**Author's response to reviews**

**Title:** Non-infections osteomyelitis of the mandible of a young female: a case report

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**Author's response to reviews:** see over
Dear Editor,

28. October 2013

Thank you very much for the excellent review performed by high recognices researchers and clinicians within the field. The review performed by professor Stuart Ralston was outstanding and gave us the opportunity to re-think the diagnose. As professor Ralston has written the diagnose is more likely non-infections osteomyelitis with Paget’s disease of the bone as a differential diagnosis. The results from our case are still very important and presenting a rare patient case. In this case we report on a unifocal disease which is very special when compared to the literature.

We do hope that this case is now ready for publication. We have point by point responded to the critique from the reviewers and the editor in the following section.

Best regards

Peter Schwarz

Editors recommendations:

1. Please include the study design in your title, i.e. Case report. For example: A presenting with B in C: a case report.

Response: The title has now been changed accordingly, see also response to reviewer 1.

2. Please include a title page as page 1. The title page should include the title, authors, author affiliations, corresponding author details and complete co-author email addresses.

Response: Changed accordingly

3. Please include the Ethnicity of the patient in the Abstract and Case presentation sections.

Response: It is a Caucasian patient, now included.

4. Please include three to ten keywords representing the main content of the article, after the Abstract section.

Response: Now included

5. Please remove the Methods section as this is not part of the Case Presentation article format.

Response: The methods section has been deleted.
6. Please include a list of abbreviations used in the manuscript and their meanings after the Conclusions section.

Response: Now included

7. Please include an acknowledgement section at the end of the manuscript before the reference list. Please acknowledge anyone who contributed towards the study by making substantial contributions to conception, design, acquisition of data, or analysis and interpretation of data, or who was involved in drafting the manuscript or revising it critically for important intellectual content, but who does not meet the criteria for authorship. Please also include the source(s) of funding for all authors. Authors should obtain permission to acknowledge from all those mentioned in the Acknowledgements.

Response: Acknowledgement section is not relevant in this manuscript. There was no funding of the case-report.

Reviewer 1

Comments to authors:
Thanks for asking me to review this paper. This is an interesting and unusual case. Unfortunately I do not think it is Paget's disease as the authors have suggested. The histological report of woven bone is non-specific as are the abnormalities on isotope scan and SPECT and these could be due to non-infections osteomyelitis of the mandible which is a recognised but unusual condition of unknown cause. This condition seems to have some similarities to SAPHO and might be a subtype of that disorder. Please see (e.g.) Pediatrics Vol. 113 No. 4 April 1, 2004 pp. e380-e384) for more information. Further investigations that might push one towards a diagnosis of PDB would be abnormal osteoclast morphology on biopsy (e.g. larger than normal multinucleated osteoclasts with inclusions) or genetic evidence (e.g. mutations in SQSTM1, TNFRSF11A) but that information does not seem to be available. Another feature against PDB is the patients age. Early onset familial PDB would be an outside possibility, but with no family history it seems unlikely. A new mutation could be possible in TNFRSF11A and maybe the authors could test for that?

Response: Thank you for your excellent suggestion. The first diagnostic test from the pathologist was non-infections osteomyelitis, as was written in our manuscript. The diagnosis of PDB was based on our best fit. We believe that your suggestion is correct and therefore we have accordingly changed the manuscript to non-infections myelitis throughout the introduction and discussion (both completely rewritten). Still this is a very rare condition we report and we therefore changed the manuscript title and wording accordingly throughout the manuscript. Other differential diagnosis has been included in the discussion as well.

Reviewer 2.

- General comments
This paper reports a single observation of mandible Paget disease. The originality of this paper is the location of the disease and the age of onset, both very atypical. However, neither the clinic nor the high level of markers of bone turnover, or the bone scintigraphy and spect-CT presented in this
article are specific to Paget's disease. Histological examination is not concordant between the 2 biopsies. The analgesic bone response after treatment with zoledronic acid is not specific for Paget's disease. So it is very difficult to confirm Paget's disease on the data presented in this article.

**Response:** We do agree and have changed the manuscript accordingly. See also our response to reviewer 1.

First, it would be interesting to verify the absence of any other localization on the skeleton, including the lower limbs.

**Response:** The patient does not suffer any symptom from other sites and by bone scintigraphy and SPECT we find no other localisation of bone activity.

Then, it is essential to discuss the differential diagnosis and in particular fibrous dysplasia, most common at this age and whose appearance, particularly in the jaw, is very close to that of Paget’s disease.

**Response:** Please consult response to reviewer 1 and furthermore now we have included differential diagnosis in the discussion.

The illustration should be complete with radiograph and a CT- scan of the jaw to highlight the features and atypical appearance of the localization on the mandible of Pagetic disease and to the differential diagnosis with fibrous dysplasia or other anomaly of bone structure.

**Response:** No further examinations of the patient are possible. However, as we have changed accordingly to the suggestions by reviewer 1 we think that all relevant diagnostic tools have been included. The SPECT-scanning as suggested are included in the manuscript.

Finally, the use of zoledronate in this age can also be discussed, the pamidronate could have be proposed

**Response:** This is now included in the discussion