Reviewer’s report

Title: Novel PYGL mutations in Chinese children leading to glycogen storage disease type VI: two case reports

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Reviewer: David A Weinstein

Reviewer's report:

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In this manuscript, Dr. Luo and colleagues present a case report with 2 patients with glycogen storage disease type VI who have different phenotypes. The case descriptions were clear, and the genetic studies were both well done and convincing. While more is needed in the literature about type VI glycogen storage disease and the genetic causes of this condition in Asia, the significance of this case report still needs better explanation. There are also several additional points with should be addressed.

1. The authors present the cases as having different severity, but the primary difference in the cases is the liver size. The liver size could be a reflection of the diet and carbohydrate intake prior to diagnosis. Otherwise, the patients clinically were similar. In fact, patient 1 (the milder case without hepatomegaly) had worse laboratory studies and growth. The response to treatment was also better for patient 2 in terms of growth. Why did the authors conclude that these children had different phenotypes? Could other factors like diet contributed to some of the differences seen?

2. The goal of any case report is to provide information that will benefit the field. The novel parts of this article are the lack of hepatomegaly and the new mutations. The lack of hepatomegaly is focused on by the authors, but it is of less significance since GSD VI has always been in the differential diagnosis of GSD VI. Therefore, the authors should but more focus on the significance of the new mutations. Do these mutations have significance for screening? Do these mutations have implications for future interventions like gene editing, gene therapy, or mRNA therapy?

3. Is type VI rare or under diagnosed in the Chinese population? Were these patients from different locations? How can this help to get other children diagnosed?

4. Table 1 requires some explanation. If the liver disease was mild in patient 1, why did the patient have high lactate? Why was the patient with "no hepatomegaly" have higher ALT/AST and triglycerides compared with patient 2. The lab abnormalities
have not been addressed. Were total protein and prealbumin concentrations checked? What were the beta-OH-butyrate concentrations?

Minor Point:

5. The authors state in the background and discussion that the clinical manifestations of GSD VI are similar to GSD I, III, IXa, and XI. I respectively disagree with this statement. GSD I and XI look vastly different from GSD VI. GSD I is much more severe, and does not have ketosis. GSD XI has malabsorption, renal abnormalities, acidosis, and a very different clinical picture

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

Not relevant to this manuscript

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