

Response to Reviewer#1

Scientific Quality: Grade E (Do not publish)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Comment 1: On the last sentence Considering that the pelvic pain symptoms continued to decrease, treatment strategies were considered to be effective.

What did 'the pelvic pain symptoms' mean? Is this phrase the symptom of bone metastases? If 'the pelvic pain symptoms' means the part of bone metastatic disease, the authors should mention of the relation of that phrase to clinical symptoms of bone metastases.

Response: Thanks a lot for the reviewer`s comment. The patient's pain comes from lumbar pain, not pelvic pain symptoms; we used the wrong word here, so we used lumbar pain in the revision.

In Page 2,line 22,“Considering that progressive decrease in the presenting lumbar pain, treatment strategies were considered to be effective.”

Comment 2: Three months later, bone imaging and MRI showed that bone metastasis was more advanced than before. What modality of bone imaging? Is it bone scan? CT scan, plane X-ray? All modality but MRI? Authors should show what modality of imagings.

Response: Thanks for the reviewer's comment. The modality of bone imaging in the paper is radionuclide bone imaging, we use the wrong word; For accurate expression, we have replaced radionuclide bone imaging in the manuscript.

Comment 3: CONCLUSION If lesions increase in bone scan, then PSA, PSMA PET-CT, and other examinations should be used to determine whether the treatment` s effectiveness. The author should definite the kind of the lesions. Is it bone metastasis lesion? Were the lesions increasing only on the finding of bone scan? Authors mentioned that MRI showed that bone metastasis was more advanced than before.

Response: Thanks a lot for the reviewer`s comment. Conclusion we express

imprecisely, in order to describe the conclusion more accurately, we make corrections.

In Page 2, Line 27, "Careful evaluation must precede treatment plan changes."

Comment 4: Introduction However, "bone flare" phenomenon occurred 3 months post treatment, and then decreased in further follow-up evaluations [2]. Please provide a specific notation for the definition of the term "bone flare" in this quote.

Response: Thanks for the reviewer's comment. It has been revised in the paper.

In Page 4, Line 10, "Following the application of novel hormonal therapy, PSA was noted to decrease significantly in some patients after treatment. However, radionuclide bone imaging showed progression of bone metastases after 3 months and with a gradual decrease noted during subsequent follow-up. Ryan et al. calls this phenomenon "bone flare"."

Comment 5 Core Tip We describe a case of metastatic hormone-sensitive prostate cancer with bone flare after apalutamide and ADT therapy, and summarized the characteristics of the clinical manifestations of bone flares after treatment with novel hormonal therapy in a patient with a prostate adenocarcinoma. The contents of the three underlines overlap. Authors could organize these sentences into shorter ones.

Response: Thanks a lot for the reviewer's comment.

In Page 3, Line 3, "In 2018, prostate cancer was ranked as the fifth leading cause of cancer-related deaths in men, worldwide. Some of such cases are metastatic hormone-sensitive prostate cancers (mHSPC) and Apalutamide has been shown to improve survival in such patients. However, a "bone-flare" phenomenon may occur during management with apalutamide. We describe a case of mHSPC with this phenomenon after apalutamide and ADT therapy, and thus demonstrate the importance of multiple bone imaging modalities—radionuclide bone imaging, MRI, PSA, PSMA PET-CT—in determining the treatment course in such patients."

Comment 6:Outcome Considering that the pelvic pain symptoms continued to decrease, treatment strategies were considered to be effective. Authors never mention about the pelvic pain symptoms complained by the patient in the part of physical examination. It is not clear this decreasing pelvic pain whether related from this disease in this sentence alone. Authors should state about pelvic pain in the part of physical examination.

Response: Thanks a lot for the reviewer's comment. The patient's pain comes from lumbar pain, not pelvic pain symptoms; we used the wrong word here, so we used lumbar pain in the revision.

Comment 7:Authors described that Ryan et al. [2] pointed out that after abiraterone treatment for 3 months, the PSA level decreased by more than 50%, while bone scans showed new progression in bone metastases or PSMA aggregation. On the other hand, the case of authors showed new progression in bone scans alone not in PSMA aggregation. Authors should state the difference between Ryan cases and their case.

Response: Thanks a lot for the reviewer`s comment. In this sentence, we intend to say that Ryan et al. discovered the phenomenon of bone flare and named it. It has been corrected in the Manuscript.

In Page 6, Line 22, "Ryan et al. [2] reported that after abiraterone treatment for 3 months, the PSA level decreased by more than 50%, but bone metastasis lesions increase. In Page 6, Line 28, "Our case revealed that bone flare phenomenon also occurs with apalutamide therapy."

Comment 8:Fig 1 Authors described that bone imaging indicated progression on bone. But bone accumulation in A, B: before the treatment decreased in CD: after treatment. This imaging absolutely showed improve of metastases after treatment. should also demonstrate MRI indicated progression of the bone metastasis three months later.

Response: Thanks a lot for the reviewer`s comment. I am sorry that the labeling of the figure in the paper is wrong and it has been corrected.

Response to Reviewer #2:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: The authors describe the evolution of metastatic prostate carcinoma after treatment with apalutamide and ADT therapy. The authors conclude that the effectiveness of such treatment should be made after PSMA-PET-CT examination that in this case report showed that aggregation of PSMA on the bone was significantly reduced. Well written manuscript and useful for clinicians facing with such problems.

Response: Thank you for your affirmation of us, we will continue to improve the manuscript.

Response to Reviewer #3:

Scientific Quality: Grade D (Fair)

Language Quality: Grade B (Minor language polishing)

Conclusion: Rejection

Specific Comments to Authors: The manuscript is not well written, text formatting is not sufficient. This case report manuscript seems to not improve the current literature at all. The aim is not represented in the discussion or in the conclusions, the whole manuscript seems to be a transcription of the patient's medical record. The final message is not strong, patients not reporting embarrassing episodes are common. The current manuscript is rejected.

Response: Thanks a lot for the reviewer's comment. The bone flare phenomenon with apalutamide has not been reported yet. In this case report, we intend to inform the readers that bone flare phenomenon can also occur during the treatment with apalutamide, and share our experience. Our manuscript does have some problems. We are sorry for the unsatisfied experience. We have made a series of changes in writing, format, language, and so on.

Reviewer #4:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: Well written case report. What is the role of bisphosphonate in bone flare? Kindly discuss on this line.

Response: Thanks a lot for the reviewer's comment. We are a little bit confused that the word Diphosphates is not mentioned in the manuscript, we are not sure if you mean alkaline phosphatase. If we misunderstand your meaning, please let us know.

Response to Science editor

This case report describes a case of bone flares in a patient with metastatic hormone-sensitive prostate cancer who was treated with apalutamide and androgen deprivation therapy and summarizes the clinical features after being treated with a novel hormonal therapy. The novel hormonal therapy (gosereline sustained-release implant 3.6 mg monthly and apalutamide 240 mg daily) may be of interest to readers. However, authors need to know that Signed Informed Consent Form(s) or Document(s) cannot be replaced by informed consent for surgery. The number of total references is few and a bit outdated, maybe a little more related references could also be cited. The figure legends should be properly annotated and easy to read and interpret so that readers can understand what is being expressed without reading the full text.

Language Quality: Grade B (Minor language polishing)

Scientific Quality: Grade C (Good)

Response: Thanks a lot for the science editor's comment. The relevant informed consent form has been signed, we are sorry that we did not upload it. In the revised manuscript we have added some corresponding references.

Response to Company editor-in-chief

Response: Thank you for handling our manuscript. We will continue to improve the manuscript.