Author's response to reviews

Title: Life-threatening hypersplenism due to idiopathic portal hypertension in early childhood: Case report and review of the literature

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Author's response to reviews: see over
Life-threatening hypersplenism due to idiopathic portal hypertension in early childhood: Case report and review of the literature

Dear Mrs Neilan,

Please find enclosed the revised version of the above mentioned manuscript for consideration for publication in the BMC Gastroenterology. All listed authors on the manuscript have seen and approved the revised version of the manuscript and take full responsibility for the manuscript. All authors report no financial support and/or conflicts of interest. The manuscript has not been published and is not under consideration for publication elsewhere. The work will not be submitted to any other journal while under consideration by the BMC Gastroenterology.

We have addressed the comments in the revised manuscript and provide a point-by-point response to the concerns below. We have also highlighted all changes made when revising the manuscript.

Yours sincerely,

Dr Jan Däbritz
- On behalf of the authors -
POINT-BY-POINT RESPONSE

Referee 1: There are still far too many grammatical errors, despite being a revised submission.

Response: The manuscript has been edited by two native English speaking colleagues (Kiran Nistala, University College London Institute of Child Health, London, United Kingdom, and Trevelyan R. Menheniott, Murdoch Children’s Research Institute, Melbourne, Australia).

Referee 1: The underlying concept of this paper is that idiopathic portal hypertension is the cause of the underlying disease, rather than hypersplenism itself from other causes. In the absence of clear documentation of elevated portal pressures, this presumption remains still unclear, and therefore the overall concept of this report remains doubtful in my mind. Decision to not measure portal pressures sounds reasonable, but it is not true that this child was "critically ill". Conclusions about portal hypertension are not proven, and therefore should be qualified.

Response: We absolutely agree that measuring portal pressures could further substantiate the underlying concept of our paper. Since this was not feasible due to the medical condition of our patient the proposed pathophysiology of idiopathic portal hypertension is not without a degree of speculation. However, the portal vein of our Turkish patient was relatively prominent with a width of at least 10 mm. Standard values of portal vein size in infants and children are limited, to some extent conflicting or controversially discussed. However, according to more recently published data of portal venous diameter in children (Soyupak S et al. Portal venous diameter in children: Normal limits according to age, weight and height. Eur J Radiol. 2010;75:245-7) the size of the portal vein in our patient was not within the normal range for age (4.0-8.38 mm, 2.5-97.5 percentiles) and/or height (4.0-8.0 mm, 2.5-97.5 percentiles). Further evidence for a hyperdynamic situation is a clear asymmetry of the renal veins (left>right) suggesting a portorenal shunt. Furthermore, we could detect the left V. gastrica sinistra by keyhole angiography, which also suggests an increased portal vein pressure. These findings are strongly confirmative of portal hypertension.

Referee 1: The concept of "uncontrolled splenic hyperperfusion...with subsequent hypersplenism" is not proven. As this case may simply represent hypersplenism, this should be qualified.
Response: We hypothesized that the primary defect in the regulation of splenic blood flow seems to be crucial for the development of IPH. This view of the pathophysiology is supported by the fact that i) liver function abnormalities do not occur in IPH, ii) the abnormal expression of eNOS and VCAM-1 was only seen in splenic but not hepatic tissue, iii) the signs of portal hypertension resolved in our patient after splenectomy, and iv) both the adult patients reported before and our young patient have not developed recurrent signs of portal hypertension, liver pathologies or complications after splenectomy.

Referee 1: Abstract - Hyperperfusion is not clearly demonstrated, therefore, the choice of therapies should be directed toward hypersplenism, not hyperperfusion

Response: Following the suggestion of the reviewer we have changed this information given in the abstract.

Referee 1: Background - Poorly worded and structured. Should be several paragraphs, not just one. Phrases such as "amongst others" should be edited. Similarly, the word "etiopathogenesis" is new to me, and not sure what it means. A careful review by a native English speaking editor would be mandatory prior to reconsider for publication.

Response: According to the suggestion of the reviewer we have restructured the Background section of our revised manuscript. The word “etiopathogenesis” has been replaced by “etiology and pathogenesis”. In addition, the manuscript has been edited by two native English speaking colleagues.

Referee 1: Background - The findings of lack of overt hepatic malfunction does not, to my mind, have anything to do with congenital causes of hypersplenism as opposed to acquired causes.

Response: According to the suggestion of the reviewer we have deleted this statement.

Referee 1: Case Presentation - Pathogenic findings is not proper heading.

Response: The heading "Pathologic findings" has been replaced by “Clinical presentation”.
Referee 1: Page 6, the phrase "antibiotic-resistant septic temperatures" is unclear. Bacteremia? Fevers? Antibiotic-resistant organisms? To be published in an English journal, phrases such as this need to be clarified.

Response: The Phrase has been replaced by “fever (despite antibiotic therapy)".