Author's response to reviews

Title: A case with transient refractive change after removal of pituitary tumor

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Author's response to reviews: see over
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Editor-in-Chief
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Dear Editor-in-Chief,

My colleagues and I thank you and the 3 reviewers for the very helpful feedback on our paper. Basically, we totally agree with all of their important comments, and have tried hard to incorporate all their suggestions into our revised manuscript. Specific and detailed responses to each and every review comment are listed below.

SPECIFIC RESPONSES TO EACH REVIEWER COMMENT

Reviewer 1:

Reviewer’s report:
The analysis presented in the paper is very interesting but has not been studied and discussed thoroughly. The authors have missed the refractive change produced by changes in anterior chamber depth like that during athalamia after glaucoma surgery or ocular trauma.

Refractive change of the eye is affected by a combination of possible changes in axial length, corneal power, anterior chamber depth and lens power. Besides, the power of the lens depends on its thickness, its curvatures and its gradient of refractive index. The authors have not accounted for possible changes in corneal power and it is not clear whether they measured corneal radius. If that were the case and they have corneal radius measurements, then they could calculate lens power for the changing distance refraction with Bennett’s formula (see references). Then they could show that the changing refraction in the hyperopic direction described was caused by a decrease in lens power.

As can be seen in the table I have made with the data they show in figure 2, the posterior pole of the lens (calculated as anterior chamber depth + lens thickness) did not change during the study period. The increase in lens thickness caused by hyponatremia matches the decrease in anterior chamber depth. If the lens was swollen in its position sustained by the zonule and the ciliary processes, then one would expect a backward movement of the posterior pole at least equal to half the increase in lens thickness. But that was not the case, as the posterior pole of the lens did not recede in this particular case. Dubbleman has shown with Scheimpflug images that, with increasing age, while the lens thickens, the posterior pole recedes a little (and the anterior chamber decreases by a similar amount) leaving the lens in its position. So one could argue that,
in this case report, the possible swelling of the ciliary processes that may have accompanied the lens swelling, somehow protruded the lens into the anterior chamber. At least, that is what is suggested by the analysis of the reported changes in lens thickness and anterior chamber depth.

Then, if that were the case, one could say that a decrease in the anterior chamber depth would produce a myopic shift, while an increase in lens thickness would produce an hyperopic shift (optically speaking, a thicker lens is less powerful). These two changes would compensate each other. What happened in the meantime with the lens curvatures and its gradient index? What happened with the lens equatorial diameter? Although these cannot be measured, if the authors have corneal power they could calculate lens power as I said. That would show that a decrease in lens power is the answer for the hyperopic shift seen with hyponatremia. If that were not the case and the authors did not measure corneal power and cannot calculate lens power, at least this hypothesis should be discussed as a possible explanation, because the increase in lens thickness and the decrease in anterior chamber depth they found, cancel each other and would produce no refractive change. I recommend that they read the following references.

Table. Anterior chamber and lens thickness changes in mm.

<table>
<thead>
<tr>
<th></th>
<th>Anterior Chamber D</th>
<th>Lens Thickness</th>
<th>Lens Posterior Pole</th>
</tr>
</thead>
<tbody>
<tr>
<td>At onset</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OD</td>
<td>3.05</td>
<td>4.21</td>
<td>7.26</td>
</tr>
<tr>
<td>OS</td>
<td>3.1</td>
<td>4.03</td>
<td>7.13</td>
</tr>
<tr>
<td>At follow up</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OD</td>
<td>3.34</td>
<td>3.89</td>
<td>7.23</td>
</tr>
<tr>
<td>OS</td>
<td>3.23</td>
<td>3.9</td>
<td>7.13</td>
</tr>
<tr>
<td>Difference (onset minus follow up)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OD</td>
<td>-0.29</td>
<td>0.32</td>
<td>0.03</td>
</tr>
<tr>
<td>OS</td>
<td>-0.13</td>
<td>0.13</td>
<td>0</td>
</tr>
</tbody>
</table>


Response: We really thank the reviewer for their helpful comments and informing us of important knowledge about refractive change. We totally agree with the reviewer’s suggestions and have read the references that the reviewer suggested. Then, we re-built the discussion section. The details are following response to Discussion.

Specific:
Abstract.
In conclusion, after the words “is proposed” there should be a “:” and after it should say “...in the aqueous humor with lens swelling”.

Response: we now changed the abstract as the reviewer suggested.

Background:
The first paragraph should be changed to add anterior chamber depth and lens power as explained. “And one cannot say that RC changes with age” as this is redundant. One should say that “Refraction changes with age”.

Response: we have now changed the background as the reviewer suggested and added the description about the refractive error changes with age.

Case presentation:
Figure 2 is very clear. There you can see that while the lens decreases thickness the anterior chamber depth increases by the same amount.

Response: We added the description about the same amount of lens decreases thickness and anterior chamber depth increases in case presentation section and Table 1 at the end of the revised text.
Discussion:
Consider discussing the conflictive findings in the anterior chamber depth and explain that possible changes in lens curvatures or gradient index may be the cause of the hyperopic shift found. To say that lens thickness change explains all the findings seems too simplistic.

Response: Now we have reconstructed the discussion section totally incorporating your suggestions. Please see the discussion section in the revised version.

Reviewer 2:
Reviewer’s report:
The authors report 62-year-old woman who experienced a temporary refractive change after trans-sphenoidal surgery.
Major Compulsory Revisions
What was the corrected visual acuity during the refractive change?

Response: Now we have added the description about the corrected visual acuity during the refractive change in the case presentation section on revised version as follows: And also, the corrected visual acuity was not changed during the follow-up.

Please provide the keratometry data before during and after the change.

Response: We totally agree with this comment. We have provided the keratometry data in Figure 2 and in the case presentation section of the revised version.

Reviewer 3:
Reviewer’s report:
While the case report is novel, the discussion is incomplete (see below). I recommend that the discussion be reworked to include a better explanation for why this patient had a hyperopic shift, and include more reference to papers about myopic and hyperopic shifts due to systemic electrolyte imbalance.

Specific:
The presented theory about increased lens thickness as the cause of the patient's hyperopic shift is inadequate. Increased lens thickness alone should result in a myopic shift. However, if the hyponatremia and resultant aqueous influx into the lens caused a decrease in the refractive index of the lens, this could counteract the increased lens thickness and result in a net hyperopic
shift. This is most likely the reason behind the patient's hyperopic shift, and should be addressed. Both hyperopic and myopic shifts have been thoroughly described in hyperglycemic patients, and the following article by Wiemer et al. provides a nice explanation and summary: Wiemer, NGM, et al. Refractive properties of the healthy human eye during acute hyperglycemia. Graefes Arch Clin Exp Ophthalmol, 2008; 246:993-8.

Response: We thank the reviewer for this comment and totally agree. In the discussion, we have now added the description about the relationship of refractive index of the lens and a net hyperopic shift.

Specific:
The first line of the case presentation should read “thyroid dysfunction” rather than “thyroidal”.

Response: “thyroidal” was now corrected to “thyroid” in the case presentation.

Altogether, we hope that our revised paper is improved. And also, we believe that our paper may be an important case report for refractive changes following systemic disorder.

Sincerely,

Hiroto Ishikawa and all co-authors

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Thank you for your consideration.
Yours sincerely,

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