Author's response to reviews

Title: "Hereditary hyperferritinaemia cataract syndrome - first cases in Switzerland?"

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Author's response to reviews:

Dianne Pangan
Journal of Medical Case Reports
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Dear Mrs. Pangan,

Firstly, we would like to thank you for the review of our manuscript "Hereditary hyperferritinaemia cataract syndrome - first cases in Switzerland?"

We are happy to insert the reviewers comments in the revision.

Below, you will find detailed comments to each point of the reviewer`s report.

Yours sincerely

A. Kröger
Reviewer 1 (Gunda Millong)

Because the English seems poor, we will have the paper proof-read by an English speaking person.

Reviewer 2 (Domenico Girelli)

Major points:

1. “HE” is not an acronym actually used for hereditary hemochromatosis: please use HH.
   - In the whole manuscript the acronym for hereditary hemochromatosis has been changed from “HE” to “HH”.

2. Since the Authors claim that these are the first cases to be diagnosed in Switzerland, it should be useful to have information about the geographical origin of the two families.
   - In both case reports you will find information about the geographical origin. The first patient is a Caucasian male probably from Switzerland. The second patient, also Caucasian, is an orphan, so there is no family history available.

3. Discussion, first sentence: please start with “HFE-related HH” rather than simply with “hemochromatosis”, since the latter term generically includes also rare forms like those related to Tfr2, HJV, HAMP and Ferroportin genes.
   - We added the term “HFE-related” in this sentence.

   - The sentence was amended and the reference from Heilmeyer et al has been cited.

5. Discussion about aceruloplasminaemia: this disease is always characterized by neurological symptoms, although indeed diabetes is generally the first
manifestation. Please delete “with or without” (neurological symptoms).

- “with or without” has been deleted.

6. Discussion about ferritin: please insert “Under normal conditions,” before “serum ferritin values correlate quite precisely with body iron stores…”.

- We rephrased the sentence to “In healthy individuals………”.

7. Moreover, glycosylated (G) ferritin is only present in serum. Re-phrase as follows: “Ferritin, the intracellular iron storage molecule, is a heteropolymer composed of 24 subunits, H and L, variously assembled. On the other hand, serum ferritin consists mainly of L subunits which can also be glycosylated (G).”

- We inserted this text in the appropriate section.

8. I do not completely agree on the sentence: “Genetic confirmation should be obtained”. Typical cases, i.e. those with otherwise unexplained hyperferritinaemia co-segregating with autosomal dominant juvenile cataract are sufficiently diagnosed by medical history and biochemical analyses. Please address this point.

- We agree and have added that there is no need for genetic confirmation in really typical cases.

9. I do not understand the meaning of the final sentence: “In the recent discovery of new proteins involved in the iron metabolism, we consider it as useful to know the clinical picture of HHCS.” It should be re-phrased or even deleted.

- The sentence has been deleted.

10. Some sentences need complete rewording: for instance: “In no other up to know examined body part in HHCS was another accumulation of L-Ferritin found”. Rephrase as: No involvement of organs other than the eye have been reported in patient’s series until now (cite: Girelli D et al. Brit J Haematol 2001; 115:334-340).

- The sentence has been re-phrased and the citation added.
11. Type errors and language inconsistencies

- Type errors and language inconsistencies in the whole manuscript have been improved and because of the poor English, we sended it to a native speaker for correction.