Dear Prof Bloomfield, Prof Peng, Prof Vento and the review committee,

We would like to thank the editor and reviewers for the invaluable comments and suggestions to our submitted manuscript entitled "**Avascular Necrosis of the First Metatarsal Head in a Young Female Adult** ".

We have revised the manuscript and addressed to our best the important points raised in a point-by-point format with highlights. We sincerely wish that the revised manuscript will now meet the expectations and allow us to share the important findings with readers of the *World Journal of Clinical Cases*. Further advices and comments would be most welcomed.

Thank you once again for considering our manuscript for publication.

Sincerely and on behalf of all authors,

Michael Ong

Company Editor in Chief

General Comments:

I have reviewed the Peer-Review Report, full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Clinical Cases, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors.

Author Response:

The author would like to thank the editorial committee for recommending a conditional acceptance for this manuscript. We hope this case study can provide additional information to clinicians on the conservative treatment toward avascular necrosis of the first metatarsal head.

Science Editor

General Comments:

The manuscript describes a Case Report of the Avascular Necrosis of First Metatarsal Head. The topic is within the scope of the WJCC. (Authors performed an interesting case report. Author should argue better therapeutic option in discussion section. The questions raised by the reviewers should be answered. Recommendation: Conditional acceptance.

Author Response:

The author would like to thank the editorial committee for recommending a conditional acceptance for this manuscript. We hope this case study can provide additional information to clinicians on the conservative treatment toward avascular necrosis of the first metatarsal head. In addition, we have added in better therapeutic approaches in the discussion section.

Comments and Suggestions for Authors	**Author's Responses**
1. The authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor	Thank you for the comment. The original images have been attached (as a PowerPoint) along with this reply.
2. PMID numbers are missing in the reference list. Please provide the PubMed numbers and DOI citation numbers to the reference list and list all authors of the references. Please revise throughout	Thank you for the comment. The missing PMID and DOI in the reference section have been added accordingly. However, we noticed that some of these references do not have DOI. Nevertheless, we have provided all those available being retrieved from PubMed.

3. To obey the publication ethics and improve the protection of all patients' rights to privacy, the authors should provide the informed consent form on which the patient's name, address, birthday, address, ward, bed number, hospital number and other private information are obfuscated	Thank you for the kind reminder. The consent form does not contain any information disclosing the patient's address, birthday, address, ward, bed number, hospital number and other private information. Only name, telephone number and email contact were listed for contact purposes.

Reviewer 1:

General Comments

A case report about an Avascular Necrosis (AVN) of the First Metatarsal Head in a Young Female Adult. The main objective was to describe an unusual form of AVN, including diagnostic and therapeutic aspects. However, although of interest for the reader, the paper has several criticisms that must be addressed. In particular, clinical condition needs more details, using questionnaire or tools for describing better the case. Treatment choice should be better described and the discussion, should be better argued about similarities and differences with what reported in literature. English must be slightly reviewed by a native English speaker.

Author Response:

The authors would like to thank the reviewers for the positive comments for this manuscript. The specific comments being raised have been addressed to our best in the following context. We definitely hope the improvements can provide additional information toward an alternate conservative treatment toward avascular necrosis of the first metatarsal head.

Comments and Suggestions for Authors	**Author's Responses**
1. "On physical examination, mild swelling of the first MTPJ was revealed, with failed interphalangeal joint (IPJ) flexion, but intact flexor hallucis longus (FHL) tendon. Clinical appearance of the feet, sensation and local perfusion of the toes were normal." It could be of interest for the reader have information about clinical aspect of your patient. It could be useful to use appropriate questionnaire for the assessment of pain, function, impairment of Activity of Daily Living (ADL) and quality of life.	Thank you for your comment. Beside the general description on the physical examination during the consultation, we actually asked simple questions regarding whether the pain has affected her quality of life. The information was added to Page 6 Line 136-140. However, it would be of interest to incorporate some proper questionnaires (e.g. ADL, SF-12, etc) as a further study.
2. Didn't you perform an X-ray evaluation as first line approach, before MRI?	Thank you for your question

	Yes, the X-ray evaluation is the general approach upon the patient's presentation. The additional MRI was performed for assessing whether there is damage on vascularization and surrounding soft tissues. Details of the X-ray have been added to Page 6 Line 146-147.
3. Did you research in medical history any risk factor, such as joint or bone trauma, fat metabolism diseases, sickle cell anemia and Gaucher's disease, or any other causes of reduced blood flow? Please specify better this aspect.	Thank you for the comment. Based on the record from this patient's previous record, we did not find any risk factor (e.g. joint or bone trauma, endocrine diseases, etc). The history of her past illness has been added to Page 5 Line 128-130.
4. In the "treatment" section you described the progression of the disease, providing few information about the treatment proposed. In particular, how the patient carried out the non-weight bearing and which kind of analgesics assumed?	Thank you for the question. The details of the treatment proposed and the methods carried out have been added to Page 7 Line 166-174.
5. Why did you not prescribed vitamin d, calcium or drugs affecting bone?	Thank you for your question. Although some literatures showed that low Vitamin D may have a correlation with the occurrence of AVN, it was shown that it was not an independent risk factor (Osunkwo, I, 2013, Current Opinion in Endocrinology & Diabetes and Obesity). Moreover, we could not find any strong evidence in literature showing that vitamin D or calcium supplements are proven treatment modalities for AVN. Moreover, it is not a common practice in our clinic to give such treatment for those with suspected AVN. As the patient was not

	presented with low bone mass or have a history of bone fractures, we believe that it was not necessary to prescribe vitamin d or other bone supplements toward the clinical benefit for this patient. Likewise, the mechanism on how these drugs (e.g. alendronate) can benefit bone in AVN remains controversial (S. Agarwala, 2002, Alendronate in the treatment of avascular necrosis of the hip). Hence, there is no supporting evidence that these prescriptions may benefit our patient.
6. Did you suggest a rehabilitation protocol for improving function?	Thank you for the question. Owing to the rare occurrence of such pathology in our daily clinic, there is currently no specific guideline for rehabilitation protocol being established. However, we do adopt a rehabilitation protocol to ease the symptoms of patient. These include non-weight bearing exercises for ambulation, and partial weight bearing with single elbow crutch then full weight bearing with no walking aids for pain symptoms. The details have been added to Page 7 Line 167-171, Line 182-183 & 189-190.
7. "autoimmune markers suggestive of SLE." How can you affirm this sentence if you did not perform laboratory assessment?	Thank you for this question. Definitely, the diagnosis of SLE would require the use of diagnostic criterion based from the American College of Rheumatology's. However, given the good past health of our patient and absence of any clinical features (e.g., fever, psychosis, delirium, seizure, alopecia, ulcers, cutaneous lupus features, etc) constituting the diagnostic criteria, it may not be our

	routine clinical practice to conduct a full SLE workup for this patients without presentation of any clinical features. However, we do agree that it would ultimately be needed for diagnosis of SLE to ascertain if the patient may be suffering from this autoimmune illness or not. Hence, this shall be a consideration on employing a proper SLE diagnosis toward our patients as our next further studies.
8. "various serum results, such as elevated C-reactive protein level an erythrocyte sedimentation rate". Although it is unlikely that your patient suffers from AR, this sentence is not appropriate due to the absence of biochemical assessment.	Thank you for this question. Definitely, the authors agreed that this patient would unlikely to be suffering from RA. However, the purpose of this statement was to state a limitation on our current study that we have not carried out a lab assessment toward RA. Without these assessment, we would not be able to conclude whether this patient might be suffering from RA or not.
9. " however, are more commonly used in the management of the typical sites of AVN, rather than the first MTT head". It could be of interest providing a brief description of similarity and differences between AVN of Metatarsal Head and others skeletal sites, in particular femoral head. Please, read and cite "Paoletta M, Moretti A, Liguori S, Bertone M, Toro G, Iolascon G. Transient osteoporosis of the hip and subclinical hypothyroidism: an unusual dangerous duet? Case report and pathogenetic hypothesis. BMC Musculoskelet Disord. 2020 Aug 13;21(1):543. doi: 10.1186/s12891-020-03574-x. PMID: 32791961; PMCID: PMC7427076."	Thank you for the suggestion. In light of the recommended reference, a brief description of similarity and differences has been added in the discussion section, as shown on Page 11 Line 311-315 and Page 12 Line 316-321.
10. In the discussion, beyond the differential diagnose with other conditions, you could argue better therapeutic option available for this condition and	Thank you for the suggestion. We have added the comparison with

compare it with your therapeutic protocol, explaining strength and limit.	different therapeutic option available for this condition and compare it with our current therapeutic protocol on Page 12 Line 318-332.
Reviewer 2:	
The author would like to thank the reviewers for the positive comments for this manuscript. We hope this case study can provide an additional information to clinicians on the conservative treatment toward avascular necrosis of the first metatarsal head.	
Comments and Suggestions for Authors	**Author's Responses**
1. Although this topic has been report in many literatures, I support to publish this case report which could be benefit for the reader regarding to more options especially conservative treatment.	Thank you for the comment. We believe this case report can help add further information toward conservative treatment for patients suffering with avascular necrosis of the first metatarsal head.