Author's response to reviews

Title: Recurrent Symptomatic Intraocular Pressure Spikes during Hemodialysis in a Patient with Unilateral Anterior Uveitis: case report

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Author's response to reviews: see over
Dear Executive Editor Aime

Thank you very much for your encouraging comments on our manuscript entitled "Recurrent Symptomatic Intraocular Pressure Spikes during Hemodialysis in a Patient with Unilateral Anterior Uveitis: case report" (MS: 7310376778258418). Enclosed is the first revised version of the manuscript. We hope that we have adequately answered the reviewer's questions. We did our best to shorten the manuscript, and we had it reviewed thoroughly by an English-proficient medical editor. The list of modifications reflected in the revised manuscript and our replies to the comments of the reviewers are also enclosed.

Additionally, we appreciate the insightful comments of Dr. Jaime Levy and Dr. alireza R. Ghaffarieh. We have revised the manuscript and provided point-by-point responses according to the two reviewers' comments, as follows.

**Response to Dr. Jaime Levy's Comments**

MINOR ESSENTIAL REVISIONS

Case Presentation

1. Did the patient have any previous uveitis episodes?

   No, he had none by past medical histories.

2. Please provide details of the fellow eye.

   We added the following sentence in "Case Presentation Section", (Page 4, Lines 9-11):

   "The unaffected fellow eye did not show abnormal findings from the full ophthalmic examination, except for laser photocoagulation scar due to diabetic retinopathy."
3. Did the authors find any gonioscopic differences between the right and left eye?

Thank you for insightful advice. We added the following paragraph.

In Case Presentation Section, (Page 4, Lines 3-7)

"The gonioscopic findings showed a wide open-angle status (Grade 4, using Shaffer's classification) and mild pigmentation (Grade 1~2+) of the trabecular meshwork without angle neovascularization or peripheral anterior synechiae in both eyes. A more densely pigmented trabecular meshwork was observed in the left eye than in the right eye."

4. Was there any difference in the hemodialysis protocol over the last years?

There was no difference in the hemodialysis protocol over the last years.

5. The treatment between HD sessions needs to be clarified (steroid drops and anti-glaucomatous treatment).

We added the following details on the use of the steroid drops and the anti-glaucomatous treatment between the hemodialysis sessions.

In Case Presentation Section, (Page 4, Lines 13-15)

"The patient was initially treated with a fixed combination of dorzolamide-timolol eyedrops (twice a day), brimonidine eyedrops (twice a day), oral methazolamide (100 mg/day) to control his IOP, and 1% prednisolone acetate every two hours to manage inflammation."
6. Was there any iris atrophy developing during follow-up period?

We added the following sentence in Case Presentation Section, (Page 4, Lines 2-3): "No sectorial iris atrophy or iris heterochromia developed during the follow-up period, which suggests herpetic keratouveitis or Fuchs' heterochromic iridocyclitis."

Discussion

1. Do the authors think the HD triggered the uveitis and subsequently, the high IOP?

After the initiation of the application of the topical steroid eyedrops, the degree of intraocular inflammation did not worsen, regardless of the hemodialysis sessions. However, the IOP spikes associated with ocular pain did not subside despite the improvement of inflammation. Therefore, the authors do not think HD triggered the uveitis and subsequently, the high IOP.

2. Please provide the differential diagnosis for hypertensive uveitis related or unrelated to the hemodialysis.

Thank you for kind advice. We agree with the reviewer's opinion that the differential diagnosis for hypertensive uveitis should be provided, so we added the following paragraph.

In the Discussion Section (Page 6, Lines 3-13)

"A wide variety of inflammatory diseases are associated with ocular hypertension, such as Fuchs' heterochromic iridocyclitis, glaucomatocyclitic crisis, herpetic keratouveitis, sarcoidosis, rheumatoid arthritis, and syphilis [14]. Therefore, careful
patient evaluation is essential for accurate diagnosis and understanding of the pathogenesis of glaucoma. Especially, specific signs, patterns of IOP elevation, and past medical histories may also be evident in certain types of uveitis [14]. In our patient, the slit-lamp examination showed an intact corneal epithelium and some keratic precipitates without sectorial iris atrophy. Moreover, the gonioscopy revealed a wide open-angle status and mild pigmentation of the trabecular meshwork without angle neovascularization or synechiae. The results of the serologic test for syphilis, the HLA-B27, and the chest radiology findings were normal. Therefore, the authors diagnosed idiopathic acute anterior uveitis."


3. May the authors provide some explanation for the disappearance of the uveitis after trabeculectomy?

Thank you for kind advice. We added the following paragraph: (Page 6, Line 25 - Page 7, Line 6)

"In a previous study of Strvrou and Murray [17], they reported that trabeculectomy might have a beneficial effect on the course of uveitis. They suggested that the improved aqueous outflow might allow the egression of inflammatory mediators from the anterior chamber. Furthermore, Weinreb [18] suggested that an anti-metabolite had a beneficial effect on intraocular inflammation, and some researchers [19] suggested that 5-FU might play a role in the management of anterior uveitis. Thus, trabeculectomy with adjunctive mitomycin C may theoretically improve uveitis and yield a successful surgical outcome."


4. Please discuss the unilateral occurrence of the intraocular high pressure besides the outflow facility.

   Thank you for insightful advice. We added the following discussion of the IOP spikes besides the outflow facility: (Page 5, Line 23- Page 6, Line 2)

   "Besides the compromised outflow facility, Rever et al. [12] reported that the anterior chamber depth decreased significantly during the HD. Moreover, Jaeger et al. [13] cited patients with narrow angles by gonioscopy who experienced an IOP rise during HD. In this context, gonioscopy is thought to be essential to the accurate diagnosis of IOP spikes related to HD."


Response to Dr. alireza R. Ghafrarieh's Comments

1. Did patient develop sign of uveitis after surgery during HD again?

Thank you for insightful advice. We added the following sentence in Case Presentation (Page 4, Line 24-25)
"Furthermore, the patient did not develop again signs of uveitis after the trabeculectomy during hemodialysis."

2. What was the condition of the angle? Any PI?

Thank you for insightful advice. We added the following paragraph.
In Case Presentation Section, (Page 4, Lines 3-7)
"The gonioscopic findings showed a wide open-angle status (Grade 4, using Shaffer's classification) and mild pigmentation (Grade 1+~2+) of the trabecular meshwork without angle neovascularization or peripheral anterior synechiae in both eyes. A more densely pigmented trabecular meshwork was observed in the left eye than in the right eye."

3. What is the cause of uveitis?

Thank you for kind advice. We agree with the reviewer's opinion that the differential diagnosis for hypertensive uveitis should be provided, so we added the following paragraph.
In the Discussion Section (Page 6, Lines 3-13)
"A wide variety of inflammatory diseases are associated with ocular hypertension, such as Fuchs' heterochromic iridocyclitis, glaucomatocyclitic crisis, herpetic keratouveitis, sarcoidosis, rheumatoid arthritis, and syphilis [14]. Therefore, careful patient evaluation is essential for accurate diagnosis and understanding of the
pathogenesis of glaucoma. Especially, specific signs, patterns of IOP elevation, and past medical histories may also be evident in certain types of uveitis [14]. In our patient, the slit-lamp examination showed an intact corneal epithelium and some keratic precipitates without sectorial iris atrophy. Moreover, the gonioscopy revealed a wide open-angle status and mild pigmentation of the trabecular meshwork without angle neovascularization or synechiae. The results of the serologic test for syphilis, the HLA-B27, and the chest radiology findings were normal. Therefore, the authors diagnosed idiopathic acute anterior uveitis."


Again, we thank you very much for giving us the opportunity to revise and improve our manuscript and for your consideration. We hope our manuscript is now suitable for publication in BMC Ophthalmology. Thank you in advance.

If you have further questions, please feel free to contact me:

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Sincerely yours,

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