Author’s response to reviews

Title: Spontaneous closure of a traumatic macular hole in a 50 year old female

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Author’s response to reviews: see over
Dear Editor
Thank you for giving us the opportunity to revise and re-submit our manuscript entitled: “A probable mechanism of spontaneous closure of a traumatic macular hole: the role of autologous serum”

With respect to the reviewers’ comments we have the following remarks:

Reviewer # 1
1. Reason behind high frequency of TMH in young population and low in older population needs to be mentioned in Introduction section.
We mention in the introduction the reason of TMH higher frequency in younger patients

2. The final consequences a patient faces due to traumatic macular holes needs to be mentioned in Introduction section.
We added a sentence in the introduction about the consequences of TMH per your request

3. Treatment available and recovery period usually required should be described in brief in Introduction section.
We added a sentence in the introduction as per your request

4. The figures should be subdivided and pointers should be used to describe the area of discussion.
We changed the figures, to match the legends and points of discussion

5. Full form of ETDRS needs to be mentioned
ETDRS abbreviation is explained in Case presentation, page 4, first paragraph

6. The case needs to be elaborated with respect to the reasons which prevent the hole closure at higher age.
We added the second paragraph in the discussion section, explaining the above, as requested

7. The details of treatment or medications administered to the patient in present case should also be demonstrated.
We added a comment at “Case presentation” first paragraph that “the past medical and ocular history was unremarkable.

Reviewer #2
Comments to authors:
Thank you for your nice comments.
As per your suggestion, the conclusion of the abstract section was revised, and the very last sentence “despite patient age and post-traumatic PVD” was removed.
Reviewer #3

1. Title: The title used for the manuscript is not appropriate. One case is not enough in order to propose a mechanism of spontaneous TMH closure. Also, the words “the role of autologous serum” cannot form part of the title either, since no autologous serum was used in the study. The only words appropriate for the title are those used by the authors as a second heading, that is “Spontaneous traumatic macular hole closure in a 50-year-old female”.

Indeed, we did not use in vivo any autologous serum, but we explain in detail page 5, second paragraph that “In our case, the clot in the TMH base (potentially a hemorrhage by-product), containing a significant quantity of platelets may have simulated the clot observed after autologous serum use, thus facilitating a similar effect. This may have stimulated glial cell migration and proliferation, thus contributing to spontaneous hole closure despite patient age”.

The title was rephrased to “Spontaneous traumatic macular hole closure in a 50-year-old female”.

2. Abstract, line 3: “We report for the first time …”. As explained in comment no.4, this is not the first time that such a case is reported. The comment “for the first time was removed as per your suggestion

3. Abstract, conclusion: The entire conclusion of the abstract is speculative. These thoughts may be included in a paragraph of the Discussion (with the appropriate reference support), but the conclusion of the abstract must be based only on the findings of the case described.

Conclusion of the abstract is indeed speculative; in the vast majority of research published (even in RCTs or experimental models) the authors explain the study findings speculating and proposing mechanisms. Our case report fell into this category.

4. Discussion, first paragraph: “Spontaneous TMH closure is common, but there are no published data in patients over 30s.” This statement is not true. Spontaneous closure of TMH has been previously reported in a 56-year-old woman (Menchini et al. Retina 2003;23:104-6).

Discussion first paragraph was changed to “but highly infrequent in patients over 30s.”

5. Discussion, second paragraph: “Three mechanisms have been proposed for TMH resolution: cell proliferation at the TMH base, contractile epiretinal membrane formation resulting in TMH shrinkage and closure and foveal PVD resulting in the release of anteroposterior traction [4].” First of all, the reference used to support this statement is a case report, and the only probable mechanism for TMH closure that it mentions is “the bridging of the protruding retinal tissue over the macular hole”. Second, the three mechanisms mentioned above by the authors have been proposed to explain spontaneous closure of “idiopathic” macular hole, not “traumatic” one. And third, epiretinal membrane and/or foveal PVD are unlikely mechanisms of macular hole closure in young patients, who constitute the group of patients mostly affected by TMH.
We removed the entire paragraph, that was referring to idiopathic MHs. Instead, we added a reference regarding TMHs and their pathophysiology, in the second paragraph of the discussion section

6. Discussion, third paragraph: “The unique feature …”. As explained in comment no.4, this is not a “unique” feature of the presented case. The wording “unique feature” was changed to “distinct feature”

7. Discussion, third paragraph: “The serum beneficial effect may be due to the presence of growth factors (…) and cytokines”. A reference is needed here. The reference was added per your suggestion

8. Discussion, third paragraph: “The serum beneficial effect …”. There has been much controversy about whether such an effect exists. Autologous serum has been used in combination with vitrectomy, so the beneficial effect could be due to the vitrectomy. Besides, a randomized clinical trial on 185 eyes from Moorfields, with a two-year follow-up, comparing natural history, vitrectomy, and vitrectomy plus autologous serum for idiopathic full-thickness macular hole, found that the “use of autologous serum did not seem to affect anatomic or visual results”, concluding that “autologous serum application does not enhance the results of surgery (Ezra et al. Arch Ophthalmol 2004;122:224-236).
We agree with your comment that the autologous serum in the studies you mentioned was used in combination with vitrectomy, so the beneficial effect could be due to vitrectomy. Nevertheless, in our case, the possible effect of autologous serum was without an additional PPV. In fact, for all traumatic macular hole cases, the possible presence of blood and serum, might play a role in promoting hole closure and this may explain in part the higher “spontaneous” closure rates in TMH cases. To speak in absolute terms, one would have to review each TMH case that closed without surgery and look for the presence of blood that might have played a role in hole closure.
Reviewer # 4
Comments to authors:
1. Please add more information on the previous systemic and ophthalmic history of the patient (i.e. any previous ophthalmic surgery or trauma, any medications used etc).
   We added a comment at “Case presentation” first paragraph that “the past medical and ocular history was unremarkable.

2. The hypothesis of a blood clot promoting closure of a macular hole is very interesting. To confirm this hypothesis, an animal model of vitreous hemorrhage and macular hole formation may be helpful. The authors could comment on this point.
   We much agree to your point but an animal model in this cases would be inappropriate, as vitreous dynamics and volume might also play a role in terms of mechanics.
   In vivo, for all traumatic macular hole cases, the possible presence of blood and serum, might play a role in promoting hole closure and this may explain in part the higher “spontaneous” closure rates in TMH cases. To speak in absolute terms, one would have to review each TMH case that closed without surgery and look for the presence of blood that might have played a role in hole closure.