Author's response to reviews

Title: Central Precocious Puberty in a 3 year-old girl with Phenylketonuria: a rare association?

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

We would like to thank the reviewers for their careful review of the manuscript and valuable suggestions that have improved the quality of our work.

In this revised version, we have addressed the points raised by the reviewers. In red ink are the reviewers’ comments and in green ink our replies point by point. Changes in the text, figures or tables are highlighted in yellow. All authors have read and approved submission of the manuscript in its final form.

We want to thank you for your kind attention and for considering our paper for publication in BMC Endocrine Disorders.

Looking forward to having your feed-back,

My best regards.

Sincerely

Dr. Claudio Giacomozzi
RE: Manuscript BMC 6394544201129689

“Central Precocious Puberty in a 3 year-old girl with Phenylketonuria: a rare association?”

Point-by-point rebuttal

Reviewer #1:

1. The discussion does not presently align with the data put forward. The data presented suggest the association between TCPP and PKU is - at best- very modest. metabolism response does not seem to suggest it is worthwhile to perform a large study on this subject, and the authors do not presently put forward other arguments (eg possible pathophysiological mechanisms) to move in this direction.

A: We changed the text in the discussion reinforcing that there is not evidence for a correlation between phenylalaninemia level and timing of pubertal onset in patients with PKU. We erased the sentences promoting further studies on this matter. However, we can not entirely exclude that some data are lacking as previous population studies did not carefully addressed this point.

2. The conclusions section is in fact a 'future directions' paragraph. It should be used for a real conclusion.

A: We changed the conclusion paragraph in: “We conclude that CPP is a rare coincidental event in children with PKU and can occur independently by the persistently high phenylalanine concentrations.” We changed abstract accordingly.

Reviewer #2:

1. Although seen in 1/10000 in European or North America, PKU is seen in 1/3500-5000 cases in Turkey and with a similar frequency in the countries with high consanguineous marriages. Interestingly with a high percentage in Ireland.

A: We added a more detailed description of the incidence of PKU in Europe. Appropriate reference has been included [16].

General comments:

We adjusted the manuscript format according to the journal style.