

Responses to Editor and Reviewers (Point-by-Point)

Reviewer: #1 (Reviewer's code: 02730436)

Comments to the Author

Authors reported a well-defined case report with successfully treated with strict hemodialysis administration and phosphate lowering medication. This case is unique due to fast occurrence of tumoral calcinosis after 24 months renal replacement therapy with peritoneal dialysis.

Response: We thank the reviewer for the positive comment.

However there are some minor concerns to be addressed:

1) Please add your native –English speaker colleague's name and signature to English editing certificate. In addition case presentation section might be divided into like “Chief complaints, History of present illness, History of past illness, Physical examination upon admission, Laboratory examinations, Imaging examinations, Pathological examinations.”

Response:

- As requested by the reviewer we have provided the Name of the native English speaker (line 240) and his signature in the “Non-Native Speaker of English Editing Certificate”.
- As requested by the reviewer we structured the case presentation in the revised manuscript accordingly (lines 90 – 150).

2) How long did the patient followed-up with CKD in pre-dialysis period?

Response: The reviewer brings up an important point. The patient was followed up with CKD in pre-dialysis period consistently for 9 years.

3) Please mention sevelamer carbonate and lantan carbonate dosage? Did the patient tolerate both these medications? When did you stop them? Is the patient still on treatment or not?

Response: The reviewer raises important questions.

- Sevelamer was started by the patient 1 month before admission with a dosage of 800 mg 1-2-1 (lines 113 – 114 and 129) due to increasing phosphate. However at admission (09/2016) the phosphate binder therapy was switched to lantan carbonate with a dosage of 1000 mg 1-1-1 (line 128 and lines 161 - 162) showing an adequate response to the treatment; this was continued until the patient underwent parathyroidectomy (07/2018). Since that time the patient has been on calcium diacetate 950 mg 0-1-1 with an adequate response to the treatment (lines 146 – 147 and lines 162 - 163).
- In addition, the patient was tolerating sevelamer carbonate and lantan carbonate.

4) Authors should implicate the rationale of using both calcitriol and cholecalciferol in this case and discuss the overuse of vitamin D in the occurrence of tumoral

calcinosis. The authors stated that “In our case the patient developed tumoral calcinosis due to insufficient quality of CAPD,” in discussion section. I suggest adding the administration of vitamin D3 medication possibly aggravated the tumoral calcinosis.

Response: The reviewer brings up an important point. The rationale of using both cholecalciferol and calcitriol in this patient was the fact that the vitamin D3 level was clearly below the reference range and the parathormone level was continuously increasing (lines 111 - 112). As suggested by the reviewer we discussed the overuse of vitamin D3 in the revised manuscript (line 184).

5) Please also speculate that potential association of rapid decrease in peritoneal Kt/V via the possible calcification in peritoneal microvasculature. It might be related with the insufficiency of peritoneal dialysis.

Response: We thank the reviewer for bringing up an alternative explanation of rapid decrease in peritoneal Kt/V. This possibility has been discussed in the revised manuscript (line 184 - 186).

6) Please change “CAT” abbreviation in the manuscript as CT as in figure descriptions.

Response: We thank the Reviewer for the comment. We made the suggested change in the revised manuscript.

Reviewer: #2 (Reviewer’s code: 00503182)

Comments to the Author

Some language changes are needed; please follow the comments and highlighted phrases.

Response: We appreciate the reviewer’s comments. We made the suggested changes in the revised manuscript.

Reviewer: #3 (Reviewer’s code: 00503179)

Comments to the Author

The topic: disturbances in calcium phosphate metabolism in chronic renal failure. A case is described with severe tumoral calcinosis around the hips. The cause was insufficient treatment and lack of compliance. After treatment had been adjusted, the calcifications disappeared. The clinical description in text is adequate with supplemental information from a table and CT-scans. Such cases had been reported

earlier. The present paper is easy to read, and modern technology are used. The presentation is pedagogic. Only small language polishing is needed.

Response: We thank the reviewer for the positive comment. We revised the language and made the change in the revised manuscript.

Reviewer: #4 (Reviewer's code: 00503254)

Comments to the Author

In this manuscript, the authors report a rare case of severe tumoral calcinosis with complete remission in a patient having end stage renal disease. This case report is clinically interesting and useful.

Response: We thank the reviewer for the positive comment.

However, there are some points that need to be addressed. Minor comments:

1. The authors should use abbreviations properly.

Response: We thank the reviewer for the comment. We made the suggested change in the revised manuscript.

2. The spacing used for abbreviations is not correct.

Response: We thank the reviewer for the comment. We made the suggested change in the revised manuscript.

3. The authors performed parathyroidectomy due to tertiary hyperparathyroidism. Why did they not use cinacalcet hydrochloride?

Response: The reviewer brings up an important point. Due to continuously increasing parathormone level the patient was indeed treated with etelcalcetid (10/2017 - 12/2017) and cinacalcet hydrochloride (12/2017 – 08/2018) (lines 144 – 145 and lines 163 - 165). However parathormone remained in a range between 600 to 1000 pg/ml, despite pharmaceutical treatment leading to the indication for parathyroidectomy.

Editor

1) Please provide the manuscript documents in word version so that we can edit.

Response: As requested by the editor we have now provided the revised manuscript as a word file.

2) Running title. A short running title of no more than 6 words should be provided. It should state the topic of the paper. For example, Losurdo G et al. Two-year follow-up of duodenal lymphocytosis. (no more than 6 words).

Response: As requested by the editor we changed the running title in the revised manuscript (lines 1-2).

3) *Author contributions: Please provide the author contributions. See the format in the attachment file-revision policies.*

Response: As requested by the editor we have now provided the authors contributions in the revised manuscript (lines 22-26).

4) *Key words: (no less than 5-10 keywords)*

Response: As requested by the editor we have now provided key words in the revised manuscript (lines 59-62).

5) *Core tip: Please write a summary of less than 100 words to outline the most innovative and important arguments and core contents in your paper to attract readers.*

Response: As requested by the editor we have now provided a core tip (lines 64-73).

6) *Under the heading of Case Presentation, the following seven aspects must be presented in this order: 1) Chief complaints; 2) History of present illness; 3) History of past illness; 4) Personal and family history; 5) Physical examination upon admission; 6) Laboratory examinations e.g., routine blood tests, routine urine tests and urinary sediment examination, routine fecal tests and occult blood test, blood biochemistry, immune indexes, and infection indexes; and 7) Imaging examinations e.g., ultrasound, plain abdominal and pelvic CT scan, high-resolution chest CT scan, and head MRI. The patient case presentation should be descriptive, organized chronologically, accurate, salient, and presented in a narrative form.*

Response: As requested by the editor we have now provided in the revised manuscript required outline of the case presentation (lines 90-150).

7) *Please provide the decomposable figure of all the figures, whose parts are all movable and editable, organize them into a PowerPoint file, and submit as "Manuscript No. - image files.ppt" on the system. Make sure that the layers in the PPT file are fully editable. For figures, use distinct colors with comparable visibility and consider colorblind individuals by avoiding the use of red and green for contrast.*

Response: As requested by the editor we have now provided and uploaded all figures as .pptx files.