OPEN PEER REVIEW

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An "Open Peer Review" process is making the details of all review process (including reviewers, associate editors, and EICs comments) as "Public" as it is agreed by EIC, Authors, and reviewers.

Advantages of "Open Peer Review" process

- More transparency, constructiveness and tactful comments of the peer review process: leads to an increase in the quality of reviews
- More motivations for all involved roles in the review process
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- Prevents reviewers from following their individual agendas and leading to the detection of reviewers' conflicts of interests

You can find out more at:
https://brieflands.com/briefland/knowledgebase/category/tree.html#opr.html

Archives of Pediatric Infectious Diseases
Article DOI: 10.5812/pedinfect.108029
Published in: Archives of Pediatric Infectious Diseases: 9(3); e108029

Peer Review Report for "Left Atrial Myxoma Misdiagnosis as Infective Endocarditis: A Case Report"

Author(s): Mohammad Rafi Khourgami, Ali Ershad, Kambiz Mozaffari

Review Timeline:

Submit Date: 29 Jul 2020
Revised Date: 20 Oct 2020
Accepted Date: 24 Nov 2020

Revision (0)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

Fariba Alaei: Reviewer | Revision (0) — 4 Aug 2020

Dear AE,
The manuscript needs some grammatical edits.
Comments for the authors:
Case report
- Your current history is not well defined.
- How did you describe limb pain? Did you have any pelvic ultrasound or orthopedic consult to R/O septic arthritis?
Discussion
- The last sentences are not well understood.
- What do you mean about infected myxoma?
Thanks.

REFEREE: Reviewer | Revision (0) — 6 Aug 2020

Dear AE,
Cardiac mixoma is a part of some endocrine syndrome like Carney complex (pigmented

skin freckling, soft tissue tumors, and endocrine neoplasia (adrenal, testicular, and ...)
Please, the authors declare in the case of the report if the patient had some features of this syndrome or was assessed for other neoplasia) or if the patient's family had a history of soft tissue or endocrine neoplasia.
Thanks.

REFEREE: Reviewer | **Revision** (0) 7 Aug 2020

Dear AE,
A microscopic description of the tumor is essential to mention in the text. Tumor gross image associated with special stainings, such as Alcian Blue or PAS or immunohistochemistry (if present) is suggested to be included.
Also, the Figure 3 legend should describe the microscopic characteristic findings of the tumor (which is present in the picture); however, in both the picture legend and text, only pathologic diagnosis is mentioned.
Thanks.

REFEREE: Reviewer | **Revision** (0) 5 Sep 2020

Dear AE,
Comments for the authors:
1- In the cardiovascular textbooks in atrial myxoma, what percentage of patients have constitutional symptoms and embolic events and obstructive symptoms respectively?
2- Due to the absence of congenital heart disease, the lack of response to medical treatment of bacterial endocarditis, and the lack of change in the size of atrial vegetation in the above patient, it seems that heart surgery and biopsy of the above mass could be performed earlier to diagnose the disease.
Thanks.

Fariba Alaei: Associate Editor | **Revision** (0) 7 Sep 2020

Dear EIC
The reviewer(s) have recommended publication, but also suggest some minor revisions to the manuscript. Therefore, I invite the author to respond to the reviewer(s)' comments and revise his manuscript.
Kind regards,

REFEREE: EIC | **Revision** (0) 10 Sep 2020

Dear Author,
The reviewers' comments are mentioned. Please correct the details as mentioned above carefully according to reviewers' request.
Thanks.

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Revision (1)

Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

Dear chief of Editor:

Thanks for the valuable comments sent to us; carefully we correct the requested items as below:
Reviewer 1:
Thank you for your fantastic case report
Microscopic description of the tumor is essential to mention in the text. Tumor gross image associated with special stainings, such as Alcian Blue or PAS or immunohistochemistry(if present) is suggested to be included.
Also Figure 3 legend should be describe the microscopic characteristic findings of the tumor (which present in the picture); however, in both picture legend and text, only pathologic diagnosis is mentioned.

We described the microscopic findings of the tumor in text and Figure 3 and highlight them.

Reviewer 2:
General comments
The manuscript needs some grammatical edition.

We edited English grammar again.

Q.1: Case report
Your current history is not well defined.
How did you describe limb pain? Did you have any pelvic ultrasound or orthopedic consult to R/O septic arthritis?

R.1: At first, we attributed limb pain to nonspecific symptoms of infectious endocarditis such as myalgia, arthralgia but retrospectively limb pain in cardiac myxoma may be due to microembolization to lower extremity and ischemia. As mentioned in the case report, rheumatology and orthopedic consultation were performed. Physical Examination with pelvic x-rays and ultrasounds of the hip joints showed no evidence of septic arthritis. We add this issue to the text.

Discussion
Q.2: The last sentences are not well understood.
What do you mean about infected myxoma?

R.2: We mentioned" We ruled out infected myxoma with a negative PCR and tissue culture result, however, systemic infections or infections of other organs in at least some period might still be probable. This possibility of course could not be documented. "
Based on our knowledge and articles the infected myxoma is extremely rare. It is documented by pathology and when microorganisms are seen on pathology or PCR but in our study this evaluation was negative. They manifest with aggravated clinical symptoms including high-grade fever, multiple embolic events, and the presence of refractory microorganisms.

Reviewer3:
Q: Cardiac mixoma is a part of some endocrine syndrome like Carney complex (pigmented skin

freckling, soft tissue tumors and endocrine neoplasia (adrenal, testicular and ...) Please, declare in case report if patient had some features of this syndrome or assessed for other neoplasia) or patient's family had a history of soft tissue or endocrine neoplasia.

R: In our patient, there were no significant symptoms and signs compatible with the Carney complex. In differential diagnosis, Carney disease was considered. The patient had no diagnostic criteria such as dermatologic manifestations (lentigines, cutaneous myxoma, pigmented skin freckling) and multiple endocrine and non-endocrine neoplasia except cardiac myxoma, so it was removed from the final diagnosis list and family history of soft tissue or endocrine neoplasia was negative.

We add this issue to the discussion.

Reviewer 4: Hi,

Q.1: In the cardiovascular textbooks in atrial myxoma, what percentage of patients have constitutional
symptoms, embolic events, and obstructive symptoms respectively?

R.1: Myxomas present with a classic triad of symptoms, including cardiac obstruction, emboli, and systemic illness.
About 80% of pediatric patients present with symptoms of valvar obstruction. Peripheral emboli occur in >70% of pediatric patients with myxomas. Constitutional symptoms, the third major component of the clinical triad, occur in ≤ 65% of pediatric patients with myxomas. (Moss & Adams Heart Disease in infants, children, and adolescents, 9th edition).
We add this sentence to the introduction.

Q.2: Due to the absence of congenital heart disease, and the lack of response to medical treatment of bacterial endocarditis and the lack of change in the size of atrial vegetation in the above patient, it seems that heart surgery and biopsy of the above mass could be performed earlier to diagnose the disease.

R.2: we managed our patient that suspicious to infectious endocarditis based on routine cardiac references including:" *i*ndications for operative intervention include significant valvular obstruction, progressive heart failure secondary to valvular insufficiency or dehiscence, fungal endocarditis, persistently positive blood cultures after appropriate antibiotics for 10 to 14 days, bacteriologic relapse after an appropriate course of therapy, and recurrent major emboli and after the surgical indication criteria fulfilled the surgery was done(Moss & Adams Heart Disease in infants, children and adolescents, 9th edition) And think the time of surgery was not late but we will reevaluate our management and we are proud to use your advice for the next management.

Sincerely yours

Ali Ershad, pediatric cardiology MD

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Revision (1)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

Fariba Alaei: Reviewer | **Revision** (1) — 26 Oct 2020

Dear AE,
Regarding the authors' revision manuscript, I appreciate this conclusive and complete response.
Thanks.

Marjan Shakiba: Reviewer | **Revision** (1) — 26 Oct 2020

Dear AE,
My question was answered properly.
The manuscript was accepted.
Thanks.

REFEREE: Reviewer | **Revision** (1) — 10 Nov 2020

Dear AE,
Thanks for adding the microscopic description in the text. It is better to conclude figure legend and replace figure legend with this sentence(Hypocellular neoplasm, composed of a few spindle and stellate cells in myxoid matrix).
Regards

Fariba Alaei: Associate Editor | **Revision** (1) — 19 Nov 2020

Dear EIC
Based on the authors' answers to the reviewers' comments, the reviewer(s) have recommended publication.
Kind regards.

REFEREE: EIC | **Revision** (1) — 24 Nov 2020

Dear Author,
The document is reviewed carefully by the reviewers. According to their comments and your revisions as requested, this manuscript is accepted.
Thanks.