably suggestive of non-surgical mortality. Blood lactate levels of this patient were 1.07, 2.02, 2.07 and 2.24 mmol/L, respectively. Low BSA, low age, LCOS, ISR during the surgery and in ICU, and mechanical ventilation duration were found to be the risk factors related with mortality (p<0.05). LCOS, decreased urine output and metabolic acidosis were determined to be the risk factors related with hyperlactatemia (p<0.05). The risk factors associated with mortality and the risk factors associated with hyperlactatemia are shown in Table 3 and Table 4.

DISCUSSION

In open heart surgery, along with the expected effects of CPB, hyperlactatemia is a commonly encountered condition. Normal blood lactate concentrations is 0.5-1 mmol/L in unstressed patients and <2 mmol/L in critical patients. Hyperlactatemia is defined as blood lactate levels between 2 and 5 mmol/L, and lactic acidosis is defined as metabolic acidosis with blood lactate levels> 5 mmol/L (7). Many studies reported increased lactate levels above the normal range, which can be related with mortality. In the previous studies, it was demonstrated that hyperlactatemia occurs due to activation of anaerobic glycolysis before the parameters showing cardiac functions are impaired (BP, urine output, mixed venous oxygen saturation) when LCOS develops, and if identified early, there is a change of successful intervention (8, 9). Increase in lactate levels due to any reason and the resultant metabolic acidosis gains a particular importance as they will lead to suppression of cardiac functions (8). There may be significant elevation in blood lactate levels

Table 3. Risk factors related with mortality

	Alive mean±SD (median)	Exitus mean±SD (median)	p value (p<0.05 significant)
BSA	0.92±0.43 (0.83)	0.35±0.02 (0.35)	p<0.001
Age	6.80±4.55 (7.00)	1.27±0.86 (1.00)	p=0.008
LCOS	0	3 (25.0%)	p<0.001
ISR (intraoperative)	8 (24.2%)	7 (58.3%)	p=0.009
ISR (intensive care unit)	9 (27.2%)	7 (58.3%)	p=0.012
MVD	8.12±3.71 (8.00)	24.25±4.19 (23.50)	p=0.006

BSA: Body surface area, LCOS: Low cardiac output syndrome, ISR: Inotropic support requirement, MVD: Mechanical ventilation duration

Table 4. Risk factors related with hyperlactatemia

	NL group mean±SD (median)	HL group mean±SD (median)	p value (p<0.050)
LCOS	0	3 (25.0%)	p=0.016
Decreased urine output	(2.0±0.52) 2.1	(1.5±0.56) 1.4	p=0.015
Metabolic acidosis	4 (12.1%)	8 (66.6%)	p=0.001

LCOS: Low cardiac output syndrome, NL: Normal lactate, HL: High lactate

due to severe hypoperfusion (without acidosis) (9-11). Increased lactate levels after paediatric open heart surgery show a parallelism with increased mortality and morbidity (12, 13). In the present study, four blood samples for lactate analysis were obtained from each of the patients undergoing paediatric open heart surgery preoperatively, intraoperatively and at 1 and 12 hours postoperatively. The mean preoperative lactate level was 1.91 mmol/L and the mean lactate level at postoperative 1 hour in the ICU was 2.67, there are differences in the upper range of lactate levels in numerous similar studies. In the HL group, which was formed according to a lactate threshold of 3 mmol/L, a borderline association was found between lactate levels and mortality (p=0,052). Of the 45 cases included in the study, 4 of them died; 3 of them were in the HL group and 1 was in the NL group; the patient who died in the NL group was intubated due to sudden onset unconsciousness and respiratory failure, and was planned to be taken to the ward as her/his hemodynamic and clinical status was stable. This situation was probably suggestive of non-surgical mortality. However, although this case had a remarkable effect on the statistical results, we determined a borderline relation between mortality and high lactate levels (p=0.052). When the lactate values obtained in the preoperative, intraoperative and at 1 and 12 hours in the postoperative period were evaluated separately, there was a significant relation between lactate values obtained at postoperative 12 hours and mortality (p=0.008). The lactate values obtained at postoperative 1 hour of the three cases who died in the HL group were 3.77, 5.4 and 3.85 mmol/L, respectively, and lactate values obtained at 12 hours were 5.42, 5.74 and 4.2 mmol/L, respectively. Başaran, Maullet, and Bolcal, in their studies emphasized the significant relation between mortality and increased lactate levels in the early period (8, 14, 15). According to the threshold value of ≥3mmol/L that we accepted, hyperlactatemia (≥3 mmol/L) frequency that developed in 12 of 45 cases was 26.7%. Risk factors related with hyperlactatemia were LCOS, decreased urine output, and metabolic acidosis (p<0.05). Low BSA, low age, LCOS, intraoperative inotrope requirement and ISR in ICU, and MVD were found to be the risk factors related with mortality (p<0.05). Different risk factors may be put forward according to different lactate thresholds. In the present study, risk factors were determined according to a lactate threshold of 3mmol/L. When hyperlactatemia threshold after open heart surgery is clarified, more reliable data can be collected and interpreted about the probable risk factors associated with mortality. In the present study that included 45 cases, LCOS is the only single risk factor related both with mortality and hyperlactatemia. As tissue perfusion is impaired in LCOS, development of hyperlactatemia is an expected situation. XCL time, CPB duration, VP, β agonist use and hyperglycaemia are considered as conditions leading to hyperlactatemia. These factors were not statistically significant in this limited patient group. In case of increased lactate levels after open heart surgery, Başaran et al. (8) recommended to evaluate cardiac functions using echocardiography, and in accordance with the results, to correct volume deficit according to central venous pressure (CVP), provide inotrope support if required, and to adjust ventilator settings in order to increase oxygenation and decrease carbon dioxide levels. Nevertheless, other than echocardiography all these procedures are routinely performed in the treatment and follow-up. In case of hyperlactatemia, at least determination of the reason of hyperlactatemia (cardiac or non-cardiac) will allow to intervene before low perfusion clinic develops or metabolic dysfunction leads to the impairment of cardiac performance. Early interventions will result in decreased mortality rates. Researchers put emphasize on early secondary markers of hypoperfusion before BP, urine output and mixed venous oxygen saturation that indicates cardiac performance is impaired. Many authors believe that hyperlactatemia can be an early indicator (5, 8, 16). Although there is a limited number of studies and no common consensus on this subject, in accordance with the current data, we think that follow-up of both intraoperative and postoperative lactate levels is beneficial as it allows early intervention before clinical symptoms of hypoperfusion develops.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Erciyes University Faculty of Medicine.

Informed Consent: Written informed consent was obtained from patients' parents who participated in this study.

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Authors' contributions: Conceived and designed the experiments or case: SO, FS, HC. Performed the experiments or case: SO, FS, HC. Analyzed the data: SO, FS. Wrote the paper: OB, KE, SO. All authors have read and approved the final manuscript.

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REFERENCES

1. Civetta JM, Taylor RW, Kirby RR, eds. Postoperative management of the adult cardiac surgery patient. Critical care. 3rd ed. Philadelhia, PA: Lippincott Williams & Wilkins, 1997.p.1147-75.
2. Vincent JL, Dufaye P, Berré J, Leeman M, Degaute JP, Kahn RJ. Serial lactate determinations during circulatory shock. Critical Care Med 1983; 11(6): 449-51. [CrossRef]
3. Bakker J, Coffernils M, Leon M, Gris P, Vincent JL. Blood lactate levels are superior to oxygen derived variables in predicting outcome in human septic shock. Chest 1991; 99(4): 956-62. [CrossRef]
4. Landow L. Splanchnic lactate production in cardiac surgery patients. Crit Care Med 1993; 21(2): 84-91. [CrossRef]
5. Ranucci M, De Toffol B, Isgrò G, Romitti F, Conti D, Vicentini M. Hyperlactatemia during cardiopulmonary bypass: determinants and impact on postoperative outcome. Crit Care. 2006: 10(6): R167. [CrossRef]
6. Sheppard AP, Granger DN. Metabolic regulation of the intestinal circulation. In Sheppard A, Granger D, editors. Physiology of the intestinal circulation. New York: Raven Press; 1984.p.33-47.
7. Valenza F, Aletti G, Fossali T, Chevallard G, Sacconi F, Irace M, Gattinoni L. Lactate as a marker of energy failure in critically ill patients: hypothesis. Crit Care 2005; 9(6): 588-93. [CrossRef]
8. Basaran M, Sever K, Kafali E, Ugurlucan M, Sayin OA, Tansel T, et al. Serum Lactate Level Has Prognostic Significance After Pediatric Cardiac Surgery. J Cardiothorac Vasc Anesth 2006; 20(1): 43-7. [CrossRef]
9. Meregalli A, Oliveira RP, Friedman G. Occult hypoperfusion is associated with increased mortality in hemodynamically stable, high-risk, surgical patients. Crit Care 2004; 8(2): 60-5. [CrossRef]
10. Friedman G, Berlot G, Kahn RJ, Vincent JL. Combined measurements of blood lactate concentrations and gastric intramuco-

sal pH in patients with severe sepsis. Crit Care Med 1995; 23(7): 1184-93. [CrossRef]
11. Claridge JA, Crabtree TD, Pelletier SJ, Butler K, Sawyer RG, Young JS. Persistent occult hypoperfusion is associated with a significant increase in infection rate and mortality in major trauma patients. J Trauma 2000; 48(1): 8-14. [CrossRef]
12. Jeng JC, Jablonski K, Bridgeman A, Jordan MH. Serum lactate, not base deficit, rapidly predicts survival after major burns. Burns 2002; 28(2): 161-6. [CrossRef]
13. Mikulaschek A, Henry SM, Donovan R, Scalea TM. Serum lactate is not predicted by anion gap or base excess after trauma resuscitation. J Trauma 1996; 40(2): 218-22. [CrossRef]
14. Maillet JM, Le Besnerais P, Cantoni M, Nataf P, Ruffenach A, Lessana A, et al. Frequency, risk factors, and outcome of hyperlactatemia after cardiac surgery. Chest 2003; 123(5): 1361-6. [CrossRef]
15. Bolcal C, Doğancı S, Demirkılıç U, Tatar H. Koroner Bypass Cerrahisi Sonrası Görülen Hiperlaktateminin Sıklığı, Risk Faktörleri Ve Sonuçları. Turkiye Klinikleri J Cardiovasc Sci 2007; 19(1): 27-31.
16. Park SJ, Kim HS, Byon HJ, Kim CS, Cheong IY, Kim JT. Intraoperative plasma lactate as an early indicator of major postoperative events in pediatric cardiac patients. Tohoku J Exp Med 2012; 228(3): 239-45. [CrossRef]

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Pathogen Bacteria of the Urinary Tract Isolated from Urine Cultures and Their Susceptibility

ORIGINAL INVESTIGATION

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ABSTRACT

Objective: The present study was aimed to determine the distribution and antimicrobial susceptibility of strains isolated from urinary tract infections in our region.

Materials and Methods: In this study, the distribution and antibiotic resistance profiles of microorganisms isolated from the urine cultures of urology outpatient clinic and ward patients between December 2011 and May 2013 were retrospectively evaluated.

Results: The most commonly isolated microorganisms in outpatient clinic patients were; *E. coli* (71%), *K. pneumoniae* (8.8%), *P. aeruginosa* (6.3%), and the most commonly isolated microorganisms in hospitalized patients were *E. coli* (61.3%), *P. aeruginosa* (12.3%) and *K. pneumoniae* (5.8%). Amikacin, gentamicin, ceftazidime, cephalothin, ciprofloxacin and trimethoprim-sulfamethoxazole resistance rates of *E. coli* strains and cefotaxime and cephalothin resistance rates of *K. pneumoniae* were higher in hospitalized patients than that in outpatient clinic patients ($p<0.05$). While *E. coli* resistance to ampicillin, amoxicillin-clavulanate, gentamicin, nitrofurantoin, cefotaxime, ceftazidime, cefuroxime, ciprofloxacin and trimethoprim-sulfamethoxazole was significantly higher among male patients who were admitted to the outpatient clinic, ceftazidime and trimethoprim- sulfamethoxazole resistance was significantly higher among hospitalized male patients, in comparison to that in the female patients ($p<0.05$).

Conclusion: As antibiotic resistance rates vary across centres, it will be beneficial that each region perform surveillance studies to determine local antibiotic resistance rates for developing treatment protocols.

Key words: Urine culture, urinary tract infection, antibiotic

INTRODUCTION

Urinary tract infections (UTI) are among the leading causes of nosocomial and community acquired infections and are defined as the presence of inflammation in the kidneys, collecting system and/or urinary bladder. This infection affecting all age groups and both genders is particularly more common in young adult females (1). Approximately 30% to 50% of the population is estimated to develop at least one urinary tract infection in their lifetime (2). Urinary tract infections account for 7 million physician visits annually in the United States of America and approximately 15% of the prescribed antibiotics are for UTIs (3, 4). While gram negative rods, which are part of the normal gut flora are responsible from the majority of UTIs, the most commonly isolated microorganism is *Escherichia coli* (5, 6). The isolation rates of bacteria including *Proteus, Klebsiella, Enterobacter, Pseudomonas* and *Serratia* in nosocomial and complicated urinary tract infections are gradually increasing (7). Due to the empirical use of antibiotics in infectious diseases and the lack of standardization in antimicrobial susceptibility tests, resistance to commonly used antimicrobial agents is increasing year by year (8, 9). Generally, community acquired UTIs are treated empirically, and urine culture/ antimicrobial susceptibility test is demanded in cases with no response to empirical treatment or those with recurrence. Therefore, knowing the common isolated uropathogens of each region and their antimicrobial susceptibility patterns is beneficial in planning treatment protocols (10, 11).

Our aim in this present study was to determine the distribution and antimicrobial susceptibility of the isolated strains from urinary tract infections in our region.

MATERIAL and METHODS

The present study retrospectively evaluated the distribution and antibiotic resistance profiles of isolated microorganisms from the urine cultures of patients treated in the urology outpatient clinic and ward of our hospital between December 2011 and May 2013. The midstream urine samples and/or samples collected in aseptic conditions were accepted by the Microbiology laboratory. Urine samples were inoculated on 5% sheep blood agar and Eosin Methylene Blue (EMB) agar medium using a standard loop, and were incubated at 37°C for 18-24 hours. Colonies that grow in culture plates were identified using gram staining, and the presence of catalase, coagulase,

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oxidase and urease enzymes and biochemical characteristics. For strains that could not be identified using conventional methods, BD Crystal ID kit (Becton, Dickinson and Company, New Jersey, USA) was used. Antimicrobial susceptibility of bacteria was evaluated according to the recommendations of the Clinical and Laboratory Standards Institute (CLSI) and available conditions using Müller Hinton Agar medium (Oxoid Limited, Hampshire, England) by Kirby Bauer disk diffusion technique. Resistance and susceptibility to the most commonly used antibiotics for empirical treatment including penicillin, ampicillin, amoxicillin clavulanic acid, piperacillin tazobactam, cefotaxime, ceftazidime, cefuroxime, cephalothin, ciprofloxacin, levofloxacin, amikacin, gentamicin, streptomycin, erythromycin, tetracycline, trimethoprim-sulfamethoxazole and nitrofurantoin were analysed.

Statistical analysis

Data analysis was performed with SPSS 16 program using chi square test. In statistical analysis, statistical significance level was set at $p<0.05$.

RESULTS

In the study, culture growth was identified in 940 (494 female, 446 male) urine samples obtained from outpatient clinic patients and 308 (66 female, 242 male) urine samples obtained from hospitalized patients. The most commonly isolated microorganisms from outpatient clinic patients in the decreasing order of frequency were *E. coli* (71%), *K. pneumoniae* (8.8%), *P. aeruginosa* (6.3%), *Enterobacter spp* (3.4%), *Citrobacter* (2%), *P. Mirabilis* (1.9%), *Enterococcus faecalis* and *Streptococcus agalactiae* (1.2%), *Pseudomonas spp* (0.8%), *Staphylococcus aureus* and *Acinetobacter* (0.7%), and other bacteria (2%). The most commonly isolated microorganism in hospitalized patients was *E. coli* (61.3%), followed respectively by *P. aeruginosa* (12.3%), *K. pneumoniae* (5.8%), *Enterobacter spp* (4.5%), *E. faecalis* (3.2%), *Citrobacter* (2.9%), *Pseudomonas spp* (2.5%), *S. aureus* (1.9%), *P. mirabilis* and *Acinetobacter* (0.9%), *S. agalactiae* (0.6%) and other bacteria (3.2%). The distribution of isolated uropathogens in outpatient clinic and ward patients is shown in Table 1.

When the antimicrobial resistance rates of *E. coli* strains isolated from the urine cultures of outpatient clinic and ward patients were evaluated, it was found that amikacin, gentamicin, ceftazidime, cephalothin, ciprofloxacin and trimethoprim sulfamethoxazole resistance was significantly higher in hospitalized patients ($p<0.05$). In comparison of the antimicrobial resistance rates of *K. pneumonia,* cefotaxime and cephalothin resistance were again higher in hospitalized patients ($p<0.05$). The antimicrobial resistance rates of Gram negative and Gram positive bacteria isolated from the urine cultures of outpatient clinic and ward patients are given in Table 2 and Table 3.

The comparisons of resistance rates of *E. coli* strains isolated from female and male patients are presented in Table 4. When the antimicrobial resistance rates of *E. coli* grown in the urine cultures of outpatient clinic patients were evaluated, it was observed that ampicillin, amoxicillin-clavulanate, gentamicin, nitrofurantoin, cefotaxime, ceftazidime, cefuroxime, ciprofloxacin and trimethoprim-sulfamethoxazole resistance was higher in male patients in comparison to females ($p<0.05$) (Table 4). There was also a statistically significant difference between hospitalized male and female patients in terms of ampicillin, ceftazidime and trimethoprim-sulfamethoxazole resistance. While ampicillin resistance (39.1%/18.4%; p=0.008) was higher in females, ceftazidime (30.4%/41.8%; p=0.01) and trimethoprim sulfamethoxazole (41.3%/63.1%; p=0.01) resistance was higher in males (Table 4).

DISCUSSION

Although the most commonly isolated agents from urinary tract infections vary, almost all of them are caused by a single bacteria type, *E. coli* being the leading (12). In the study of Temiz et al the most frequently isolated microorganism was *E. coli* with a rate of

Table 1. Distribution of uropathogens isolated from outpatient clinic and ward patients

	Outpatient Clinic			Ward		
BACTERIA	**Female**	**Male**	**Total n (%)**	**Female**	**Male**	**Total n (%)**
E. coli	380	283	663 (71)	46	141	187 (61.3)
K. pneumoniae	46	37	83 (8.8)	2	16	18 (5.8)
P. aeruginosa	12	48	60 (6.3)	5	33	38 (12.3)
Enterobacter spp.	8	24	32 (3.4)	3	11	14 (4.5)
Citrobacter	13	6	19 (2.0)	2	7	9 (2.9)
P. mirabilis	10	8	18 (1.9)	-	3	3 (0.9)
Enterococcus faecalis	2	10	12 (1.2)	5	5	10 (3.2)
S. agalactiae	12	-	12 (1.2)	-	2	2 (0.6)
Pseudomonas spp.	1	7	8 (0.8)	-	8	8 (2.5)
S. aureus	4	3	7 (0.7)	1	5	6 (1.9)
Acinetobacter	1	6	7 (0.7)	-	3	3 (0.9)
Other	5	14	19 (2.0)	2	8	10 (3.2)
Total	494	446	940	66	242	308

Table 2. The types and antibiotic resistance rates of uropathogens isolated from outpatient clinic patients. (%)

BACTERIA	AMK	AMP	AMC	GEN	LVX	NIT	TZP	CTX	CAZ	SFR	CEF	CIP	SXT	STR	TET	ERY	PEN
E. coli	0.4	21.4	18.4	28.2	4.0	5.8	3.6	11.6	28.9	16.1	17.6	40.8	40.5	-	-	-	-
K. pneumoniae	0	16.8	22.8	15.6	2.4	27.7	7.2	3.6	26.5	20.4	10.8	20.4	31.3	-	-	-	-
P. aeruginosa	26.6	3.3	5	61.6	1.6	-	6.6	20.0	48.3	-	-	65.0	-	-	-	-	-
Enterobacter spp	-	15.6	-	31.2	25.0	-	-	-	-	-	-	53.1	3.1	18.7	62.5	28.1	9.3
Citrobacter	0	21.0	47.3	5.2	-	26.3	0	1.6	10.5	15.7	36.8	10.5	15.7	-	-	-	-
P. mirabilis	0	11.1	0	5.5	0	38.8	-	0	0	0	5.5	11.1	50.0	-	-	-	-
E. faecalis	-	25.0	0	33.3	-	8.3	-	-	-	-	-	41.6	-	25.0	50.0	25.0	8.3
S. agalactiae	-	25.0	0	0	-	-	-	-	-	-	-	8.3	8.3	0	66.6	41.6	8.3
Pseudomonas spp.	37.5	-	0	75.0	-	-	12.5	-	37.5	-	-	87.5	-	-	-	-	-
S. aureus	-	0	0	0	-	-	-	-	-	-	-	0	-	0	0	0	57.1
Acinetobacter	-	14.2	14.2	57.1	-	57.1	42.8	42.8	42.8	42.8	14.2	57.1	57.1	-	-	-	-
Other	0	10.5	10.5	21.0	5.2	15.7	0	5.2	5.2	10.5	15.7	36.8	36.8	-	-	-	21.0

AMK: Amikacin, AMP: Ampicillin, AMC: Amoxicillin clavulanic acid, GEN: Gentamicin, LVX: Levofloxacin, NIT: Nitrofurantoin, TZP: Piperacillin tazobactam, CTX: Cefotaxime, CAZ: Ceftazidime, SFR: Cefuroxime, CEF: Cephalothin, CIP: Ciprofloxacin, SXT: Trimethoprim-sulfamethoxazole, STR: Streptomycin, TET: Tetracycline, ERY: Erythromycin, PEN: Penicillin

Table 3. The types and antibiotic resistance rates of uropathogens isolated from ward patients (%)

BACTERIA	AMK	AMP	AMC	GEN	LVX	NIT	TZP	CTX	CAZ	SFR	CEF	CIP	SXT	STR	TET	ERY	PEN
E. coli	2.1	23.5	24.0	37.4	3.7	8.5	3.2	17.1	39.0	19.7	29.4	65.2	58.2	-	-	-	-
K. pneumoniae	0	27.7	27.7	16.6	0	38.8	11.1	22.2	38.8	27.7	33.3	27.7	38.8	-	-	-	-
P. aeruginosa	23.6	-	-	57.8	0	-	2.6	15.7	57.8	-	-	63.1	-	-	-	-	-
Enterobacter spp	-	14.2	-	21.4	14.2	-	-	-	-	-	-	42.8	-	21.4	42.8	21.4	7.1
Citrobacter	11.1	22.2	55.5	33.3	-	33.3	11.1	11.1	44.4	22.2	33.3	22.2	22.2	-	-	-	-
P. mirabilis	0	0	0	0	0	100	-	0	0	0	0	0	33.3	-	-	-	-
E. faecalis	-	50.0	0	50.0	-	0	-	-	-	-	-	70.0	-	50.0	60.0	40.0	20.0
S. agalactiae	-	0	0	0	-	-	-	-	-	-	-	0	-	0	0	0	0
Pseudomonas spp.	12.5	-	12.5	37.5	-	-	25.0	-	25.0	-	-	62.5	-	-	-	-	-
S. aureus	-	0	0	0	-	-	-	-	-	-	-	33.3	-	0	0	0	50.0
Acinetobacter	-	33.3	33.3	33.3	-	66.6	33.3	0	66.6	0	66.6	100	66.6	-	-	-	-
Other	-	0	10.0	0	0	20.0	10.0	0	0	10.0	0	0	10.0	-	-	-	20.0

AMK: Amikacin, AMP: Ampicillin, AMC: Amoxicillin clavulanic acid, GEN: Gentamicin, LVX: Levofloxacin, NIT: Nitrofurantoin, TZP: Piperacillin tazobactam, CTX: Cefotaxime, CAZ: Ceftazidime, SFR: Cefuroxime, CEF: Cephalothin, CIP: Ciprofloxacin, SXT: Trimethoprim-sulfamethoxazole, STR: Streptomycin, TET: Tetracycline, ERY: Erythromycin, PEN: Penicillin

* The underlined resistance rates show a statistically significant difference when compared with the resistance rates of outpatient clinic patients ($p<0.05$)

71%, followed by *Klebsiella* strains with 13% (13). In the study of Yılmaz and colleagues in which they evaluated the results of three-year urine culture-antimicrobial susceptibility tests, similarly *E. coli* and *Klebsiella* were on the first two ranks (14). Rifaioğlu et al evaluated the urine cultures of outpatients and hospitalized patients separately, and found that the first three most commonly isolated microorganisms in outpatient clinic patients were *E. coli* (67.2%), *P. mirabilis* (7.5%) and *K. pneumoniae* (3.9%), while the corresponding order for hospitalized patients was *E. coli* (49.6%), *P. aeruginosa* (10.5%) and *K. pneumoniae* (5.3%) (15). Urbarlı et al also demonstrated that the most commonly isolated microorganism in both outpatient clinic and ward patients was *E. coli* (75%), followed by *P. aeruginosa*(8%) and *Klebsiella* (5%) (16). Consistent with the results of the other studies, the present study demonstrated that *E. coli* (outpatient clinic: 71%, ward: 61.3%) was the most common pathogen isolated in both outpatient clinic and ward patients, followed by *K. pneumoniae* (8.8%) and *P. aeruginosa* (6.3%) in outpatient clinic patients, and *P. aeruginosa* (12.3%) and *K. pneumoniae* (5.8%) in ward patients. No significant difference was determined between the outpatient clinic patients and hospitalized patients regarding the isolated bacteria type (Table 1).

Table 4. Antibiotic Resistance Rates of *E. coli* strains according to gender

	Outpatient Clinic			Ward		
ANTIBIOTIC	**Female (%)**	**Male (%)**	**p value**	**Female (%)**	**Male (%)**	**p value**
Amikacin	0.2	0.7	0.57	4.3	1.4	0.254
Ampicillin	17.3	27.9	0.002	39.1	18.4	0.008
Amoxicillin-clavulanate	12.1	27.2	<0.001	15.2	26.9	0.117
Gentamicin	18.4	40.9	<0.001	30.4	40.4	0.294
Levofloxacin	2.8	5.3	0.15	2.1	4.2	0.98
Nitrofurantoin	3.4	9.8	0.001	13.0	7.0	0.22
Piperacillin tazobactam	2.6	4.5	0.20	4.3	2.8	0.63
Cefotaxime	6.5	18.7	<0.001	17.3	17.0	0.66
Ceftazidime	19.4	42.0	<0.001	30.4	41.8	0.01
Cefuroxime	12.6	20.8	0.005	26.0	18.4	0.29
Cephalothin	14.4	21.9	0.14	19.5	31.9	0.13
Ciprofloxacin	26.8	59.7	<0.001	60.8	66.6	0.48
Trimethoprim-sulfamethoxazole	29.2	53.0	<0.001	41.3	63.1	0.01

The increasing antimicrobial resistance throughout the world make the treatment of UTIs difficult every passing day. The reasons for antibiotic resistance may be the improperly adjusted treatment doses or frequent use of antibiotics in the treatment of various infections, as well as the acquisition of resistance in bacteria with low susceptibility by selection / spontaneous mutation or development of resistance in enteric bacteria by R plasmids responsible from multiple drug resistance (17). In previous studies, there is a discrepancy in antibiotic resistance rates of *E. coli* strains isolated from UTIs.

Ağca et al, in their study performed in two centres, reported that *E. coli* isolated from outpatient clinic patients and hospitalized patients were mostly susceptible to imipenem and amikacin, respectively (7). In this study, *E. coli* strains showed the lowest resistance rate to amikacin and piperacillin tazobactam; these rates were 0.4% and 3.6% in outpatient clinic patients and 2.1% and 3.2% in hospitalized patients. The low resistance rates detected for these antimicrobials may be attributed to the uncommon use of amikacin, piperacillin tazobactam and carbapenem group antibiotics in the empirical treatment of UTIs, and the use of these antibiotics only in hospitalized patients according to culture results.

Fluoroquinolones are wide spectrum antibiotics that are prescribed frequently for the treatment of complicated and uncomplicated urinary system infections; hence, resistance rates to these antibiotics are quite high. Various studies reported different quinolone resistance rates for *E. coli*. Yaşar and colleagues, in their study in which they evaluated the effects of extended spectrum beta lactamase (ESBL) production on antibiotic resistance in *E. coli* strains, determined ciprofloxacin resistance as 52.2% (18). Rifaioğlu et al reported ciprofloxacin susceptibility in *E. coli* strains isolated from outpatient clinic patients as 15.4% and ward patients as 40.2% (15). Ağca et al in their study performed in two centres found that ciprofloxacin resistance of one of the centres was 19% in outpatient clinic patients and 63% in ward patients, while the corresponding figures were 23% and 24% in the other centre (7). In this present study, ciprofloxacin resistance in *E. coli* strains in outpatient clinic and ward patients were 40.8% and 65.2%, respectively. Resistance to levofloxacin, a third generation fluoroquinolone which is commonly used in empirical treatment, was 4% and 3.7%, respectively.

Trimethoprim-sulfamethoxazole resistance in *E. coli* strains are reported between 22.1% and 60% in many studies performed in our country (19). In this study, co-trimoxazole resistance in *E. coli* strains was 40.5% in outpatient clinic patients and 58.2% in ward patients.

The *E. coli* resistance rates to ampicillin, amoxicillin-clavulanate in the present study show a wide difference from the rates reported in the literature. Temiz et al. reported ampicillin and amoxicillin-clavulanate resistance as 76.1% / 65.7% in outpatient clinic patients and 79.3% / 68.8% in hospitalized patients (13). These rates were 69% / 36% and 82% / 58%, respectively, in the study of Bayraktar et al. (20). In the present study, the resistance rates to ampicillin were 21.4% and 23.5% in outpatient clinic patients and that to amoxicillin-clavulanate were 18.4% and 24% for ward patients. According to these results, it should be bear in mind that aminopenicillins may be a good option for treatment of community acquired UTI caused by *E. coli* in our region.

An aminoglycoside derivative, gentamicin, has an important place in antimicrobial treatment, primarily in Gram negative infections. When the studies on gentamicin susceptibility in *E. coli* are evaluated, it is observed that there is an increasing trend of resistance in the last ten years. Kaya et al. reported that gentamicin resistance in *E. coli* strains increased from 4% to 16% within four years; Kurutepe and colleagues also reported that gentamicin resistance in *E. coli* strains from outpatient clinic patients increased from 7% to 13.8% in a six years period (19, 21). In this study gentamicin resistance rates of *E. coli* isolates (outpatient clinic: 28.2%, ward: 37.4%) were consistent with the increasing trend of resistance in the literature. This situation emphasizes the necessity of regular monitoring of antimicrobial susceptibility of uropathogens.

The problem of increasing resistance is also observed in studies evaluating the effects of cephalosporin group antibiotics on *E. coli*. Kaya et al reported that cefuroxime resistance increased from 9.6% to 32.1%, cefotaxime resistance from 1% to 27.5%, and ceftazidime resistance from 1% to 24.6% between 2000 and 2003 (19). Among the cephalosporins included in antimicrobial susceptibility test, *E. coli* strains isolated in the present study exhibited higher rates of resistance to ceftazidime, compared to literature (outpatient clinic: 28.9%, ward: 39%). Cefuroxime and cefotaxime resistance rates were consistent with the results of other studies (Table 2-3).

In comparison of the resistance rates of *E. coli* strains isolated from UTI between female and male patients, it was found that male patients had a higher resistance to numerous antibiotics. Linhares et al, in their ten-year surveillance study determined that strains isolated from male patients were more resistant to fluoroquinolones, penicillin, nitrofurantoin and to first and second generation cephalosporins (22). Another surveillance study in USA and Canada reported that ciprofloxacin, levofloxacin and trimethoprim-sulfamethoxazole resistance was higher in males (23). Mc Gregor et al, in their study in which they evaluated sex- and age-specific antibiotic resistance patterns found that *E. coli* isolated from male patients was more resistance to ampicillin, amoxicillin-clavulanate, ciprofloxacin and nitrofurantoin (24). In this study, ampicillin, amoxicillin-clavulanate, gentamicin, nitrofurantoin, cefotaxime, ceftazidime, cefuroxime, ciprofloxacin and trimethoprim sulfamethoxazole resistance was statistically significantly higher in male outpatient clinic patients compared to that in females. While ampicillin resistance was higher in female hospitalized patients, ceftazidime and trimethoprim-sulfamethoxazole resistance was higher in males.

In the present study, amikacin, levofloxacin and piperacillin tazobactam were the most effective antibiotics whereas trimethoprim sulfamethoxazole, ceftazidime and cephalothin had the highest resistance rates to *K. pneumoniae* strains, the second most commonly isolated microorganism in outpatient clinic patients and the third most commonly isolated microorganism in hospitalized patients. In the study of Abdullah and colleagues where only *Klebsiella* isolates were investigated, amoxicillin (0.1%) and nitrofurantoin (15.5%) showed the lowest susceptibility, while imipenem (97.7%) and piperacillin tazobactam (95.7%) were reported as the most effective antibiotics (25).

In our study, when the resistance profiles of the isolated *P. aeruginosa* strains were assessed, it was observed that ciprofloxacin, gentamicin and ceftazidime resistance rates were high in both outpatient clinic and ward patients (Table 2-3). Our results were similar to the results of the study of Temiz et al, in which ciprofloxacin, gentamicin and ceftazidime resistance were found as 68.1%/38.8%, 54.5%/50%, and 59%/44.4%, respectively in outpatient clinic and ward patients (13).

CONCLUSION

The selection of antibiotics for treatment of urinary tract infections is important for both treatment success and prevention of resistance development. Urine culture should be performed in every outpatient clinic and ward patient before starting empirical treatment, antibiotic susceptibility of the isolated microorganism should be determined and empirical treatment should be rearranged according to antimicrobial susceptibility results. As antibiotic resistance rates show variations across centres, it will be beneficial that every region perform surveillance studies to determine local antibiotic resistance rates for the development of treatment protocols.

Ethics Committee Approval: Ethics committee approval was received for this study from the local ethics committee of Bozyaka Training and Research Hospital.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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REFERENCES

1. Özsüt H. İdrar yolu infeksiyonları. In Topçu AW, Söyletir G, Doğanay M, editors. İnfeksiyon Hastalıkları ve Mikrobiyolojisi Cilt 1. Sistemlere Göre İnfeksiyonlar, İstanbul: Nobel Tıp Kitapevi; 2002.p.1059-64.
2. Dimitrov TS, Udo EE, Emara M, Awni F, Passadilla R. Etiology and antibiotic susceptibility patterns of community-acquired urinary tract infections in a Kuwait hospital. Med Princ Pract 2004; 13(6): 334-9. [CrossRef]
3. Foxman B. Epidemiology of urinary tract infections: incidence, morbidity, and economic costs. Dis Mon 2003; 49(2): 53-70. [CrossRef]
4. Mazzulli T. Resistance trends in urinary tract pathogens and impact on management. J Urol 2002; 168(4): 1720-2. [CrossRef]
5. Sobel JD, Kaye D. Urinary tract infections. In: Mandell GL, Bennett JE, Dolin R (editors). Principles and Practice of Infectious Diseases. 6th ed. New York: Churcill Livingstone; 2005.p.875-905.
6. Sucu N, Boz G, Bayraktar Ö, Çaylan R, Aydın K, Köksal İ. Üropatojen Escherichia coli suşlarının antibiyotik duyarlılıklarının yıllar içerisindeki değişimi. Klimik Dergisi, 2004; 17(2): 128-31.
7. Ağca H, Toklu GD. İdrar örneklerinden izole edilen bakteriler ve antibiyotik duyarlılıkları. J Clin Anal Med 2013; 4(1): 30-3. [CrossRef]
8. Tuncer İ. Antibiyotik direnç mekanizmaları. XXIX. Türk Mikrobiyoloji Kongresi; Antalya; 2000.p.213-9.
9. Öztürk Mİ, Koca O, Kalkan S, Kaya C, Karaman Mİ. Üroloji kliniklerinde görülen patojenlere karşı antimikrobiyal direncin güncel durumu. Türk Üroloji Dergisi 2008; (3): 363-7.
10. Akata F. Üriner sistem infeksiyonlarında uygun antibiyotik kullanımı. Klimik Dergisi 2001; 14(3): 114-23.
11. Hryniewicz K, Szczypa K, Sulikowska A, Jankowski K, Betlejewska K, Hryniewicz W. Antibiotic susceptibility of bacterial strains isolated from urinary tract infections in Polan. J Antimicrob Chemother 2001; 47(6): 773-80. [CrossRef]
12. Demirtürk N, Demirdal T, Eldemir H, İnce R, Altındiş M. İdrar örneklerinden izole edilen bakterilerin antibiyotiklere duyarlılıkları. Türk Mikrobiyol Cem Derg 2005; 35(2): 103-6.

13. Temiz H, Akkoç H, Gül K. Laboratuarımızda idrar kültürlerinden izole edilen gram negatif bakterilerde antibiyotiklere direnç. Dicle Tıp Dergisi 2008; 35(4): 234-9.
14. Yılmaz E, Özakın C, Sınırtaş M, Gedikoğlu S. Uludağ Üniversitesi Tıp Fakültesi Bakteriyoloji Laboratuvarı›nda 1999-2002 yılları arasında idrar örneklerinden izole edilen mikro-organizmalar ve antibiyotik duyarlılıkları. İnfeksiyon Dergisi 2005; 19(1): 91-6.
15. Rifaioğlu MM, Yıldırım A, Başok EK, Keskin SK, Özgüneş N, Tokuç R. Son dört yıl içerisinde idrar kültürlerinden izole edilen bakterilere karşı gelişen antibiyotik direncindeki değişim. Turkish J Urology 2009; 35(3): 201-9.
16. Urbarlı A, Arı A, Erdenizmenli M, Fidan N, Özgenç O. İdrar örneklerinden soyutlanan Gram-negatif bakteriler ve antibiyotik direnç oranları. İnfeksiyon Dergisi 2001; 15(2): 249-53.
17. Söyletir G, Günalp A. İdrar yolu enfeksiyonlarından izole edilen E.coli'lerin çeşitli antibiyotiklere duyarlılıkları ve bu enfeksiyonlarda metabolik defektli suşların rolü. Mikrobiyol Bul 1985; 19(4): 210-7.
18. Yaşar KK, Pehlivanoğlu F, Şengöz G. Alternatif tedavi seçeneği olarak fosfomisinin komplike üriner sistem infeksiyonlarından izole edilen GSBL pozitif Escherichia coli suşlarına etkinliği. ANKEM Derg 2011; 25(1): 12-6.
19. Kaya O, Akçam FZ, Uyar C, Demir C, Yaylı G. 2000-2004 yılları arasında izole edilen üropatojen Escherichia coli suşlarında artan antibiyotik direnci. S.D.Ü. Tıp Fak Derg 2006; 13(4): 22-6.
20. Bayraktar B, Özcan N, Borahan S, Başarı F, Bulut E. Yatan ve ayaktan hastalardan izole edilen üriner sistem infeksiyonu etkeni gram negatif çomaklarda antibiyotiklere direnç. ANKEM Derg 2004; 18(3): 137-40.
21. Kurutepe S, Surucuoğlu S, Sezgin C, Gazi H, Gülay M, Özbakkaloğlu B. Increasing antimicrobial resistance in Escherichia coli isolates from community-acquired urinary tract infections during 1998-2003 in Manisa, Turkey. Jpn J Infect Dis 2005; 58(3): 159-61.
22. Linhares I, Raposo T, Rodrigues A, Almeida A. Frequency and antimicrobial resistance patterns of bacteria implicated in community urinary tract infections: a ten year surveillance study (2000-2009). BMC Infect Dis 2013; 13: 19. [CrossRef]
23. Zhanel GG, Hisanaga TL, Laing NM, DeCorby MR, Nichol KA, Palatnik LP, et al. Antibiotic resistance in outpatient urinary isolates: final results from the North American Urinary Tract Infection Collaborative Alliance (NAUTICA). Int J Antimicrob Agents 2005; 26(5): 380-8. [CrossRef]
24. McGregor JC, Elman MR, Bearden DT, Smith DH. Sex and age specific trends in antibiotic resistance patterns of Escherichia coli urinary isolates from outpatients. BMC Family Practice 2013; 14: 25. [CrossRef]
25. Abdullah FE, Mushtaq A, Irshad M, Rauf H, Afzal N, Rasheed A. Current efficacy of antibiotics against Klebsiella isolates from urine samples-a multicentric experience in Karachi. Pak J Pharm Sci 2013; 26(1): 11-5.

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Swelling and Elongated Uvula with Unilateral Vocal Cord Paralysis after General Anesthesia

CASE REPORT

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ABSTRACT

Swelling and elongated uvula and vocal cord paralysis are very rare complications of general anesthesia. This report illustrates that these rare complications might occur together after general anesthesia. An adult male patient was operated for glomus tumor in left hand middle finger and six hours after the operation acute respiratory distress was diagnosed. There was no drug allergy in his medical history and breathing difficulty had not been observed after the operation which had been performed under general anesthesia ten years ago. Medical therapy with dexamethasone combined topical epinephrine was applied and complete recovery was obtained without surgery.

Key words: Anesthesia, general, intubation, uvula, vocal cord paralysis

INTRODUCTION

Complications of endotracheal intubation (ETI) includes laryngeal edema, sore throat, swallowing difficulty, vocal cord paralysis, laryngeal ulcer, uvular edema or necrosis and infection, however both of uvular edema and vocal cord paralysis are very rare (1, 2). Swelling and elongated uvula may cause a life-threatening airway obstruction which has to be treated quickly. In this report, medical treatment of uvular edema with unilateral vocal cord paralysis after general anesthesia is presented.

CASE REPORT

A 42-year-old man admitted to the Hand Surgery Unit with complaints of unbearable pain in his left middle finger, which aggravated by cold or by touching, continued for ten months. On his examination, the nail bed was pale and swollen. A hand magnetic resonance imaging (MRI) detected a radiopaque mass 3 mm in diameter under the nail bed. The lesion was diagnosed as a glomus tumor and an operation was suggested.

His preopreative physical status was ASA-I and his airway was assessed as Mallampati Class-I. The body-mass index was 23.35 kg/m^2. The patient was a non-smoker and his medical history was unremarkable except an operation for acute appendectomy ten years ago.

The operation was performed under general anesthesia for one hour. No premedication was used. A 20 gauge anjiocut was inserted and serum physiologic was infused throughout the surgery. Anesthesia was induced with fentanyl 2 µg.kg^{-1} *i.v.*, propofol 2.5 mg.kg^{-1} (Propofol 1% Fresenius, Kabi, Australi, GmbH) in a dose of adequate to block verbal response. Atracurium 0.5 mg.kg^{-1} was administered to facilitate the orotracheal intubation. A size 8.0 endotracheal tube (ETT) was used for intubation. The patient was manually ventilated and anesthesia was maintained with a mixture of 50% oxygen/air and 1-1.5% end-tidal sevoflurane. There was no important problem about anesthesia during the operation. Intubation and extubation were done without any difficulty but before extubation the back of throat was suctioned roughly. There was no trouble after extubation and the patient was comfortable in the recovery room. During the observation half an hour after the surgery only complaint was sore throat and no allergic reaction, no rash or respiratory distress were observed and vital signs were unchanged. The signs of serious airway obstruction, however, were observed, such as fear of death, gagging and choking at six hour after the operation. An epyglottical edema was suspected and arterial blood-gasses were examined at first, however, elongated and swelling uvula was observed and hoarseness was recognized on physical examination (Figure 1). The oxygen saturation and P_{CO2} were measured as 87% and 50 mmHg, respectively. Then supplemental oxygen (2.5 L/min) via nasal canule, topical epinephrine and 8 mg. *i.v* dexamethasone were administered. The saturation improved to 98% and P_{CO2} decreased to 42 mmHg and symptomatic relaxation was obtained in one hour.

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A unilateral vocal cord paralysis was diagnosed with fiber optic laryngoscope and it was related to hoarseness and breathless. The right vocal cord paralysis clinic type was assessed as cadaveric type and it is occurred when recurrent laryngeal nerve is damaged (Figure 2). MRI did not show any mass or tumor causing to vocal cord paralysis in head, neck or thorax.

The patient was hospitalized one more day and i.v. dexamethasone and topical epinephrine administration again at the twelve hour after the first medical administration. By the next day, significant symptomatic relief and reduction of uvular size were observed. Only complaint was hoarseness and it had been kept on following two months.

DISCUSSION

Swelling and elongated uvula is a rare complication of general anesthesia, on the other hand, it was also reported after regional anesthesia (2, 3). The reasons of uvular edema such as hereditary angioneurotic edema, irritant inhalation and allergy except infection can also cause Quincke's edema (4). In this case, possible reasons of uvular edema are direct trauma of endotracheal tube (ETT), displacement of ETT then pressure on uvula or suctioning trauma.

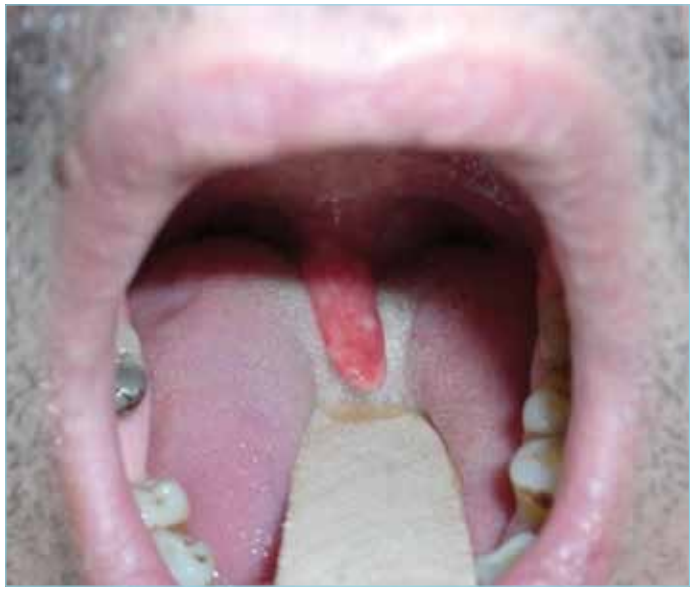

Figure 1. Swelling and elongated uvula was seen at six hour after general anaesthesia

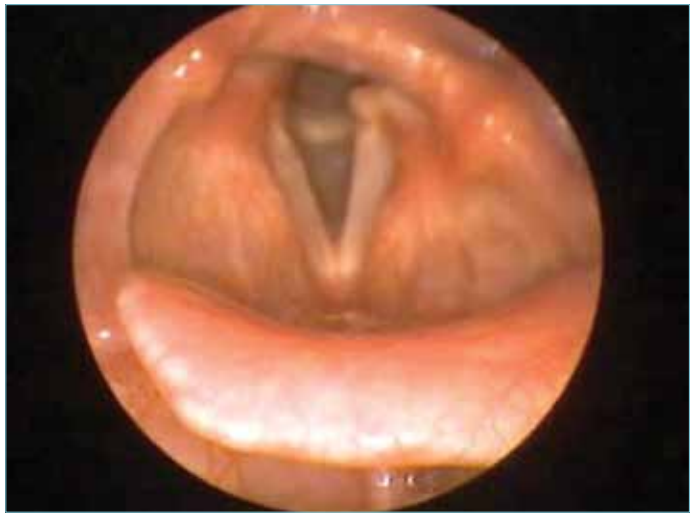

Figure 2. Paralytic right vocal cord in intermediate position was diagnosed by fiberoptic laryngoscope

Vocal cord paralysis is also another rare complication of general anesthesia and most usually seen in children (1). Major symptoms of vocal cord paralysis are hoarseness and respiration difficulty. Possible reasons include hard intubation, malposition of the ETT, surgical trauma, using big size ETT or laryngeal mask, nerve traction, accompanied infection, over inflated cuff pressure on the vocal cord (1). These traumas might be harmful for anterior branch of recurrent laryngeal nerve, tube cuff pressure compress the nerve against the posteromedial aspect of thyroid cartilage and it might cause vocal cord paralysis and sometimes differential diagnosis between nerve injury and arytenoid dislocation needs additional imagine scans, especially a neck computerized tomography (5, 6).

To the best of our knowledge, while vocal cord paralysis and uvular edema after general anesthesia had been reported separately however cooccurrence of these complication had not been reported. Herein we present the first case complicated with vocal cord paralysis and uvular edema after general anesthesia. Cooccurrence of these complications requires a life-threatening emergency and carefully treatment.

Epinephrine causes bronchodil ation and decreases serous secretion in upper and lower airway (4, 6). Steroids prevent to mucosal edema by increasing capillary permeability and also have anti-inflammatory effects (6). Dexamethasone has long half-life and its anti-inflammatory effect is very strong and it is still essential therapy for uvular edema (7). Diphenhydramine was another option, however, since allergic reaction was not considered, diphenhydramine was not given (4, 5). When uvular edema can be related with drug allergic reactions after anesthesia, diphenhydramine can be used (7).

CONCLUSION

We conclude that ETI can be cause of life –threatening respiratory obstruction due to uvular edema and unilateral vocal cord paralysis in rarely. Respiratory distress occurred a few hours after the operation is required upper airway examination. Oral examination simply reveals a uvular edema but if there is a suspect about vocal cord paralysis bronchoscopy should be done. Conservative treatment can be enough for the treatment but surgery should be in mind if medical therapy insufficient.

Informed Consent: Written informed consent was obtained from the patients who participated in this study.

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REFERENCES

1. Salem MR, Wong AY, Barangan VC, Canalis RF, Shaker MH, Lotter AM. Postoperative vocal cord paralysis in paediatric patients. Reports of cases and a review of possible aetiological factors. Br J Anaesth 1971; 43(7): 696-700. [CrossRef]
2. Harris MA, Kumar M. A rare complication of endotracheal intubation. Lancet 1997; 350(9094): 1820-1. [CrossRef]
3. Neustein SM. Acute uvular edema after regional anesthesia. J Clin Anesth 2007; 19(5): 365-6. [CrossRef]
4. Welling A. Enlarged uvula (Quincke's Oedema)--a side effect of inhaled cocaine? -A case study and review of the literature. Int Emerg Nurs 2008; 16(3): 207-10. [CrossRef]
5. Kashyap SA, Patterson AR, Loukota RA, Kelly G. Tapia's syndrome after repair of a fractured mandible. Br J Oral Maxillofac Surg 2010; 48(1): 53-4. [CrossRef]
6. Brimacombe J, Clarke G, Keller C. Lingual nerve injury associated with the ProSeal laryngeal mask airway: a case report and review of the literature. Br J Anaesth 2005; 95(3): 420-3. [CrossRef]
7. Mallat A, Roberson J, Brock-Utne JG. Preoperative marijuana inhalation--an airway concern. Can J Anaesth 1996; 43(7): 691-3. [CrossRef]

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Dissociative Identity Disorder Presenting as a Suicide Attempt or Drug Overdose: A Case Report

CASE REPORT

Abdullah Akpınar, Arif Demirdaş

ABSTRACT

The major feature of dissociative identity disorder is the existence of at least two different identities that alternately control a person's behavior. Dissociative identity disorder is known as a rare disorder due to underdiagnosis and misdiagnosis. One of the presenting symptoms in dissociative identity is a suicide attempt. In this case, dissociative identity disorder and overdose drug intake, which emerges during the treatment of depression with fluoxetine, is identified. With regard to this complex case, the issues of overdose drug intake, suicide attempt, depression, antidepressant-associated suicide or side effects in dissociative disorder and their relations with each other will be discussed.

Key words: Dissociative identity disorder, suicide, drug intoxication

INTRODUCTION

Dissociative identity disorder is known as a rare disorder due to its being underdiagnosed and misdiagnosed (1). The major feature of Dissociative Identity Disorder (DID) is the existence of at least two different identities that alternately control a person's actions. DID is also strongly linked to severe experiences of early childhood trauma (2). Suicide attempt is one of the presenting symptom in DID (3, 4). Suicide is sometimes a complicating condition in psychiatric practices. Suicide rates decrease after the treatment of depression but rarely suicide emerges related to antidepressant treatment in patients with depression that it is generally seen in adolescents and it seems to be associated to bipolarity (5-8).

Adjunctive antidepressants were accepted as a treatment option for DID in clinical practice (9). Despite extensive use of antidepressants in clinical practice, the unfavorable effects of antidepressant on dissociative identity has not been determined.

In this case we determined a dissociative identity and high dose drug intake which emerged during the fluoxetine therapy in treatment of depression. With the regard to this complex case, the issues of dissociative identity, high dose drug intake, suicide attempt, depression, antidepressant associated suicide or side effects and their relations will be discussed in dissociative identity disorder.

CASE REPORT

An 18 year-old student was found by her friends at the student dormitory unconscious and close to the drugs. She had been discharged from hospital after three days of intensive care treatment. Physical examination, laboratory tests, and cranial computer tomography did not reveal any pathology. She was referred to the psychiatry outpatient clinic. In her interview it was understood that she responded to the treatment of fluoxetine 20 mg/day, which was begun a month previously with major depression symptoms in the third week of treatment, and the treatment of fluoxetine 20 mg/day was continued. She reported that she had no idea or plan for suicide before the high-dose drug intake and she did not know why she acted in this way. She said that before intensive care at the hospital she remembered things in a very confused way and like a dream, she felt she was like a child, she played with candies of various colors (probably drugs), and then, she ate all of the candies. She stated that she did not know why she was in the hospital when cooperation was built. When it was reported that she took drugs, she responded that they were candies, not drugs, and she stated that she was confused with this situation. Additional drug, alcohol or other material intake was not reported. No hypermanic or manic episode in the past was identified. No suicide history in the past or in the family was found. No psychiatric disorder was found in the family. It was stated in the history that there had been several months of abuse by a person when she was 5-6 years of age. She identified herself as more childlike and immature compared to her peers. No additional story related to the existence of an additional identity or other dissociative cases, was recorded from her. Informed consent was obtained from patients who participated in this case. The mental status examination

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found that she was conscious, cooperative, full oriented, affect and mood; euthymic, physiological symptoms of fatigue, lack of energy. Hamilton Depression Rating Scale's was detected as 6 point.

DISCUSSION

Dissociative identity disorders are either underdiagnosed or misdiagnosed secondary to the mistaken belief that dissociative disorders are rare (1). Sar et al. (10) found that DID constituted 6 % of patients among emergency psychiatric admissions. DID generally has a reported history of childhood abuse, with the frequency of sexual abuse being higher. Patients who have been diagnosed with DID frequently report chronic suicidal feelings with some attempts (11). In this case; the patient had sexual abuse, existence of a different identity (child identity was eating the candies), drug overdose due to child identity (appears to be a suicide) and the proper diagnosis was DID. Psychiatric examination of the patient revealed that she had a different identity, and the act was not a suicide attempt but that it was a drug overdose. This case leads us to suggest that patients with a suicide attempt or drug overdose condition might have comorbid dissociative experiences, which cannot be identified easily.

In the differential diagnosis, several questions come to mind with regards to the case due to complication of this case's intake overdose drug. Was high dose drug intake associated to antidepressants or a depressive condition? Was it associated to the underlying bipolar disorder (5-8). Was the high dose drug intake related to antidepressant side effect; such as dysphoria, akathisia, anxiety, impulsiveness and agitation (12). It was found that major depression has begun a month previously in the patient, she responded to the anti-depressant treatment and no side effect related to the drug emerged in this period. It was found that there was no suicide idea or plan before present situation. No evidence of bipolarity was found in the past or at present. The patient did not understand why she had acted in this way. It was evaluated that the interview was reliable. No case or possibility of stigmatization with relation to drug intake was found. The case of abuse was also detected in this case. Taking into account all of these findings, it is thought that there had been drug (candy) intoxication related to dissociative identity (child type) which emerged during the treatment of fluoxetine 20/day.

Despite extensive use of antidepressants in the clinical practice of DID (10), the unfavorable effects of antidepressant on dissociative ıdentıty have not been determined. In only one study, dissociative disorder emerged following an electroconvulsive therapy during the depression treatment (13). Our observation (dissociative identity emerged during the treatment of fluoxetine) was that it might be determined by coincidence or fluoxetine may have a trigger effect on dissociative identity in a person who has a history of sexual abuse. So it is difficult to make general statements about this observation.

Suicide is one of the most observed symptoms in the DID and suicide rates were reported as 70-72% in DID and also the presence of a dissociative disorder was the strongest predictor of a suicidal tendency (3, 4, 11). Taking into account this case, the cases of suicide in DID's should be evaluated with care, and it should be discussed whether the case is not a suicide but another act (like the act of eating candies in a child identity) appearing to be a suicide related to a dissociative identity. Unresolved suicide cases in DID consequently will be at greater risk of recurrent suicidal behavior.

CONCLUSION

This case has several important implications. Clinically, the case points to the risk of drug overdose due to child identity which accompanies dissociative identity disorders, suggesting that greater efforts should be made to screen for this disorder and highlighting the need for vigilant attention to safety issues when working with dissociative identity patients. With better understanding of these cases, it will be possible to take preventive measures and provide treatments towards possible repeater acts of the patient in the future. Incorporation of this new finding into everyday (suicide with DID patients) emergency psychiatry practice is urgently needed.

Informed Consent: Written informed consent was obtained from patients who participated in this case.

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Authors' contributions: Conceived and designed the experiments or case: AA. Performed the experiments or case: AA, AD. Analyzed the data: AA, AD. Wrote the paper: AA. All authors have read and approved the final manuscript.

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REFERENCES

1. Coons PM. The dissociative disorders. Rarely considered and underdiagnosed. Psychiatr Clin North Am 1998; 21(3): 637-48. [CrossRef]
2. Kaplan and Sadock's Synopsis of Pscychiatry. Behavioral Sciences/Clinical Psychiatry. Lippincott Williams Wilkins, Ninth Edition, 2003; 1: 680-4.
3. Putnam FW, Guroff JJ, Silberman EK, Barban L, Post RM. The clinical phenomenology of multiple personality disorder: review of 100 recent cases. J Clin Psychiatry 1986; 47(6): 285-93.
4. Ross CA, Norton GR. Suicide and parasuicide in multiple personality disorder. Psychiaty 1989; 52(3): 365-71.
5. Rihmer Z. Suicide risk in mood disorders. Current Opinion in Psychiatry 2007; 20(1): 17-22. [CrossRef]
6. Zisook S, Trivedi MH, Warden D, Lebowitz B, Thase ME, Stewart JW, et al. Clinical correlates of the worsening or emergence of suicidal ideation during. SSRI treatment of depression: an examination of citalopram in the STAR-D study. J Affect Disord 2009; 117(1-2): 63-73. [CrossRef]
7. Friedman RA, Leon AC. Expanding the black box-depression, antidepressants, and the risk of suicide. N Engl J Med 2007; 356(23): 2343-6. [CrossRef]
8. Rihmer Z, Gonda X. Antidepressant-resistant depression and antidepressant-associated suicidal behaviour: the role of underlying bipolarity. Depress Res Treat 2011; 2011: 906462.
9. Sno HN, Schalken HFA. Dissociative Identity Disorder: diagnosis and treatment in the Netherlands. Eur Psychiatry 1999; 14(5): 270-7. [CrossRef]
10. Sar V, Koyuncu A, Ozturk E, Yargic LI, Kundakci T, Yazici A, et al. Dissociative disorders in the psychiatric emergency ward. Gen Hosp Psychiatry 2007; 29(1): 45-50. [CrossRef]
11. Foote B, Smolin Y, Neft DI, Lipschitz D. Dissociative disorders and suicidality in psychiatric outpatients. J Nerv Ment Dis 2008; 196(1): 29-36. [CrossRef]
12. Mihanovic M, Restek-Petrovic B, Bodor D, Molnar S, Oreskovic A, Presecki P. Suicidality and side effects of antidepressants and antipsychotics. Psychiatr Danub 2010; 22(1): 79-84.
13. Zaidner E, Sewell RA, Murray E, Schiller A, Price BH, Cunningham MG. New-onset dissociative disorder after electroconvulsive therapy. J ECT 2010; 26(3): 238-41. [CrossRef]

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A Very Rare Case of a Bronchogenic Cyst Localized on the Scapular Region

CASE REPORT

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ABSTRACT

Cutaneous bronchogenic cysts (CBC) are rare lesions that originate from the primitive tracheobronchial tree. Lesions that are located subcutaneously over the scapula are the rarest type of cutaneous bronchogenic cyst. This is the 14th case of cutaneous bronchogenic cyst in the literature. In this study, we aimed to investigate those CBC located to the scapular region and review the reported cutaneous bronchogenic cyst cases in the literature.

Key words: Cutaneous, bronchogenic cyst, scapula

INTRODUCTION

Cutaneous bronchogenic cysts (CBC) are rare lesions that originate from the primitive tracheobronchial tree. Bronchogenic cysts are generally located generally intrapulmonary; the most common extrapulmonary location is the mediastinum. Other extrapulmonary sites are the lingua, intra-abdominal and cutaneous regions (1). Lesions located subcutaneously in the capular area are the rarest type of CBC (2, 3).

We report a bronchogenic cyst localized subcutaneously in the scapular region and review its clinical properties and previous cases in this report.

CASE REPORT

A four-year-old boy was brought to our clinic a few months ago with a growing swelling on his back on his right scapula. The swelling was painless and 2 x 2 cm in dimension. All the other system examinations were normal. Upon USG examination the swelling was reported as a cystic lesion with a highly dense fluid content, 20 x 11 mm in dimension and 2 mm from the epidermal surface in depth. The patient was then evaluated by CT scan. There was a mass, 26 x15 mm in dimension, on the right scapular region located subcutaneously close to the bone structures and there was no enhancement after intravenous radioopaque solution injection (Figure 1). We operated on the patient with a pre-diagnosis of cystic lesion. The swelling was excised through a transverse incision. The dimensions of the swelling were 20 x15 mm. There was a connection to the spine of scapula via a fibrotic band. The patient was discharged after a three-hour observation. In the histopathological examination, a pseudostratified ciliated epithelium-lined cyst wall was seen, with lymphoid cell infiltration with germinal centres under the epithelium (Figure 2). Thus, the swelling was reported as a bronchogenic cyst. His postoperative follow-up period was uneventful.

DISCUSSION

Cutaneous bronchogenic cysts are very rare masses mostly seen in childhood because of their congenital origin. The number of described cases of CBC in the literature is approximately 70. The most common locations for these lesions are neck, the suprasternal notch and presternal and scapular areas (4).

There are two main embryologic theories for the development of CBC. The primitive tracheal structures develop at the fifth week of gestation. The left and right mesenchymal plates of the sternum close at the ninth week. In the first theory it is considered that the bronchogenic cyst, which already exists, leaves the thorax during sternal closure and migrates to the cutaneous region (5). The cyst simply arises abnormally from the developing tracheal bud during closure of the mesenchymal plates in the other theory (6, 7). There is no connection between the cyst and the thoracal cavity in CBC cases, except in a few cases (3). There was a connection of the CBC to the scapula in two patients who had scapular CBC (2, 8). This patient is the third patient identified with a connection to scapula. As the lesions are mostly solitary and unconnected in most cases, the second theory (the pinch-off theory) can

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explain the formation of the cyst in most of cases. So the proper mechanism has not yet been determined.

There is no specific imagining method for diagnosis. Ultrasonography may be preferred to bring out characteristics of the cyst. Fistulography is an alternative diagnostic tool if there is a tract. X-ray, CT and MRI are other imagining methods for diagnosis (9).

The pathological diagnosis can be made by the demonstration of one or more tracheobronchial structures in the cyst wall. Pseudostratified ciliated columnar or cuboidal cells, hyaline cartilage, smooth muscle cells, elastic fibres, fibrous tissues, neural cells and seromucous glands could be seen in most cases (6, 8). The surface epithelium may be changed to squamous epithelium in 2% of CBC cases and lymphoid follicles may be seen due to chronic infections (8). The diagnosis in our patient was confirmed with the demonstration of pseudostratified ciliated columnar epithelium in the wall of the cyst (Figure 2).

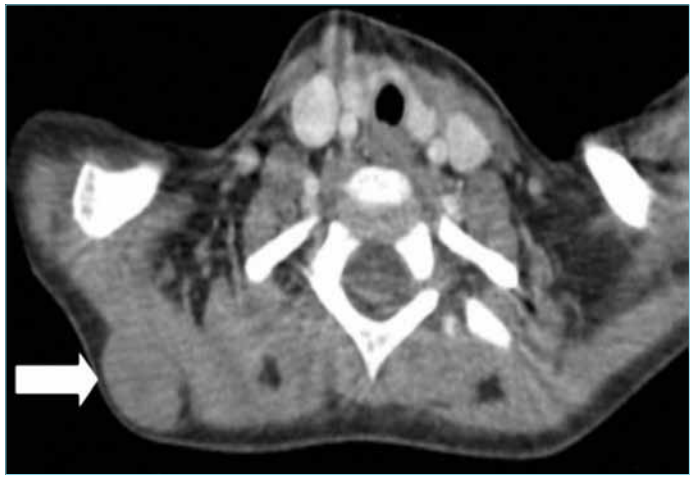

Figure 1. View of cystic lesion on CT (Arrow shows the lesion)

Only 14 of 70 CBC cases were located in the scapular area. These cases are shown in table 1. Three of these patients were female. Thus it could be said that this lesion has male dominance, like other locations of CBC. Most of the patients were 4 years of age or younger. Either a growing or non-growing mass draining fluid is a common complaint of patients, or there may be no complaint

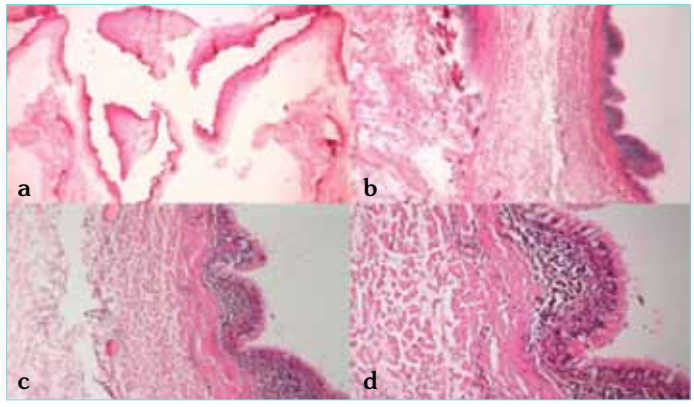

Figure 2. Bronchogenic cyst. Panoramic view of surgically excised material (a), closer view of the epithelial lining (right) and connective tissue in the subepithelial layer (b), much closer view of the pseudostratified epithelial cells and lymphoid tissue beneath the epithelium (c), ciliated respiratory epithelium and goblet cells between the pseudostratified cylindrical epithelial cells (d), (Hematoxylin-eosin, x10 (a), x40 (b), x100 (c), x200 (d), respectively)

Table 1. Details of the scapular CBC patients in the literature

Case no	Sex	Age at presentation	Symptoms	Histopathological findings	Reference
1	Male	4 months	Mass	PCCE and SMC	Pul and Pul (3)
2	Male	10 years	Mass	PCCE and lymphoid aggregates	Miller and Tyler (7)
3	Male	8 months	Asymptomatic	NS	Fraga et al. (8)
4	Male	30 months	Asymptomatic	NS	Fraga et al. (8)
5	Male	1 year	Asymptomatic	NS	Fraga et al. (8)
6	Male	4 years	Mass	PCCE, GC, SMC and mucous glands	Yu et al. (14)
7	Male	46 years	Growing mass	PCCE, sebaceous glands, SSE and malignant melanoma	Tanita et al. (11)
8	Male	Newborn	Growing mass	PCCE	Tressner et al. (15)
9	Male	1 year	Growing mass	PCCE, GC and SMC	Jona (16)
10	Male	4 years	Mass	SSE alternating with PCCE, GC, sebaceous glands and SMC	Putte et al. (17) Van der
11	Female	8 years	Asymptomatic	PCCE, GC and mucus secreting glands	Manconi et al. (18)
12	Female	1 year	Draining sinus	PCCE alternating with SSE, mucous glands	Özel et al. (10)
13	Female	4 years	Mass, draining fluid	PCCE, SMC and seromucinous glands	Blanchard et al. (9)
14	Male	4 years	Growing mass	PCCE, lymphoid cell infiltration	Current case

PCCE: Pseudostratified ciliated columnar epithelium, NS: Not specified, SMC: Smooth muscle cells, SSE: Strafied squamous epithelium, GC: Goblet cells

related to this disease. Our patient suffered from a growing mass (Table 1).

The treatment method for CBC is surgical excision. There is a potential risk of infection and malignant degeneration (10, 11). Lymphangioma, epidermal, sebaceous and aneurysmal bone cysts should be considered in the differential diagnosis for CBC (6, 8, 10, 12, 13).

It can be said, in conclusion, that bronchogenic cysts should be kept in mind if there is a cutaneous cystic lesion, especially in children, and must be excised surgically.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of University of Erciyes.

Informed Consent: Written informed consent was obtained from patient's parents who participated in this study.

Peer-review: Externally peer-reviewed.

Authors' contributions: Conceived and designed the experiments or case: MG, MK. Performed the experiments or case: MG, MK. Analyzed the data: MG, OK, AY. Wrote the paper: MG. All authors read and approved the final manuscript.

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REFERENCES

1. Özel SK, Tuğtepe H. A very rarely seen congenital anomaly: presternal bronchogenic cyst. Fırat Tıp Dergisi 2001; 6(3): 490–2.
2. Das K, Jackson PB, D'Cruz AJ. Periscapular bronchogenic cyst. Indian J Pediatr 2003; 70(2): 181–2. [CrossRef]
3. Pul N, Pul M. Bronchogenic cyst of the scapular area in an infant: case report and review of the literature. J Am Acad Dermatol 1994; 31(1): 120-2. [CrossRef]
4. Zvulunov A, Amichai B, Grunwald MH, Avinoack I, Halevy S. Cutaneous bronchogenic cyst: delineation of a poorly recognized lesion. Pediatr Dermatol 1998; 15(4): 277-81. [CrossRef]
5. Başaklar C, Sönmez K. Yenidoğanın Üst solunum yolu tıkanıklıkları ve solunum desteği. In A. Can Başaklar, Editor. Bebeklerin ve Çocukların Cerrahi ve Ürolojik Hastalıkları. Ankara: Palme Yayıncılık; 2006. p.247-71.
6. Magnussen JR, Thompson JN, Dickinson JT. Presternal bronchogenic cysts. Arch Otolaryngol 1977; 103(1): 52-4. [CrossRef]
7. Miller OF 3rd, Tyler W. Cutaneous bronchogenic cyst with papilloma and sinus presentation. J Am Acad Dermatol 1984; 11(2): 367-71. [CrossRef]
8. Fraga S, Helwig EB, Rosen SH. Bronchogenic cyst in the skin and subcutaneous tissue. Am J Clin Pathol 1971; 56(2): 230-8.
9. Blanchard M, Kadlub N, Haddad D, Cassier S, Boudjemaa S, Vazquez MP, et al. Scapular cystic lesion: Bronchogenic cyst, a rare diagnosis. Journal of the Saudi Society of Dermatology & Dermatologic Surgery 2011; 16(1): 19-20. [CrossRef]
10. Özel SK, Kazez A, Köseoğulları AA, Akpolat N. Scapular bronchogenic cysts in children: case report and review of the literature. Pediatr Surg Int 2005; 21(10): 843-5. [CrossRef]
11. Tanita M, Numagami KK, Ogoshi K, Suzuki T, Tabata N, Kudoh K, et al. Malignant melanoma arising from cutaneous bronchogenic cyst of the scapular area. J Am Acad Dermatol 2002; 46(2 Suppl Case Reports): S19-21.
12. Narcı A, Şahin Ö, Şen TA, Özkaraca E, Çetinkurşun S. An unusual localization of a bronchogenic cyst: Cervical region-A case report. Int J Ped Otorhinolaryngol Extra 2009; 4(2): 56-8. [CrossRef]
13. Tandoğan R, Hücümenoğlu S, Benli T, Aydın E, Yücetürk A. Unusual causes of scapular clicking. Lymphangioma of the thoracic wall and aneurysmal bone cyst of the scapula. Arch Orthop Trauma Surg 1997; 116(8): 516-8.
14. Yu HJ, Kwon HM, Park JW, Hwang DK, Ahn DK, Park YW. A case of cutaneous bronchogenic cyst over the left scapula. J Dermatol 2001; 28(10): 572-5.
15. Tressner NJ, Dahms B, Berner JJ. Cutaneous bronchogenic cyst of the back: a case report and review of the literature. Pediatr Pathol 1994; 14(2): 207-12. [CrossRef]
16. Jona JZ. Extramediastinal bronchogenic cysts in children. Pediatr Dermatol 1995; 12(4): 304-6. [CrossRef]
17. van der Putte SCJ, Toonsra J. Cutaneous 'bronchogenic' cyst. J Cutan Pathol 1985; 12(5): 404-9. [CrossRef]
18. Manconi R, Bolla G, Pavon I. Cutaneous subcutaneous bronchogenic cyst of the back. a case report and review of the literature. Pediatr Med Chir 2003; 25(5): 364-6.

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Use of Tornus for a Lesion That is Easily Balloon Crossable but No Expandible Despite High Pressure

CASE REPORT

Ahmet Temiz[1], Mehmet Bostan[2]

ABSTRACT

Coronary angiography (CAG) was performed on a 78-year-old female patient due to class III angina. A calcified critical obstruction was demonstrated in the right coronary artery (RCA). An attempt at percutaneous transluminal coronary angioplasty (PTCA) failed to dilatate the lesion despite high balloon pressure. In a second attempt the lesion was dilatated with the balloon after implementing a tornus penetration device, and then a stent was implanted. A dissection occurred after the stent implantation and it was treated with another stent. The treatment of lesions that cannot be dilatated using conventional PTCA techniques and the role of the tornus penetration device in such cases are discussed.

Key words: Percutaneous transluminal coronary angioplasty, coronary artery stenosis, calcification

INTRODUCTION

Since the first percutaneous coronary intervention (PCI) was performed, the techniques and technology available for the procedures developed in parallel to their difficulties. One of the most common difficulties is calcified and non-expandable lesions (CNELs). These lesions are usually aged, and performing PCI on them may be complicated by insufficient expansion of the balloon, dissection, perforation and acute occlusion (1). If expansion of the lesion via balloon inflation is insufficient, cutting the balloon (1, 3-5), deploying a FX miniRAIL balloon (6) and rotablation (1, 7) are most often used to facilitate the procedure. The tornus is a penetration device developed for chronic total occlusions (CTOs) (1, 8-12) and there are limited data about its use in CNELs.

The tornus device was originally developed for CTOs when the smallest available balloon failed to cross the lesion. In such casees the problem was an inability to cross the lesion. A large sized non-compliant balloon could cross the lesion easily but couldn't dilate the lesion despite high inflation pressure. The use of tornus in this condition is not well studied and we report the first use of tornus in our laboratory.

CASE REPORT

A 78-year-old woman was referred to us with class III anginal chest pain and chest pain after meals. She had had an anterior myocardial infarction 20 months previously, which was successfully treated with streptokinase infusion and then stenting the left anterior descending (LAD) artery. She had a history of known hypertension for 10 years. She was on ramipril 10 mg, aspirin 100 mg, metoprolol 100 mg and atorvastatin 40 mg daily therapy. AN electrocardiogram revealed no specific abnormalities except a loss of R wave progression in leads V1 and V2. Echocardiography showed apical hypokinesis with an ejection fraction of 0.54, and mild aortic and mitral regurgitation. We planned coronary angiography for the patient and, as shown in figure 1, the coronary angiography revealed 99% stenosis in the proximal segment of the right coronary artery (RCA) (30–40% instent restenosis in mid LAD, 60% stenosis of the first diagonal ostium, 40% stenosis in the second diagonal artery and 30% stenosis in the obtus marginalis). We planned PCI for RCA after loading 600 mg clopidogrel and intravenous unfractioned heparin (100 IU per kg) lesion was crossed with 0.014 inch floppy guidewire. We used a 2.0x20 mm balloon first without success and then tried 2.5x20 and 2.5x12 mm non-compliant balloons at high inflation pressures (22 atm) but there was no change. Figure 2 illustrates a 3.25x12 mm non-compliant balloon at 22 atm that finally inflated. Unfortunately (as shown in figure 3) there was no change in the lesion at this point so we stopped the procedure and decided to use tornus at another time because it was not available in the moment. In the second procedure a 2.6F tornus (Asahi Intecc, Aichi, Japan) crossed the lesion easily with counterclockwise rotation in a few seconds and the lesion was degraded so we would be able to implant a stent. Figure 4 shows the vessel after using the tornus use. Next we implanted a 2.75x34 mm drug eluting stent at 20 atm inflation pressure. The stent was implanted with no residual stenosis but a dissection occurred

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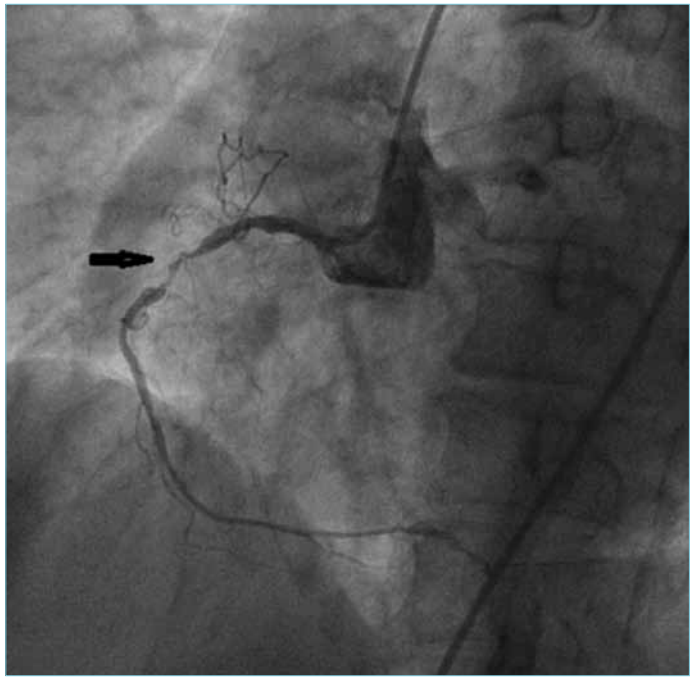

Figure 1. Right coronary angiogram at the left anterior oblique tube position. Arrow shows the irregularly shaped and calcified critical obstruction

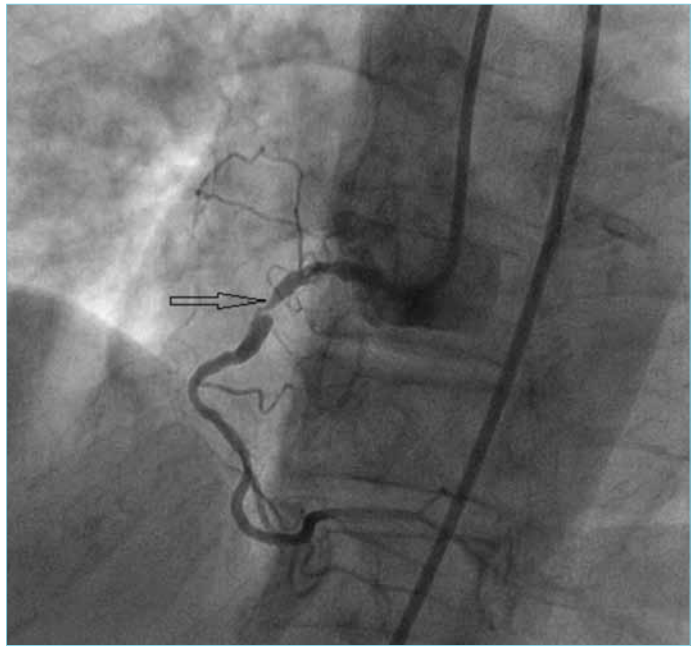

Figure 3. Right coronary angiogram after inflating a 3.25*12 mm non-compliant balloon up to 22 atm pressure at the lateral anterior oblique tube position. Arrow shows the tight lesion that is not dilated

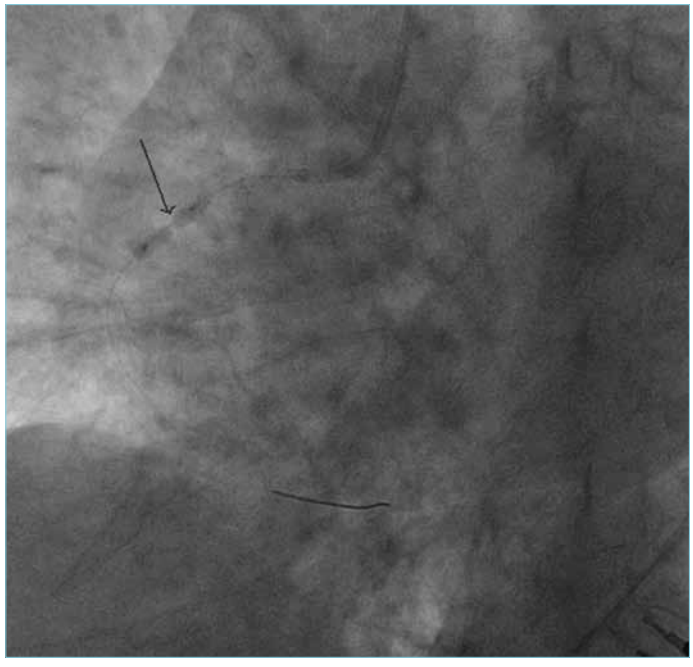

Figure 2. 3.25x12 mm non-compliant balloon inflated at 22 atm pressure in the right coronary artery. Arrow shows the notch on the balloon indicative of no expansion

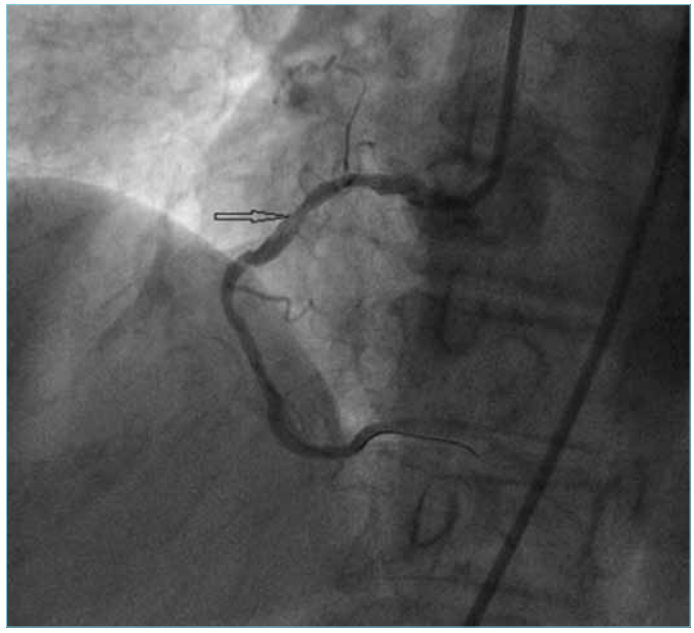

Figure 4. Right coronary angiogram at the left anterior oblique tube position after penetrating the lesion with the tornus device before stent implantation. Arrow shows the dilatated lesion after tornus use

from the proximal part of the stent to the RCA ostium. Figure 5 illustrates the dissection. We implanted a second drug eluting stent (2.75x16 mm) to overcome this problem and post-dilatation was then applied to the overlapping stent segments and RCA ostium with 2.75x18 mm and 3.25x15 mm non-compliant balloons. Finally we achieved Trombolysis In Myocardial Infarction (TIMI) III flow with no residual stenosis. Figure 6 shows the final angiography of the RCA. The patient was discharged from the hospital and at the first month followup she was free of angina.

DISCUSSION

Despite new strategies and technological developments, CNELs are still challenging problems. As compared with non-calcified lesions, the risk of complications or failure of the procedure are higher in

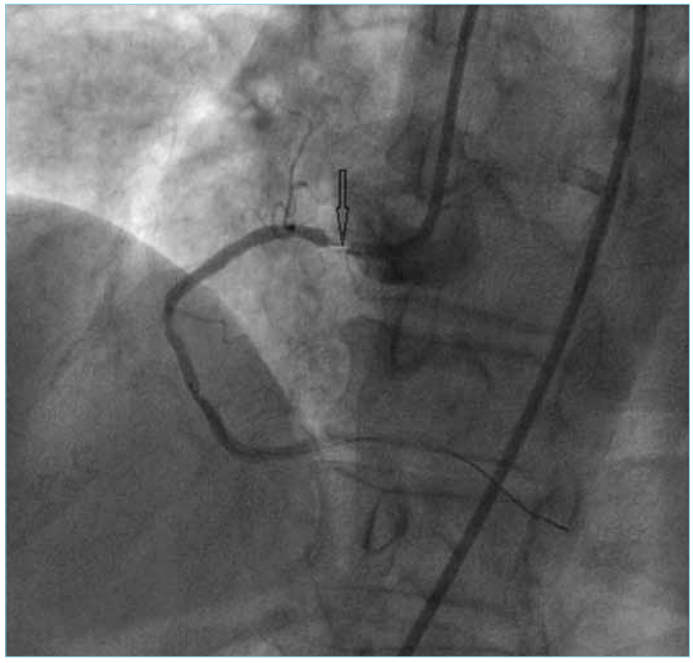

Figure 5. Right coronary angiogram at the left anterior oblique tube position after stent implantation. Arrow shows the dissection in the proximal right coronary artery

CNELs. Non-expandable lesions typically include heavy calcification and superficial circumferential calcification, but sometimes the calcification may be localized (1). If the stent is deployed before dilatation of the vessel it may cause stent thrombosis or restenosis due to insufficient expansion. The operator must be aware of the lesion's characteristics. In particular, radioopacities on the scan prior to contrast injection are warning clues about a lesion's expandability. Some investigators use intravascular ultrasound (IVUS) to further evaluate the calcifications. If the calcification is greater than 270˚ of vessel circumference they recommend the direct use of rotablation (1).

A cutting balloon, the FX MiniRAIL balloon and rotational atherectomy are techniques that are used to overcome CNELs (3-7). A cutting balloon consists of three microknifes and is effective in degrading plaque, but its high profile hinders its use in tortuous vessels (3-5). The FX MiniRAIL balloon system looks like a cutting balloon but it has two wires over the balloon instead of microknifes (3, 6). Rotablation atherectomy is mostly used in CNELs. The rotational atherectomy system abrades inelastic plaque inside the vessel into small particles. It requires a system that consists of an advancer, drive shaft, burr and a monitoring console (3, 7). Rotablation is the preferred procedure today and the European Society of Cardiology (ESC) guidelines recommend the use of rotablation in CNELs with class IC indication (2).

The tornus device was originally developed for CTOs (8-12) and has been used in CNELs, but data about its use in this context is insufficient to date, so its level of indication is class IIbC in the European Society of Cardiology (ESC) guidelines (2). Tornus and rotablation were compared in a small study regarding success rate, complications and procedure duration. Major and minor complications were the same but the device success rate was lower and procedure duration was longer with the tornus (10).

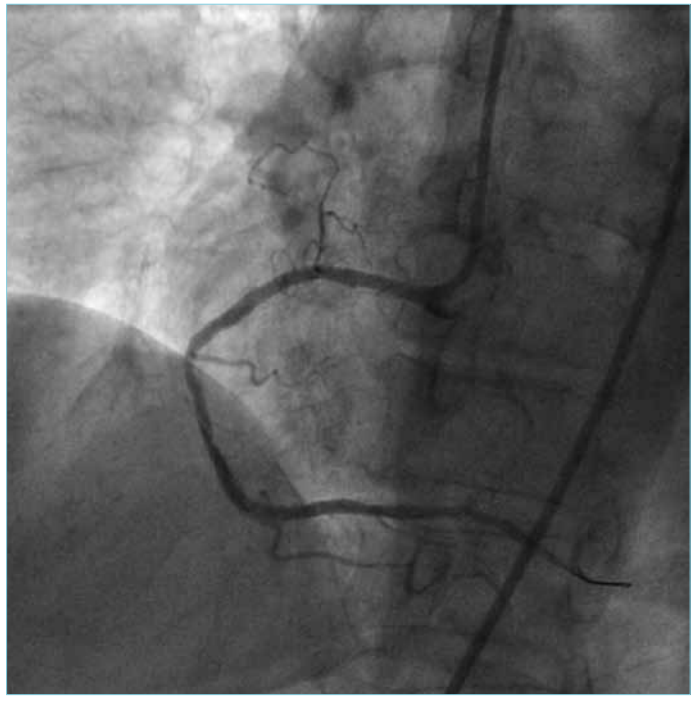

Figure 6. Final right coronary angiogram at the left anterior oblique tube position after stenting the dissection with another stent

In our case we used a tornus because of availability. The lesion was crossed in a few seconds, balloon dilatation was successful after tornus use and then a stent could be implanted. Dissection occurred proximal to the stent and was successfully treated with another stent. The main shaft of the tornus is a coreless stainless coil, with eight wires stranded in the coil in a right-handed fashion (clockwise) (8). It can cross through lesions easily with a counterclockwise rotation along with a guidewire. It is important to emphasise that while rotating the tornus the guidewire must be fixed and must not rotate with the tornus to avoid complications such as spiral dissection, rupture, device failure and acute vessel occlusion. Although we used the tornus properly, dissection still occurred proximal to the stent. The best therapy for dissection is stenting the dissected part of the vessel, as we did in our case.

CONCLUSION

Although the tornus was primarily developed for CTOs, which are impossible to cross with low profile balloons, it can also be used in conditions where the problem is a lesion that can easily be crossed but still cannot be dilatated.

Informed Consent: Written informed consent was obtained from the patient who participated in this study.

Peer-review: Externally peer-reviewed.

Authors' contributions: Conceived and designed the experiments or case: AT, MB. Performed the experiments or case: AT, MB. Analysed the data: AT. Wrote the paper: AT, MB. All authors have read and approved the final manuscript.

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REFERENCES

1. Colombo A, Stankovic G. Problem Oriented Approaches in Interventional Cardiology. 1st ed. Informa UK 81 ltd; 2007. p.73-9.
2. Wijns W, Kolh P, Danchin N, Di Mario C, Falk V, Folliguet T, et al. Guidelines on myocardial revascularization. The Task Force on Myocardial Revascularization of the European 83 Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). European 84 Heart Journal (2010) 31, 2501–55.
3. Moses JW, Carlier S, Moussa I. Lesion preparation prior to stenting. Rev Cardiovasc Med 2004; 5(Suppl 2): S16-21.
4. Lee MS, Singh V, Nero TJ, Wilentz JR. Cutting balloon angioplasty. J Invasive Cardiol 2002; 14(9): 552-6.
5. Ajani AE, Kim HS, Castagna M, Satler LF, Kent KM, Pichard AD, et al. Clinical utility of the cutting balloon. J Invasive Cardiol 2001; 13(7): 554-7.
6. Vitrella G, Sangiorgi G, Kornowski, Mosseri M, Almagor Y, Ischinger T, et al. FX MiniRAIL catheter usage for treatment 90 of de novo complex coronary lesions: results from the "OFFAR". J Interv Cardiol 2006; 19(3): 250-7. **[CrossRef]**
7. Moussa I, Di Mario C, Moses J, Reimers B, Di Francesco L, Martini G, et al. Coronary stenting after rotational atherectomy in calcified and complex 92 lesions. Angiographic and clinical follow-up results. Circulation 1997; 96(1): 128-36. **[CrossRef]**
8. Tsuchikane E, Katoh O, Shimogami M, Ito T, Ehara M, Sato H, et al. First clinical experience of a novel penetration catheter for 94 patients with severe coronary artery stenosis. Catheter Cardiovasc Interv 2005; 65(3): 368-73. **[CrossRef]**
9. Buller CE, Dzavik V, Carere RG, Mancini GB, Barbeau G, Lazzam C, et al. Primary stenting versus balloon angioplasty in occluded coronary 96 arteries: the Total Occlusion Study of Canada (TOSCA). Circulation 1999; 100(3): 236-42. **[CrossRef]**
10. Fang HY, Fang CY, Hussein H, Hsueh SK, Yang CH, Chen CJ, et al. Can a penetration catheter (Tornus) substitute traditional rotational 98 atherectomy for recanalizing chronic total occlusions? Int Heart J 2010; 51(3): 147-52. **[CrossRef]**
11. Reifart N, Enayat D, Giokoglu K. A novel penetration catheter (Tornus) as bail-out device after balloon 100 failure to recanalise long, old calcified chronic occlusions. EuroIntervention 2008; 3(5): 617-21. **[CrossRef]**
12. Liu R, Pershad A. Tornus catheter facilitated recanalization of chronic total occlusions--another niche device 102 for a difficult lesion subset. Indian Heart J 2008; 60(2): 155-7.

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Gastrointestinal Stromal Tumor in the Stomach Co-Existent with Renal Cell Carcinoma

CASE REPORT

Ebubekir Gündeş[1], Tevfik Küçükkartallar[1], Muzaffer Haldun Çolak[1], Adil Kartal[1], Hacı Hasan Esen[2]

ABSTRACT

Gastrointestinal stromal tumours (GIST) are the most common mesenchymal tumours of the gastrointestinal system (GIS). They may co-exist with renal cell cancers (RCC). While a couple of cases have been reported in literature, these are in the form of case reports. This case report presents the case of a patient with GIST in the stomach and simultaneously detected RCC. Within the scope of the treatment, wedge resection to the stomach and partial nephrectomy were performed. The patient, who had no post-op complications, was discharged on post-op day 7. Gastrointestinal stromal tumours (GIST) are the most common mesenchymal tumours of the gastrointestinal system (GIS). They may co-exist with renal cell cancers (RCC). While a couple of cases have been reported in literature, these are in the form of case reports. This case report presents the case of a patient with GIST in the stomach and simultaneously detected RCC. Within the scope of the treatment, wedge resection to the stomach and partial nephrectomy were performed. The patient, who had no post-op complications, was discharged on post-op day 7.

Key words: Gastrointestinal stromal tumour, renal cell carcinoma, synchronous development

INTRODUCTION

Gastrointestinal stromal tumours (GIST) are generally located within a wide clinical spectrum ranging from asymptomatic progressive tumours to rapidly progressive aggressive tumours. They are the most frequently seen gastrointestinal mesenchymal forms of malignancy (1). They comprise less than 1% of all GIS malignancies (2). Primary GIST cases are most frequently seen in the stomach (50–70%) (1). Most patients present between the 5th and 7th decades (2). The main treatment for GISTs is surgery (3). RCCs account for 80–90% of adult primary renal tumours and for 2% of all cancer types. They are generally seen over 40 years of age (4). RCCs and GISTs are familial tumours and mutations in the c-MET and c-KIT proto-oncogenes are seen. Both of these have tyrosine kinase receptors (5). A secondary primary tumour co-existent with GIST tumours is a very rare condition. In this study, we aim to present the case of a simultaneous existence of GIST in the stomach and RCC alongside a review of the literature.

CASE REPORT

A 60-year-old female patient presented to our clinic complaining of abdominal pain. During the examination a palpable, painless, mobile lesion of about 8x6 cm in the epigastrium was detected. Computerized tomography revealed a 12x8 cm mass in the greater curvature of the stomach which had heterogeneous density with distinctive lobule contoured borders and no invasion into the surrounding structures, most of which had intensive contrast (Figure 1). Further, a solid lesion of about 4x3 cm with smooth contours was detected in the right renal lower pole posterior that had diffuse heterogeneous contrast involvement showing exophytic extension from the cortex to the surrounding. Following surgery it was seen that the patient had a smooth contoured mass of about 10x8x6 cm in the greater curvature of the stomach (Figure 2) and a smooth contoured mass of about 4x3 cm in the lower pole of the right kidney (Figure 3). Neither of the masses had invaded the surrounding tissues. A wedge resection of the stomach and partial nephrectomy were performed on the patient.

The stomach tumour was encapsulated and composed of spindle cells growing in the form of fascicles. Tumour invasion into the muscularis and serousa layer were also reported. Seventeen mitoses were counted on 50 HPF. Immunohistochemistry was performed by the streptavidin biotin peroxidase method. Tumour cells were positive for tyrosine-protein kinase Kit (c-KIT), CD34 and vimentin, but were negative for S-100 and smooth muscle actin (SMA). The pathological analysis of the lesion resected from the stomach revealed that it was a high-grade gastrointestinal stromal tumour (Figure 4a - b). Pathological analysis of the nephrectomy material revealed that it was renal cell cancer (Figure 5). It was seen that the surgical borders were negative for both tumours. The patient, who had no post-op complications, was discharged on post-op day 7 with her treatment plan organized. Imatinib 300 mg/

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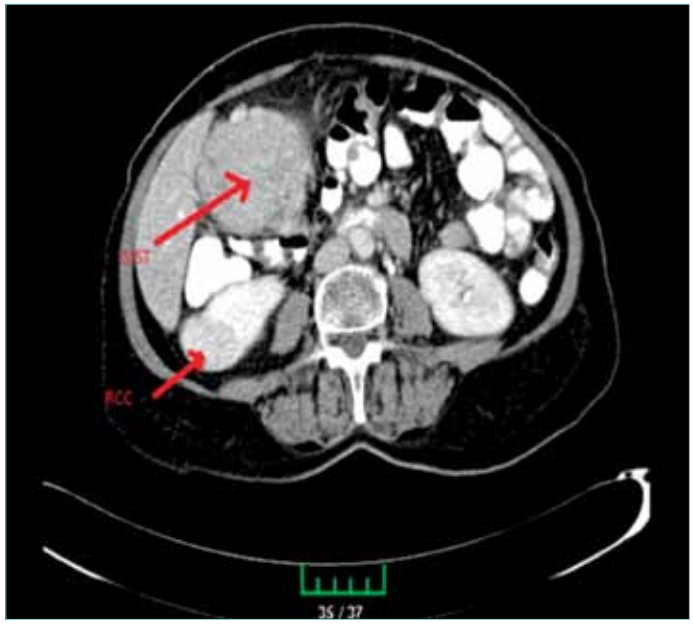

Figure 1. Abdominal computed tomography findings of gastric gastrointestinal stromal tumour and renal cell cancer

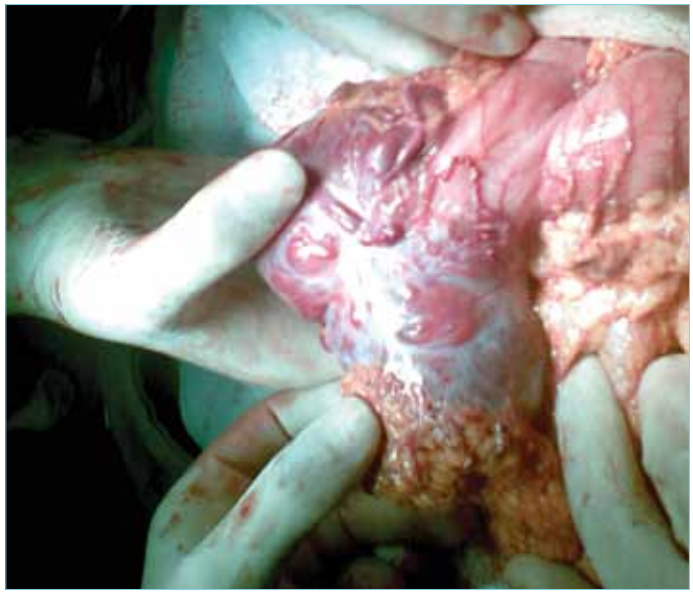

Figure 2. Gross finding. Even though the size of the mass was 10 cm, the mass was successfully resected and retrieved without any breakage (GIST)

day was started as adjuvant therapy. Postoperatively, the patient continued imatinib therapy and no recurrence or metastasis was found in the right kidney at the twelve-month follow-up.

DISCUSSION

Mazur and Clark first coined the term GIST to refer to a distinct group of gastrointestinal sarcomas in 1983. Although GISTs are the most common mesenchymal tumours, they account for 1–3% of all malignancies of the gastrointestinal system (2). Primary GIST cases are most frequently seen in the stomach (50–70%) and small intestine (25–35%), colon and rectum (5–10%), mesenterium or omentum (7%), and the oesophagus (<5%), respectively (1). GISTs

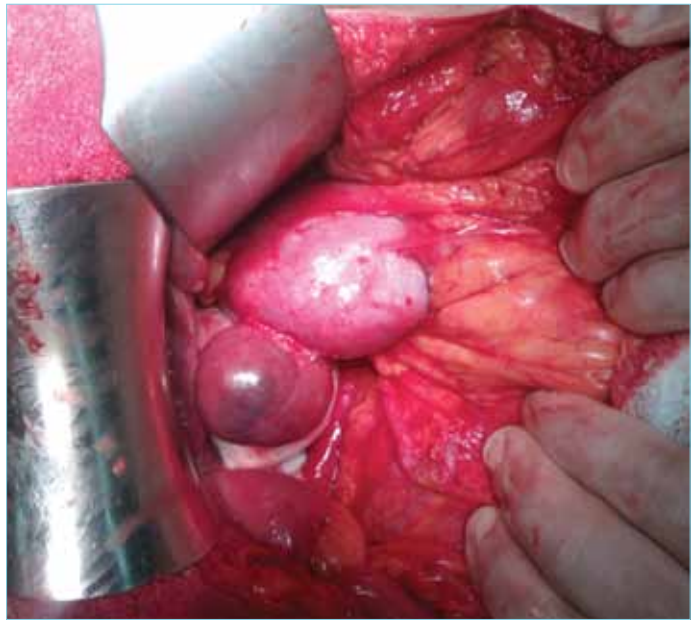

Figure 3. Intraoperative images of the lower pole renal mass (solid arrow)

are mesenchymal tumours and are generally brought about by neoplastic mutation of Cajal intestinal cells (6). Patients with these tumours present most frequently with complaints of bleeding, bowel obstruction, abdominal pain, and palpable mass, or these tumours can randomly be detected during surgical, radiological, or endoscopic procedures (7, 8). Our patient's presenting symptoms were abdominal pain and abdominal mass.

GISTs may co-exist with colorectal cancers, prostate cancers, and lymphoid tissue cancers (9).

The surgical removal of the tumour is the most significance chance for cure in these patients. Metastasis to the lymph nodes is infrequent with GISTs and is seen in about 5% of patients. Therefore, dissection of the lymph nodes is not recommended. There is still no treatment protocol for adjuvant chemotherapy or radiotherapy (3). The effectiveness of imatinib treatment in totally resected tumours by surgery is a controversial issue (1, 10). Our patient had surgical resection. Imatinib treatment was initiated as adjuvant treatment.

Renal cell carcinoma accounts for 2% of all cancers, while it comprises 80% of malignant renal tumours. Its incidence in male patients is twice that in female patients (5). The patients are generally over 40 years of age. The most frequently detected symptoms are haematuria, abdominal pain, and palpable mass. Its primary treatment is surgery and five year survival rate is an average of 70% (4). Studies in literature reported co-existence of renal cell carcinoma with lymphoma, colon, breast, thyroid, ovary, and stomach cancers (11-16).

RCCs and GISTs are familial tumours caused by mutations in the c-MET and c-KIT proto-oncogenes, both of which have tyrosine kinase receptors (5). These two tumours, however, may co-exist as sporadic cases. This condition has been suggested to be related to the potential of imatinib mesylate (Gleveec), used in the treatment of gastrointestinal stromal tumours, to cause secondary tu-

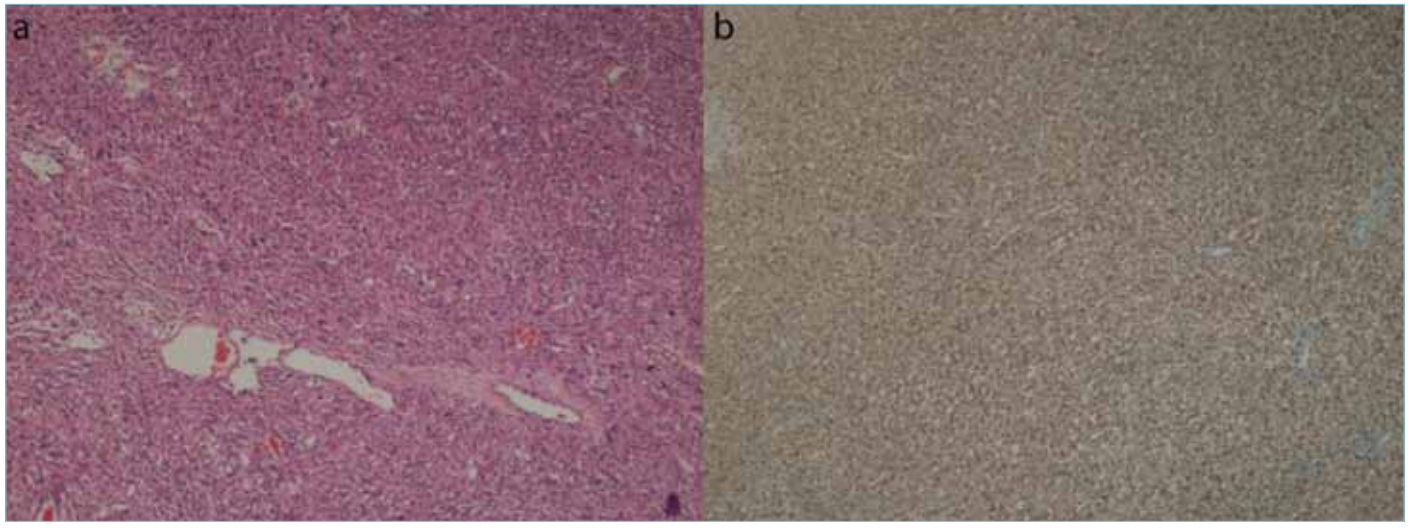

Figure 4. **Gastrointestinal stromal tumor HEx10 (a) CD117 positive immunostaining (b)**

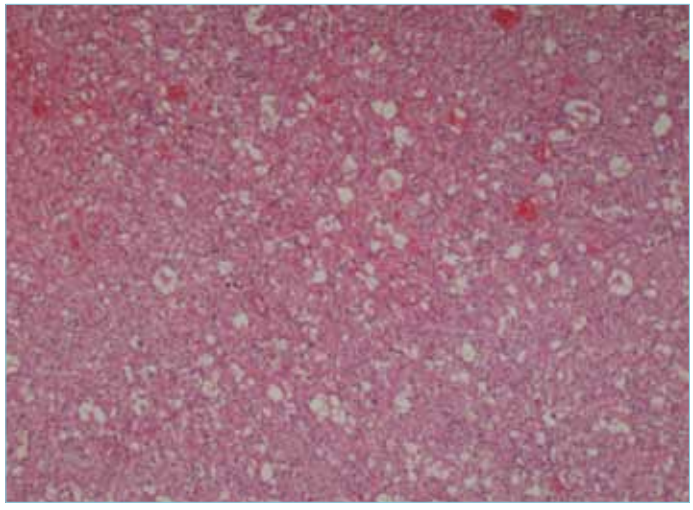

Figure 5. **Papillary renal cell carcinoma (HEx20)**

mours, especially papillary renal cell cancers (17). However, GIST and RCC were detected simultaneously in our case and a surgical procedure was performed regarding both tumours in the same session.

CONCLUSION

GIST may also co-exist with malignancies in other organs. But its synchronized existence with RCC is a rare condition. Although it has been reported that this is related to certain mutations, multicentre studies with a wide scope need to be conducted on the issue.

Informed consent: Written informed consent was obtained from patient who participated in this study.

Authors' contributions: Conceived and designed the experiments or case: EG, TK. Performed the experiments or case: AK, MHÇ. Analyzed the data: EG, HHE. Wrote the paper: EG, MHÇ. All authors read and approved the final manuscript.

Conflict of interest: No conflict of interest was declared by the authors.

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REFERENCES

1. Beham AW, Schaefer IM, Schüler P, Cameron S, Ghadimi BM. Gastrointestinal stromal tumors. Int J Colorectal Dis 2012; 27(6): 689-700. [CrossRef]
2. Nowain A, Bhakta H, Pais S, Kanel G, Verma S. Gastrointestinal stromal tumors: Clinical profile, pathogenesis, treatment strategies and prognosis. J Gatroenterol Hepatol 2005; 20(6): 818-24. [CrossRef]
3. Somerhausen Nde S, Fletcher CD. Gastrointestinal stromal tumours: an update. Sarcoma 1998; 2(3-4): 133-41. [CrossRef]
4. Küçükzeybek Y, Görümlü G, Cengiz E, Karaca B, Erten Ç, Gül MK, et al. Renal Cell carcinoma with metastases to Thyroid Gland and Parotid Gland: A Case report and Review of the Literature. International Journal of Hematology and Oncology 2013; 23(4): 167-72.
5. Au WY, Ho KM, Shek TW. Papillary renal cell carcinoma and gastrointestinal stromal tumor: a unique association. Ann Oncol 2004; 15(5): 843-4 [CrossRef]
6. Afuwape OO, Irabor DO, Ladipo JK. Gastrointestinal stromal tumour in Ibadan, Nigeria: a case report and review of current treatment. Afr Health Sci. 2011; 11(1): 134-8.
7. Caterino S, Lorenzon L, Petrucciani N, Iannicelli E, Pilozzi E, Romiti A, et al. Gastrointestinal stromal tumors: correlation between symptoms at presentation, tumor location and prognostic factors in 47 consecutive patients. World J Surg Oncol 2011; 9: 13. [CrossRef]
8. Fletcher CD, Berman JJ, Corless C, Gorstein F, Lasota J, Longley BJ, et al. Diagnosis of gastrointestinal stromal tumors: A consensus approach. Hum Pathol 2002; 33(5): 459-65. [CrossRef]
9. Agaimy A, Wünsch PH, Sobin LH, Lasota J, Miettinen M. Occurence of other malignencies in patients with gastrointestinal stromal tumors. Semin Diagn Pathol 2006; May; 23(2):120-9. [CrossRef]
10. Gold JS, Dematteo RP. Combined surgical and molecular therapy: the gastrointestinal stromal tumor model. Ann Surg 2006 Aug; 244 (2): 176-84. [CrossRef]
11. van Oosterom AT, Judson IR, Verweij J, Stroobants S, Dumez H, Donato di Paola E, et al. Update of phase I study of imatinib (STI571) in advanced soft tissue sarcomas and gastrointestinal stromal tumors: a report of the EORTC Soft Tissue and Bone Sarcoma Group. Eur J Cancer 2002; 38(5): 83-7. [CrossRef]
12. Hanawa Y, Tanomogi H, Hasegawa S. Renal cell carcinoma in a patient with malignant lymphoma: a case report. Hinyokika Kiyo 1999; 45(12): 843-5.

13. Santos I, Barrio MT, Florez S. Association of colon and renal adenocarcinoma. Description of a new case. An Med Interna 1991; 8(9): 469-70.
14. Broto A, Ortuno R, Pena R, Marsal S. Synchronous colonic adenocarcinoma and hypernephroma. Med Clin 1995; 105(7): 276-7.
15. Jimenez RA, Roldan VAM. A synchronous association of a double colonic adenocarcinoma and hypernephroma: an infrequent case of multiple primary neoplasms. An Med Interna 1992; 9(4): 183-5.
16. Kurihara T, Ishida T, Miyamoto Y, Mishima T, Suda A, Izuo M. A case of quartet cancer--a carcinoma of the breast followed by three synchronous cancers (kidney, thyroid and colon). Gan No Rinsho 1989; 35(8): 955-62.
17. Resorlu B, Baltaci S, Resorlu M, Kankaya D, Savaş B. Coexistence of papillary renal cell carcinoma and gastrointestinal stromal tumor in a case. Turk J Gastroenterol 2007 Mar; 18(1): 47-9.

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