Author's response to reviews

Title: Natural Course of Intra-Articular Shifting Bone Marrow Edema Syndrome of the Knee

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Author's response to reviews: see over
Dear Dr. Marlee,

Thank you for you interest in our manuscript “Natural Course of Intra-Articular Shifting Bone Marrow Edema syndrome of the Knee” (MS: 2127681501659051). Below you will find a point-by-point response to the concerns of the reviewers. All the comments have been addressed to in the revised manuscript.

Reviewer 1:

1) The formulation that there is a consensus as to the vascular etiology of BMES is not correct. This sentence has been removed from the manuscript. The statement that there are some different theories regarding the pathogenesis is more appropriate.
2) All the information requested by the reviewer has been added in the text. Patients with trauma, corticosteroid medication and avascular necrosis (in the knee and other joints) were not included in the study.
3) Pictures of a second patient with shifting BMES have been added.
4) A table describing MRI findings at different timepoints has been added to the manuscript as proposed by the reviewer.
5) The discussion was proofread by a native English speaker.

Reviewer 2:

1) Page 4, para 3, line 4: data regarding varus deformity are provided (3 and 4gr. Hip/ankle angle)
2) Page 6, line 6: no axe deformities were seen in these patients
3) Page 6, para 1, last line: this statement has been corrected in the text
4) Page 9, para 3, line 8: the term has been changed in the text
5) Page 10, para 3, line 4: This sentence was removed from the text.

Reviewer 3:

1) The fact that this study deals about a small and retrospective series of 8 patients has already been mentioned in the manuscript.
2) It is true that BMES is a self limited disease and that many authors treat their patients conservatively. Other working groups prefer core decompression (as Hofmann et al. 2000, 2004, 2005, 2006, Plenk et al. 2001, Leder and Knahr 1993, Aigner et al. 2002,
Berger et al. 2006 and others) as the long duration of pain and immobilisation (up to 12 months) can essentially be shortened by this operative treatment.

3) It is not correct that the use of iloprost is not documented in literature (Aigner et al. 2001, 2002, 2005, Meizer et al. 2005, Petje et al. 2004, Disch et al. 2005, Mayerhoefer et al. 2007, Hofmann et al. 2005, 2006, Breitenseher 2006). The drug is not intraarticularly injected but administered by infusions. This stable prostacyclin analogue is approved for therapy of critical ischemia secondary to peripheral arteriosclerotic obliterative disease or diabetic angiopathy. The substance has an impact on the rheological properties of the terminal vascular bed. It induces vasodilation and reduction of capillary permeability and inhibits platelet aggregation. Apart from this rheological efficacy on the terminal vascular bed, it diminishes the concentration of free oxygen radicals and leukotrienes.

We hope that all corrections in the manuscript as well as the responses to the concerns of the reviewers are complete and that the manuscript can be published soon.

Sincerely

Nicolas Aigner, MD
Consultant