Author's response to reviews

Title: Severe and isolated headache associated with severe hypertension as unique symptom of posterior reversible encephalopathy syndrome

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Author's response to reviews:

Manuscript (Case report): “Severe and isolated headache associated with severe hypertension as unique symptom of posterior reversible encephalopathy syndrome” (Gregorio Paolo Milani, Alberto Edefonti, Giacomo Tardini, Elisa Arturi, Claudia Maria Cinnante, Emanuela Anna Laicini, Ernesto Leva, Alberto Maria Cappellari, Carlo Agostoni, Emilio Filippo Fossali)

Dear Dr. Catherine Olino:

Thank you very much for your recent letter. We were pleased to know that our manuscript was rated as potentially acceptable for publication in “BMC Pediatrics”, subject to adequate revision and response to the raised comments. We carefully considered both the constructive criticisms raised by the expert reviewers.

Specifically following changes have been made and explanation may be given.

Reviewer # 1

• Comment # 1. Firstly, calling this as a “posterior cerebral edema syndrome”. Hinchey et al had described this syndrome as a posterior reversible leukoencephalopathy syndrome, reflecting the predominant white matter involvement (Ref 1 manuscript), with a subsequent report proposing the posterior cerebral edema syndrome (ref 2). This condition is now frequently referred to as the posterior reversible encephalopathy syndrome (PRES), in recognition of the grey matter involvement (see Bartynski et al. AJNR Am J Neuroradiol 2006;27:2179–90 for example). Whilst cerebral oedema may occur as a result of this condition, particularly in the sicker patients, this is not invariable and certainly...
unlikely to be the case in this patient. Furthermore, the imaging of the patient
does not support this. As such, the formulation of this being a posterior cerebral
edema syndrome is dated, and clinically inaccurate.

The manuscript was modified as suggested by the Reviewer. We reworded both
title and text conforming to these queries.

• Comment # 2. headache is one of the commonest symptoms reported in
patients with PRES. Whether this is related to the full blown syndrome involving
seizures is irrelevant as I would struggle to find a clinician who would not
consider this as a differential diagnosis with the history of severe headache and
arterial hypertension in a child with a renal co-morbidity. The authors could
perhaps reformulate the primary message to be that the early recognition
prevented a progression to the full blown syndrome, rather than the novelty of the
isolated headaches and arterial hypertension.

We really thank the reviewer for the constructive criticism. We reformulate the
primary message as suggested. Although we do think that headache associated
with severe hypertension is a really common symptom both in children and
adults, the radiological picture of PRES in the absence of other clinical findings
suggestive of this syndrome, especially visual symptoms and alteration of
conscious level, is really atypical and never described so far in literature.

• Comment # 3. Finally, the 4 figures could be merged so the before and after
visual impact could be emphasised. The abnormal changes could be further
highlights by some arrows (minor essential).

Thanks for the query. The figures were modified as suggested and arrows
included.

Reviewer # 2

• Comment # 1. Background: Sensorium is an unusual choice of words, as most
reports of PRES would discuss instead alterations of conscious level.

Thanks. The symptom was reworded as suggested by the Reviewer.

• Comment # 2. Case report

Centile ranges for the blood pressure values would be helpful for readers not
familiar with normal values in childhood.

We included centile ranges for each stage of hypertension in our child.

• Comment # 3. Case report: The investigations listed would be possibly easier to
follow if in a table.

We included a table with the list of investigations.

• Comment # 4. The figures demonstrating the MRI findings could be presented
side by side to ease comparison. Are axial images also available to demonstrate
the posterior position of these lesions and the extent of the cerebellar changes

The figures were modified as suggested.

• Comment # 5. I would also be interested in whether these signal abnormalities
were associated with any changes on diffusion weighted imaging?
Thanks for the interesting question. Diffusion weighted images did not show any restriction of diffusivity. We included the sentence in the text, too.

• Comment # 6. It is possibly worth underlining the notable negative features on the neurological examination.
We add some crucial information about neurological examination in the revised manuscript.

• Comment # 7. Discussion: A little more detail of the distribution of reported neuroimaging would likely be of interest to the reader, e.g. brainstem changes, thalamic changes etc These are nicely reviewed by Staykov and Schwab (2012).
We addressed this query writing more in detail neuroimaging findings described in the syndrome and adding the reference suggested by the reviewer

• Comment # 8 The authors discuss that if untreated PRES may be fatal. It is also important to recognize that reversibility in PRES may not be spontaneous, and it has been described that delay in treatment can lead to permanent damage to the affected area of the brain. The interesting finding of this case is the PRES in the absence of altered conscious level, seizures or neurological abnormalities. Do the authors speculate that the early recognition in this case may have led to prompter treatment, preventing the development of other features. Alternatively, is it likely that in a number of mild cases PRES like changes might be present on neuroimaging in children with headache alone in the context of hypertension, but that these cases are more often not imaged?
Thanks for the query. We addressed this crucial criticism in the text. We speculate that early diagnosis and treatment of the syndrome prevent the progression of the symptoms.

Therefore we hope that with these careful corrections our manuscript is acceptable for publication in BMC Pediatrics. Please do not hesitate to contact me again if you feel that further corrections are required.

Kind regards.

Gregorio Milani, 28th of April, 2014