

Dear Editor,

We'd like to thank the reviewers for their careful readings and valuable comments concerning our manuscript entitled "**Clinical and genetic features of cerebrotendinous xanthomatosis**" (Manuscript NO: 57897). We believe the constructive feedback will improve the manuscript and increase its potential impact to the community. We read the comments carefully and made revision according to the suggestions. Revised portions are marked in red in the manuscript. The main corrections in the manuscript and the responses to the reviewer's comments are as follows:

Responses to the reviewer's comments:

Reviewer #1:

1. Response to comment: "The patient is a 47-year-old male mainly manifesting psychiatric signs but none of the cardinal features of CTX such as cataracts, cerebellar ataxia, pyramidal signs and chronic diarrhea", this sentence is not accurate as the patient has enlarged Achilles tendons and nodules on the bilateral tibial tubercles.

Response: We have re-written this sentence according to the reviewer's suggestion. "The patient is a 47-year-old male mainly manifesting psychiatric signs but without some cardinal features of CTX such as cataracts, cerebellar ataxia, pyramidal signs and chronic diarrhea."

2. Response to comment: The patient had a poor mental state, did he evaluated by any neuropsychiatric scale?

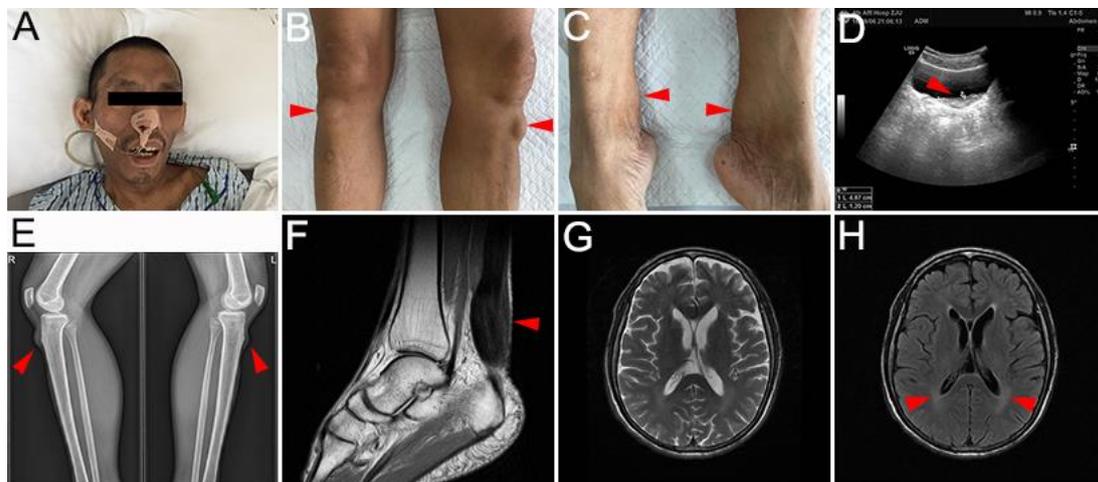
Response: No. We are regretful that we failed to achieve the patient's cooperation on neuropsychiatric scale evaluation because he was unable to answer questions during the most time of his hospitalization, though it is really true as reviewer suggested that neuropsychiatric scale is important for recording and comparing the patient's condition.

3. Response to comment: "Cerebrospinal fluid (CSF) was mildly elevated: 680.4 mg/L (normal range: 150-400 mg/L)." What does this sentence mean?

Response: We are very sorry for our confusing writing and have made correction as follows: "Cerebrospinal fluid (CSF) protein was mildly elevated: 680.4 mg/L (normal range: 150-400 mg/L)."

4. Response to comment: Specific abnormalities in figures should be marked with arrow(s) to more clearly point out abnormalities for non-CTX experts. Figure 2H, white matter defects.

Response: As reviewer suggested, we added two arrowheads in Figure 2H to clearly point out the abnormal hyperintense signal around the ventricle posterior horn bilaterally.



5. Response to comment: First-line treatment of CTX is based on chenodeoxycholic acid (CDCA) replacement therapy. Authors need to explain why this patient did not receive CDCA treatment.

Response: We are very sorry for our negligence of reporting the CDCA treatment in this patient. He was provided with 0.25g of CDCA three times per day in our hospital. He has persisted this medication until now.

6. Response to comment: As a Chinese CTX case report, I suggest the authors to cite some of the Chinese CTX reports, such as: Tao et al. Clinical and genetic characteristics of Chinese patients with cerebrotendinous xanthomatosis. *Orphanet J Rare Dis.* 2019 Dec 3;14(1):282. doi: 10.1186/s13023-019-1252-9. Chen et al. Clinical and molecular genetic features of cerebrotendinous xanthomatosis patients in Chinese families. *Metab Brain Dis.* 2017 Oct;32(5):1609-1618.

Response: We thank the reviewer for mentioning the papers of Tao et al.(2019) and Chen et al. (2017). Both papers are certainly related work and should be discussed, with which we were previously familiar but neglected to cite. Tao and Chen's papers identified novel mutations in CYP27A1 and concluded clinical and genetic characteristics of Chinese patients with CTX. We have included them as references in the revised version.

Special thanks to you for your good comments.

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