Author's response to reviews

Title: Bilateral macular hemorrhage as a complication of drug induced anemia: A case report

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Author's response to reviews: see over
Kindly attention of the Editors,

Thank you very much for your reviewer’s considerations on our paper “Bilateral macular hemorrhage as a complication of drug induced anemia: A case report”. All of the suggestions of the referee were attended. The comments of the referee are indicated below, in bold, and followed by the respective amendments:

Referee 1:

This is an interesting case of drug-related bilateral macular hemorrhage. Bilateral macular hemorrhage has been reported in a case of autoimmune hemolytic anemia, as the authors cited. The present ocular finding due to drug toxicity in this case is rare, but not so surprising if cause-effect relation existed. The authors hypothesized that substitution of folic acid with folic acid might be the contributing factor causing bilateral macular hemorrhage, via bone marrow toxicity. The authors, however, should explain and discuss why macular hemorrhage could occur in the absence of thrombocytopenia. Namely, the link between bone marrow toxicity, absence of thrombocytopenia and macular hemorrhage should be discussed.

R1: The explanation for retinal hemorrhages in the presence of anemia without thrombocytopenia is not clear. Factors such anoxia, venous stasis, angiospasm, and increased capillary permeability have been implicated in the pathogenesis of anemic retinopathy. This information has been added to the discussion and references were added to support it.

Specific comments:

1. Specify the prior ocular findings of toxoplasmosis in this patient.

R2: At presentation in our emergency room the patient only had a small focal area of retinal scar from his previous ocular toxoplasmosis 3 months before. This was further explained in the case presentation.
2. Specify the duration of medication prior to this episode.
R3: This information was added to the case presentation.

3. 4 gr should be 4 gm (?); 7,5 mg should be 7.5 mg
R4: Units were corrected: 4 gr as 4g (grams) and 7,5 to 7.5 mg.

4. Is the recovery time course (Hgb from 4.2 to 10.8) compatible with the drug-induced bone marrow toxicity?
R5: Yes, this recovery time is compatible with the bone induced anemia since the patient had stopped using the medication 15 days prior to his visit to the emergency room.

5. Discuss the contributing role of anemia and neutropenia to macular hemorrhage (especially when thrombocytopenia is not present).
R6: Detailed in response R1.

Referee 2:

I recommend the publication of this case with minors revisions. I think that the information written in the introduction may be support by references.
R7: References were added to support the information in the introduction.

Still in introduction I suggest that the authors may include SNC infection as clinically important.
R8: We agree with that CNS infection is clinically important, but in the introduction we were enumerating particular patients in which toxoplasmosis is clinically relevant. We did not detail clinical findings of immunosuppressed patients or children with congenital infection.

Finally the patients with ocular toxoplasmosis must be treated for 4 to 6 weeks instead of 6 to 8 weeks.
R9: Changed from 6 to 8 weeks to 4 to 6 weeks.

Thank you very much for your comments, we concur that those changes enriched our manuscript.

Sincerely yours,