Reviewer’s report

Title: Clinical characteristics and role of whole body bone scan in multifocal osteonecrosis

Version: 0 Date: 14 Oct 2018

Reviewer: Domenico Albano

Reviewers report:

ABSTRACT:

- Line 9, MRI and X-rays of the hips or other anatomic districts too?

- Please, report the statistical tests used

INTRODUCTION

- Lines 29-32, I wouldn't say that MRI is used to guide biopsy, since biopsy is not commonly performed to achieve the diagnosis and MRI is not actually used to guide this kind of procedure, although it allows to detect ON when X-ray and CT are still falsely negative.

- Please rewrite the last sentence of the Introduction section to better convey the purpose of the study

MATERIALS AND METHODS

Subjects

- Line 7, X-rays were performed on hips, knees, and ankles, but it is not clear what anatomical district was investigated by MRI, please clarify.

- Inclusion and exclusion criteria? Were randomly searched in your PACS or in your Orthopedic database? How long time from ankle sprain and MRI? This could have affected the evaluation of the AITFL since late fibrotic changes make difficult to differentiate a partial from a complete tear.

Simple radiographs and MRI

- Line 60, 3 T instead of 3.00
Please include in MeM how you calculated we calculated the amount of prednisone received by all patients. If they received dexamethasone, please include the prednisone-dexamethasone conversion used.

RESULTS

- Lines 7-9, MRI was performed on more anatomical districts to identify multifocal ON? I guess that 24 cases of multifocal ON were evident only on WBBS because MRI was performed on a single district and not falsely negative. This should be clarified.

- Lines 21-26, how you divided the causes of ON should be included in the MeM section instead of the results.

Wbbs, mri and xray results

- How can you compare WBBS, which is a whole body examination, with local MRI? Did all these patients perform MRI of all joints or some joints were not evaluated in some cases (this data should be reported)? Did they undergo a whole body MRI? It's still unclear how these patients were evaluated on MRI, although it's very important when comparing these modalities, especially considering that MRI is the most accurate imaging procedure. As I see from figure 1, there are several cases that you considered positive on WBBS and negative on MRI, it should be clarified if in these cases MRI of the affected segment was not available, alternatively authors should justify how WBBS can see ON not detected by MRI. In the latter case, a figure with images of the patient would be of interest.

Discussion

- The authors focused their study on the differentiation of oligofocal ON from multifocal ON, but they did not report if ON lesions were located in metadiaphyseal or epiphyseal regions. However, the location of ON is clinically much more important than the information regarding the number of ON lesions. Indeed, in metadiaphyseal ON, bone collapse does not occur, while in epiphyseal ON the involvement of articular surface gradually leads to osteochondral fragmentation and surface collapse. Epiphyseal osteonecrosis is usually more symptomatic, although in some cases it can be totally asymptomatic. May you please report this crucial data? I suggest to use the following interesting paper to discuss this important point [Osteonecrosis detected by whole body magnetic resonance in patients with Hodgkin Lymphoma treated by BEACOPP. Eur Radiol (2017) 27:2129-2136; DOI 10.1007/s00330-016-4535-8].

- Second page of the discussion, lines 13-24. I disagree since other recent papers have already demonstrated the utility of whole body MRI to detect multifocal ON in riskful patients [Eur Radiol (2017) 27:2129-2136; Br J Haematol. 2017 Feb;176(4):637-642; PLoS One. 2017 Jul 17;12(7):e0181069]. MRI, and thereby whole-body MRI, has higher sensitivity and specificity
than scintigraphy [Semin Musculoskelet Radiol 15:281-300], besides avoiding radiation exposure, which is crucial in younger patients with longer life expectancy and at higher risk of radiation-induced long-term effects. The conclusion of the paper cannot be that WBBS is useful for evaluating younger patients, especially in the light of the directive 2013/59 by the European Union which states that if a radiation-free imaging technique allows the same diagnostic results to be obtained, it should always be used [Eur Radiol (2018) 28:1187-1193]. Based on this recommendation, WBBS should not be considered the best option. I suggest to better discuss the point of radiation exposure, the potential role of whole body mri in this setting, and I would rephrase the conclusion.

- I would better underline that WBBS might have missed some locations and that the selection bias might have affected the results, since corticosteroids are well known as the most important cause of ON [Orthopedics 2011;34:39-48]

- There are few outstanding grammatical and syntax errors, but overall English is ok

- A figure with a case of the study population, including WBBS, MRI, and x-ray should be added.

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

Yes

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Unable to assess

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

Yes

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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Please indicate the quality of language in the manuscript:

Acceptable
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