Author’s response to reviews

Title: "Crying without tears" in infancy. An early diagnostic sign-post of triple A (Allgrove) syndrome: two case reports

Authors:

Daniel Tibussek (daniel.tibussek@gmx.net)
Sujal Ghosh (sujal.ghosh@med.uni-duesseldorf.de)
Angela Huebner (angela.Huebner@uniklinikum-dresden.de)
Joerg Schaper (joerg.Schaper@med.uni-duesseldorf.de)
Ertan Mayatepek (mayatepek@med.uni-duesseldorf.de)
Katrin Koehler (katrin.koehler@uniklinikum-dresden.de)

Version: 2 Date: 31 May 2017

Author’s response to reviews:

Dear editors,

Thank you for considering our manuscript entitled “"Crying without tears" in infancy. An early diagnostic sign-post of triple A (Allgrove) syndrome: two case reports.” to be resubmitted to the BMC Pediatrics.

We would like to thank the reviewers for their invaluable input that certainly has significantly improved our paper.

Editorial revisions:

1. Please amend the first section title to Background and please also add the title 'Case presentation'. Similarly, please add the title 'References' before the reference list.

Ad 1) We have made the changes accordingly.
2. Please re-upload the abstract in the submission system so that it includes the section titles.

Ad 2) Abstract has been re-uploaded including section titles.

3. Please move the declarations to the end of the main text (to after the conclusions section) and insure that you have included all the sections with the correct titles as follows:

- Ethics approval and consent to participate
- Consent to publish
- Availability of data and materials
- Competing interests
- Funding
- Authors' Contributions
- Acknowledgements

Please insure that you include details about the consent to publish the case report sought from the parents in the consent to publish section. Where a mandatory Declarations section is not relevant to your study design or article type, please write "Not applicable" in these sections.

Ad 3) Changes have been made accordingly.

4. In the authors’ contributions section please refer to each author by their initials and please also include a statement to confirm that all the authors read and approved the final version of the manuscript.

Ad 4) Changes have been made accordingly
5. Please include the relevant page numbers in the CARE checklist.

Ad 5)

The CARE checklist has been attached.

Response to Reviewers:

We have addressed the reviewers’ concerns and suggestions as outlined below:

Reviewer #1:

According to the reviewer’s suggestions, the following changes have been made.

Introduction:

Line 35- we have changed “alacrima as a clinical sign post” to “alacrima as an important clinical sign”

Case 1

Line 46- We have changed “truncated protein is most likely” to “truncated protein was most likely”

Case 2

Page 5- Line 53-We have changed “first child of non-related German” to “first child of non-consanguineous”

Line 53: We have changed “he was presented” to “He presented”

Page 6

Line 2 – we have changed “weigh < 3 percentile” to “Weight <3 rd percentile”

Line 24- We have removed “During the ultrasound examination” Start with The mother reported…. 
Line 26: We have changed “subsequently triples-A syndrome was suspected to “subsequently triple-A syndrome was suspected”

Discussion

Line 56: We have changed “early diagnostic signpost is stressed” to “early diagnostic sign is stressed”

Reviewer #2: “Both cases are well-known clinical variants of Triple A syndrome. In the paper, the Authors aimed to emphasize the significance of alacrima in such cases. The 2 cases were admitted to the hospital with non-ocular complaints and diagnosed as Triple A syndrome. Where should we put the presence of alacrima in these patients? The paper describes the syndrome, but it does not mention what is given in the title. Do the Authors believe that there was a delay for the diagnosis? There is only report of mothers for alacrima or absence of tears. Were the patients examined by the ophthalmologists? How were the tear tests? What about the lacrimal glands, was there any imaging of them?”

Answer to reviewer 2:

By publishing our two cases with Triple-A syndrome we aimed to stress that is is often the simple things that could have lead to the clinical diagnosis early in the course. In this case this is the “dry eye” or “crying without tears”. It is our observation that this clinical sign is underappreciated. This in fact had lead to a delay of specific diagnostic testing for a possible underlying disease, especially in the first case.

In that sense it was not the focus of our paper to present a detailed descriptions of the ophthalmological findings. Rather, we strongly feel that this is just another example of the importance of properly taking a detailed history, listening to parents and patients and, in our cases even more important, consider every unusual finding clinically relevant. If that would have happened, in our case 1 the diagnosis could have been made earlier. In case 2, alacrima eventually was the clinical key to diagnosis.

No tear tests or imaging studies of the lacrimal glands were performed in our patients.
Although we agree with the reviewer that these were “well-known” clinical variants of triple-a syndrome, this does only apply to experts in the field. Triple-A-syndrome is a rare disease that was not known to the vast majority of colleagues in our paediatric and ophthalmology department.

Therefore, we also aimed to provide a clinical “engram” for paediatricians: dry eye=think underlying disease, including Triple-A-syndrome.

We are looking forward to your favourable response

Yours sincerely

Daniel Tibussek, MD