Author's response to reviews

Title: A complicated case of pachydermoperiostosis with spondyloarthropathy: a case report

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Author's response to reviews: see over
Dear Editors and Reviewers,

Thank you for arranging a timely review for our manuscript. We have revised our manuscript according to the reviewer’s comments. We also thank the reviewers for their time and thoughtful comments. We found the reviewers’ comments very helpful and have revised the manuscript accordingly. Itemized replies to the reviewer’s comments are appended below.

Best regards,

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Reviewer 1:
Comments to the Author

1. The case described is interesting. However, there are some aspects that remain unclear. The patient has sufficient criteria to thing that possibly has also an undifferentiated spondyloarthritis: inflammatory pain, peripheral synovitis, very high acute phase reactants, imaging findings, positive HLA-B27. Furthermore, IgA nephropathy is also associated with SpA(s). Thus, in this case, we would have a patient with a 3 fortuitous association diseases: pachydermoperiostosis, IgA nephropathy and B27 spondyloarthritis.

Failure to respond to TNF blocking agents does not rule out a SpA because there are patients who do not respond to these agents. Moreover, it is possible that this sclerosing bone-forming phenotype of SpA is less responsive to anti-TNF biological agents than other more inflammatory phenotypes. Furthermore, the good response to
zoledronic acid does not exclude a SpA, due to there are small series, with AS in particular, showing good response to several iv bisphosphonates. All these points should be commented in the Discussion.

**Response:** Thank you for the comment. Revision was made accordingly (TITLE, page 1; 1\(^{st}\) paragraph, DISCUSSION Section, page 6; CONCLUSION Section, page 8).

2. Other important points: Was sacroiliac MRI performed? What were the findings?

**Response:** Thank you very much for the suggestion. MRI was not performed for our patient. Instead, CT scan was done, with the report shown in the 3\(^{rd}\) paragraph, CASE PRESENTATION Section, page 5.

3. Was Doppler signal observed in ultrasound examination?

**Response:** Ultrasound of the knees indicated synovitis, without Doppler signal suggesting of flow. This result was in the 3\(^{rd}\) paragraph, CASE PRESENTATION Section, page 5.

4. What is the prevalence of HLA B27 in the Chinese population?

**Response:** The prevalence of HLA-B27 in the Chinese population is 2%-7%. Anyway, we deleted this part in the 1\(^{st}\) paragraph, DISCUSSION Section, page 6, according to the comment 1. Thank you.

5. Minor changes: There are several wrong gramaticals:

Page 6: 2\(^{nd}\) line: radiographs; 10 line: response; 12\(^{th}\) line: refractory arthritis.
Page 6: 2\(^{nd}\) para: colchicine?; first-line drugs.
Page 7: at the end of 1st paragraph: Provide some reference to the following sentence: “The mechanism of action of bisphosphonates in HOA remains unclear but it is commonly accepted that they have both antiresorptive and anti-inflammatory benefits.”

Reference(s)

Figure legends: Fig 2: X-ray images of the hands...

Response: These syntax/grammar mistakes were corrected accordingly.

Reviewer 2:

Comments to the Author

1. When the patient was diagnosed with pachydermoperiostosis, he was treated with prednisone, methotrexate, salicylazosulfapyridine 2g/d, calcium and alendronic acid with poor response. Then, he was treated with intravenous zoledronate and knee joints synovectomy. It is unclear whether all treatment was withdrawn. If only alendronate was withdrawn it is possible that the benefit observed was due to the rest of the treatment.

Response: Thank you for the comment. Alendronic acid was withdrawn, and prednisone was tapered rapidly in 2 weeks, due to the poor response. The symptoms improved soon after the use of intravenous zoledronate and knee joints synovectomy. We do not think the benefit was due to the rest of other medications, because methotrexate and salicylazosulfapyridine both acted slowly. Revision was made accordingly (4th paragraph, CASE PRESENTATION Section, page 5).

2. The patient meet ASAS criteria for spondyloarthropathy. As the authors comment the association between spondyloarthropathy and IgA nephropathy, is well known. Not so an association between pachydermoperiostosis and IgA nephropathy.
Response: Thank you very much for the suggestion. We added it according to the reviewer’s comment (1st paragraph, DISCUSSION Section, page 6).

3. Recently it has been described some effect of zoledronic acid in spondyloarthropathy (Ann Rheum Dis. 2011 Jun; 70(6):1091-4. Doi: 10.1136/ard.2010.142539. Epub 2011 Feb 22), and probably this was the effect observed in the patient. I think the case probably could better be presented as an association between spondyloarthropathy and pachydermoperiostosis.

Response: Thank you for the comment. Revision was made accordingly (TITLE, page 1; 1st paragraph, DISCUSSION Section, page 6; CONCLUSION Section, page 8).

Other comments from Editors:
1. Please change the description of the patient’s gender from “man” to “male”.

Response: It was corrected accordingly (2nd paragraph, ABSTRACT Secion, page 2; 1st paragraph, CASE PRESENTATION Section, page 4).

2. Please include a list of abbreviations used in the manuscript and their meanings after the Conclusions section.

Response: We added this part accordingly (page 8).

3. Please remove the patient’s face in the figure files as the journal does not publish these type of figures.

Response: The figure files were corrected accordingly (page 11).
We thank the reviewers again for their helpful comments!