Author's response to reviews

Title: Isolated enophthalmos: an uncommon gateway to orbital tumors in pediatrics. 9 month-old female presenting with isolated enophthalmos as the unique sign of a metastatic orbital tumor: a case report.

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Version: 4  Date: 4 August 2014

Author's response to reviews: see over
Isolated enophthalmos: an uncommon gateway to orbital tumors in pediatrics.

9 month-old female presenting with isolated enophthalmos as the unique sign of a metastatic orbital tumor: a case report.

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Key words: Enophthalmos, Exophthalmos, Proptosis, Infantile orbital tumors, Neuroblastoma, Pediatric tumors.

Authorship contribution:
ST conceived the study, and participated in its design. ST Drafted and revised the manuscript for content including medical writing for content, analysis and interpretation of data.

EB conceived the study, participated in its design and revised the manuscript.

All authors read and approved the final manuscript.

Financial support: None of the authors have any financial interests to disclose.

Conflict of interest: No conflicting relationship exists for any author.

Consent: Informed consent of the parents was obtained for the publication of this case report.
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Article type: Case report

Criterion: Unexpected or unusual presentations of a disease
Malignant orbital tumors are a rare and hazardous entity in both adult and paediatric populations. Histological origins are various and they are different in adults and children. Knowing the prognosis of malignancy at such location (near the central nervous system and important vascular features), clinicians are expected to prioritize their early diagnosis. Exophthalmos is the most commonly known symptom of such tumors especially in children where the neoplastic tissue tends to grow outwards given the narrowness of their bony structures. However, clinicians should not neglect that other signs can reveal these neoplasms and should remain cautious before the least symptom. As such, enophthalmos has already been described as a rare symptom of orbital tumors in adults in a few case reports. However it was generally the satellite of other preponderant accompanying signs that one usually cannot miss (mass, erythema, edema…) and more importantly it has never been reported as the unique indicator of an orbital neoplasm in paediatrics. The importance of early diagnosing these tumors is justified by their potentially disastrous prognosis and argues for the need of a perfect knowledge of their clinics, including the scarcest signs. Among these, enophthalmos is probably one of the least known. The case of this little girl alarmed us and made us choose to publish her story because the obvious lack of knowledge of this unusual association was brought to our attention at her expense. Her case deserves being reported because the diagnosis of her tumor was delayed by at least 3 months, which probably modified the prognosis, because of a lack of knowledge of this unusual association. She in fact had been referred to 4 different paediatricians and pediatric
ophthalmologists at different teaching hospitals; however, all of them stated that her enophthalmos was nothing but a constitutional feature. The most important part of the story was that even the pediatric radiologists declined performing a CT scan because they believed that there was no valid justification for seeking an orbital tumor before enophthalmos alone. We report the case of a paediatric metastatic neuroblastoma revealed by enophthalmos alone and remind the importance of this sign as a revealing symptom of orbital tumors in children. The specificity of this case shows that enophthalmos can be the *unique indicative sign* of such hazard, which has not been clearly described elsewhere. The association between enophthalmos and orbital tumors is extremely rare in children and unfortunately *not known in common practice of pediatrics*. The authors believe it is extremely important to remind this statement to all practitioners because there can be no tolerance for ignoring this sign and delaying a potentially lethal diagnosis.
Revisions:

Reviewer 1

Thank you for this interesting exchange of ideas on the subject and for this precise observation that brings to light very accurate remarks.

In fact, in Figure 1a, the baseline bar does not sit on the lateral bony wall edge on the right side. And we agree that we have failed mentioning the cause of this phenomenon in the manuscript. This is actually because of the osteolytic and bony reorganization process. The integrity of the lateral bony wall edge of the right side was compromised by the tumor, and you can notice the osteocondensation of the right wall edge that therefore seems smaller but thicker and more heterogeneous (see black star). As explained in the manuscript, the corresponding lesion would be that of the right zygomatic arch. We shall go further in the explanation by confirming the quality of the baseline bar’s horizontality by comparison with the perfectly horizontal black double arrow located posteriorly that serves as point of reference.

If one looks carefully, the orbital bony cavity does seem to be increased in the right side at Figure 1b. The osteolytic process at the inferior wall of the right orbit, and the osteocondensation with bone neoformation at the superior wall of the left orbit associated with soft tissue inflammation as yourself perfectly noticed, denotes less space available for the right globe as compared to the left globe which remains inside its orbit.

Interestingly, a superior orbital soft tissue density in Figure 1b might
provoke exophthalmos on the left side. No exophthalmos was denoted in any cross section of the CT scan. Enophthalmos on the opposite was confirmed radiologically (in the light of the explanations mentioned herein and the oculo orbital index).

The authors denoted excellent explanations of enophthalmos in discussion section, however, for this case report, they need to show specific causes for the case providing evidences from imaging scan.

We believe that in the light of the latest explanations, Enophthalmos seems to be due to the fact that bony walls were compromised architecturally leading to an extension of the orbit volume. Less soft tissue was denoted on the right side.

Minor Essential Revisions:

1. Make paragraphs in the manuscript : see manuscript
2. Figure 1a: explain the mean of arrows : see manuscript
3. Figure 2: the tumor needs to be maked with several arrows instead of a thick line (thick line represents the size of the tumor, black arrows mark the tumor itself)

All modifications were included in the manuscript file as suggested.