Author’s response to reviews

Title: Macular and optic disc edema and retinal vascular leakage in familial amyloid polyneuropathy with a transthyretin Val30Met mutation: a case report

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Author’s response to reviews: see over
Dear Editor,

We would like to thank the reviewers for their analysis of this manuscript. We will address, point by point, the suggestions expressed by both reviewers:

Reviewer: Dr. Ruifang Sui

**Comment:** Please describe the changes in the peripheral retinal, both eyes.

**Answer:** We thank you for this important observation. The following sentence was added to the Case Presentation section: “No vitreous opacities were observed and the retinal periphery was normal bilaterally”.

**Comment:** Please perform LPP and follow at least a month before report this case.

**Answer:** Intravitreal dexamethasone implant and LPP were performed and the follow up is reported.

Reviewer: Dr. Tatjana Josifova

**Comment:** Laboratory results considering the liver function are not given in the study.

**Answer:** We agree that this data is important and should be present in the manuscript. Therefore, the following sentence was added: “Liver function tests were also unremarkable (aspartate aminotransferase 27 U/l, alanine aminotransferase 30 U/l,
gamma-glutamyl transferase 26 U/l, alkaline phosphatase 132 U/l, lactate dehydrogenase 421 U/l, total bilirubin 1.30 mg/dl, albumin 4.40 g/dl).”

**Comment:** Only the past history medication could not be relevant for the recent statues and cannot exclude the probability of retinal changes due to medication at present.

**Answer:** The reviewer raises an important issue. It is true that we cannot exclude the possibility that these retinal changes could be related to patient’s medication. In this regard, the following sentences were added to the discussion: “We cannot exclude the hypothesis of toxic microangiopathy related to drugs such as sirolimus or tacrolimus. However, the limitation of this reaction to the eye and the positive response to local intravitreal therapy favors, in our opinion, the hypothesis of FAP related ocular complications. Thus, this is probably the first report of optic disc edema, retinal vascular leakage and cystoid macular edema in a patient with FAP.”

**Comment:** The FA findings on fig. 1 do not exactly show a leakage of the small capillary vessels. A combination of staining and leakage could be detected parafoveal. On the other hand the OCT findings showing an advanced CMS -subfoveal do not match at all with the FA findings. It's very unlogical that the advanced intraretinal and subretinal CME seen at the OCT findings is not present at the FA findings.

**Answer:** It is true that the cystoid macular edema revealed by the OCT (figure 2) does not seem to match the one seen on FA (figure 1). However, we believe that an angiogram picture taken at a later stage than the one we presented would certainly show more macular hyperfluorescence. Unfortunately, we do not have a proper later frame to show.
Comment: Fig. 3 showing the FA of the right eye does not exactly present an optic nerve edema, but it shows a pulling of the dye at the edges of the optic nerve.

Answer: The reviewer is right at this point. We thank you for the comment and the corresponding change was made in the manuscript: “RE FA at 4’00’’ reveals staining of the optic disc margins (bottom left).”

Comment: The further recommended treatment of the right eye at this stage of the "changes" is not necessary since no ME or ischemic retinal changes are detected on the FA or OCT results. Moreover the recommended LPP does not explain the treatment modality (focal or panretinal) LPP.

Answer: We agree it is not advisable to treat the right eye at this stage. Therefore we removed that point from the discussion section. Panretinal laser photocoagulation modality of the left eye was specified in the text.

Comment: It is not clear why does the initial treatment of the left eye include only two injections of intravitreal anti-VEGF therapy when the recommended up-loading dosage always includes three injections application. No OCT results are presented after the second injection to show that two injections were enough for a successful therapy.

Answer: Given the lack of studies regarding the effect of intravitreal injection of anti-VEGF in FAP retinal complications we decided to adopt a treat-and-observe strategy. Given the incomplete response to this drug we decided to try intravitreal corticosteroids
which proved to be more effective. A macular OCT following the second injection of bevacizumab was added to the manuscript (figure 4).