Dear reviewers

Re: Manuscript ID: 79238 and Title: Multiple myeloma presenting with amyloid arthropathy as the first manifestation: two case reports and a literature review

Thank you for your letter and the reviewers' comments concerning our manuscript entitled "Multiple myeloma presenting with amyloid arthropathy as the first manifestation: two case reports and a literature review" (ID: 79238). Those comments are valuable and very helpful. We have read through comments carefully and have made corrections. Based on the instructions provided in your letter, we uploaded the file of the revised manuscript. The responses to the reviewer's comments are presented following. We would love to thank you for allowing us to resubmit a revised copy of the manuscript and we highly appreciate your time and consideration.

Sincerely.

Bingzong Li.

Reviewer #1:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: The text under review is very interesting and well written. The pictures add curiosity to the manuscript. The sections into which the text is divided are well organized and understandable. In the discussion, however, I recommend emphasizing the trend of signs of arthropathy in relation to myeloma treatment if a common trend was observed in selected patients. I also recommend enriching the bibliography by citing the work of authors who have been interested in the same topic before you. In addition, it is rare that informed consent is obtained before a case report is published. In the text you also refer to patients who died before submission of the manuscript; if possible, could you clarify the information regarding this aspect? Kind regards

First, we supplemented the changes in symptoms and signs associated with arthropathy after treatment in two patients. And we added one citation on amyloid arthropathy. On the issue of informed consent for patients, we decided to report on both patients when both patients were alive and consented. But by the time we finished writing, one of the patients had passed away due to progression.

Reviewer #2:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors: These are two interesting cases, which are of great significance to the clinical diagnosis of MM complicated with amyloidosis. question 1The pictures are blurred. Can you provide clear pictures? 2 It is best to summarize it into diagnostic points. 3 Myeloma-FISH [del(17p), IgH translocations, del13, 1q21 gain, and Rb1 deletion) were negative? All these are negative? 4 median nerve lysis? Median neurolysis? Should it be median nerve release? 5 Can it be concluded that amyloidosis should also be considered when MM has joint symptoms? Suggest publication These are two interesting cases, which are of great significance to the clinical diagnosis of MM

complicated with amyloidosis. question The pictures are blurred. Can you provide clear pictures? It is best to summarize it into diagnostic points. Myeloma-FISH [del(17p), IgH translocations, del13, 1q21 gain, and Rb1 deletion) were negative？ All these are negative? median nerve lysis？ Median neurolysis? Should it be median nerve release? Can it be concluded that amyloidosis should also be considered when MM has joint symptoms? Suggestions are revised and published after review

First of all, we tried to improve the clarity of all the images again. Second, we resummarize the main points of the diagnosis of MMA in the concluding section. Then we made changes to the ambiguous content and the wrong surgical name. Finally, we believe that MMA should also be considered in patients with MM with joint symptoms. Of course, MM can also be combined with rheumatoid diseases. Therefore, the final diagnosis still requires pathological results.

Reviewer #3:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: the authors presented to cases of Amyloid Arthropathy as the first manifestation of multiple myeloma. this manuscript is well written, the explanation is complete and the related figures have been added. I think it is ready to publish.

Reviewer #4:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: This is an excellent case reports on multiple myeloma-associated amyloid arthropathy (MAA). The case presentation, discussion and results are both generally well described. I would advise that this report could be even better. I hope you will find it helpful. [Regarding case 1] The patient presented with inflammation of muscles, ligaments and joints throughout the body as of August 2018. The diagnosis at this point was 'arthritis', but what was presumed to be the cause? And if the joint fluid obtained during the injection treatment of both knees and shoulders joints had been examined in pathological detail, would the patient have been led to a more appropriate diagnosis and treatment at an earlier stage? [Regarding case 2. The patient is described as having started walking in the first post-operative month. The rehabilitation of a patient with multiple myeloma (MM) who is prone to fractures requires close attention. Were there any special efforts made in the patient's rehabilitation? [Discussion. The authors describe in detail the differentiation and complications of rheumatoid arthritis (RA) and MAA. How is the relationship between these diseases considered? For example, does RA exacerbate MAA or vice versa? The authors plainly state that MAA should be considered as one of the differential diseases in arthritis associated with renal failure and anaemia. I agree with this opinion. However, patients requiring treatment for arthritis often have diabetes and hyperuricaemia. In such cases, anaemia and renal failure are common complications. Therefore, it is not practical to perform congo red or crystal

violet staining in all arthritis operations with renal failure and anaemia. Are there any additional symptoms that the authors consider useful to further suspect MAA?

[Regarding case 1] The patient presented to the rheumatology department for symptoms of arthritis, and the rheumatologist did not consider that the patient might have plasma cell disease, but considered that the patient had seronegative rheumatoid arthritis. Therefore, the rheumatologist did not screen for relevant indicators and tissue biopsies.

[Regarding case 2] The patient did not resume walking 1 month after surgery, but was assisted by crutches, and there may be a problem with the expression.

[Discussion] Patients with MM may have MMA or rheumatoid arthritis. MMA is similar to rheumatoid arthritis, which is a clonal plasma cell disease. When CARB symptoms appear, doctors should first screen for plasma cell disease, that is, blood and urine M protein screening. These screenings can detect the vast majority of patients with plasma cell disease. If necessary, bone marrow is performed. In this regard, we have revised the conclusion section of this article to add elaboration on this issue.