Author's response to reviews

Title: Congenital cystic eye associated with a low-grade cerebellar lesion that spontaneously regressed

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

We are grateful that you consider our paper interesting for publication in your journal. We revised the paper according to the reviewers suggestions. We provided a cover letter giving a point-by-point response to the concerns. All the corrections have been highlighted in yellow in the text.

**Major compulsory revisions**

1. Although the authors state that cerebellar lesion of possible glial origin has not been previously reported in association with congenital cystic eye, this is not the first report. Mehta et al. (J Pediatr Ophthalmol Strabismus. 2010 Aug 23;47 Online:e1-4. doi: 10.3928/01913913-20100818-13. Congenital cystic eye: a clinicopathologic study,) also reported ectopic glial tissue in the brain in association with a congenital cystic eye. The authors may consider revising their paper in regard with this publication (especially localization?).

   In discussion section, we mentioned the report of Mehta et al. and revised the statement of the “first report” in the light of this paper. We emphasized the cerebellar localization, not previously described as the site of glial tissue, associated with the congenital cystic eye.

2. Additionally, the suggestion to perform early MRI in children with ocular malformations, as the authors state in their conclusion, is not novel, since it is well-known that MRI is necessary in congenital cystic eye due to the presence of ocular and non-ocular intracranial abnormalities.

   In reporting this rare association, we could highlighted that the practice of early perform a brain MRI in children with congenital cystic eye is correct. This is not a novel way of acting, but the confirmation of a right approach. We consider it as a crucial message for clinicians.


   Suggested references have been added in the text and the biological behavior of our lesion has been revised as not peculiar but at least “unusual”.

4. Do the authors have an explanation for the coincidence of these two clinical entities or they believe that the findings are accidental (which appears to be the case)? This should be briefly discussed in the manuscript.

   We have no explanation, supported by scientific literature, to explain the link between these two clinical entities; so we consider it an accidental but interesting association, worthy of being reporting. We specified this statement in the conclusion section.

5. Some language editing would definitely improve the manuscript

   An accurate revision of the English language was performed. Details highlighted in the main document.
Background

6. The background is partially a redundancy of the abstract, maybe the authors could add more information regarding the ocular associations, MRI findings, unilateral / bilateral, treatment and prognosis of congenital cystic eye. The actual clinical and laboratory findings and the clinical course should be moved to the case presentation.

Background section has been extended according to suggestions of the reviewer. The clinical course and finding has been moved to the case presentation section.

Case presentation

7. When did the parents notice the cystic lesion? At birth or later?

The parents noticed the cystic lesion at birth, as added in the text.

8. The authors performed genomic hybridization testing. Could they please specify briefly what conditions they were looking for / excluded? Karyotype? SOX2 / PAX6 mutations?

No SOX2 / PAX6 mutations were evidenced, as added in the text. Karyotype was normal.

9. The lesion was partially excised? Could the authors please briefly explain why a total resection was not performed / not possible?

We explained in the case presentation the surgical decision of a partial excision.

Discussion

10. In general, the manuscript would benefit by discussing the authors’ findings more in regard to previous published cases, instead of performing a literature review.

In discussion section, we added details in regard to previous published cases, providing a review of literature.

11. Some discussion on further differential diagnoses (and their clinical signs), such as microphthalmos with cyst (much more common), cystic teratoma, cephalocele, heterotopic brain tissue, anophthalmos (true anophthalmia is extremely rare, although at birth the cystic eye may resemble anophthalmia)

In regard to the differential diagnoses, the discussion has been extended with more details.

12. The risks of a brain biopsy could be briefly discussed, as it would support the authors’ suggestion of a wait-and-see policy.

In discussion section, the risks related to a brain biopsy have been explained.

13. Some information on the surgical treatment / options of congenital cystic eye would be interesting. Also recurrence (please check Robb et al., Ophthalmic Genetics 2003)? Mean age at diagnosis?

In discussion section, the options of treatment of congenital cystic eye and the risk of recurrence have been added. The suggested reference has been added. The disorder is most commonly diagnosed at birth.

Figures
14. An image of the pre- and post-operative appearance of the congenital cystic eye would be extremely interesting. Is it available?

**The Figure 1 and its legend have been modified according to suggestions.**

**Minor essential revisions**

**Abstract**

15. 4th line: “unilateral anophthalmos” is a different diagnosis, please consider correcting

We replaced “unilateral anophthalmos” with “congenital cystic eye”

16. 6th line: what do the authors mean by “based on absence”…? Absence of neurological signs? Please specify / rewrite?

We rewrote this sentence in order to clarify.

17. 7th line: please consider revising “unexpectedly”, see above (regression of glial tumours is not as rare and unexpected, as the authors state later in the manuscript).

We rewrote this sentence in order to clarify.

**Background**

18. 5th line: “unilateral anophthalmos” is a different diagnosis, please consider correcting

We replaced “unilateral anophthalmos” with “congenital cystic eye”

19. 9th line: “please consider replacing “bioptic procedure” with “biopsy”

We replaced “bioptic procedure” with “biopsy”

**Case presentation**

20. It is stated that “follow-up MRI, one year after surgery disclosed…”, but the figure number is not included at the end of this sentence. Please correct. Fig 3a-c?

We added in the text Figure 3 a-c

21. Please correct brain “RMI” to “MRI”

We replaced “RMI” with “MRI”

**Discussion**

22. What is the estimated number of reported cases of congenital cystic eye that the authors have reviewed? Guthoff et al. 2004 reported 33 cases.
We reviewed about 30 cases of congenital cystic eye and we added the paper of Guthoff et al in the reference section.

23. Please correct “hystopathologic” to “histopathologic”.

We replaced “hystopathologic” with “histopathologic”

24. Also, some epidemiology regarding glial tumours of childhood / location / age would help the reader.

The epidemiology of childhood glial tumours has been detailed in the discussion section.

Figures

25. An image of the pre- and post-operative appearance of the congenital cystic eye would be extremely interesting. Is it available?

The Figure 1 and its legend have been modified according to suggestions.

References

26. Please consider including in your list / discussion the following papers

Gupta et al. BMC Ophthalmology 2003, 3:7

The suggested references have been added in the text.

Additional Editor’s Request:

Title Page

Please include a title page at the front of your manuscript file. It should contain, at minimum, the names, institutions, countries and email addresses of all authors, and the full postal address of the submitting author.

We provided a title page containing all the requested data.

Please put the consent section after the Conclusion section.

We modified according editor’s suggestion.

Please put the figure legends after the references.

We modified according editor’s suggestion.
Best regards,

Angela Mastronuzzi, MD