Author’s response to reviews

Title: Effect of GH replacement therapy in a boy with Dent’s disease

Authors:

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Author’s response to reviews:

Dear,

I am addressing you revised manuscript “Effect of GH replacement therapy in a boy with Dent’s disease”. We made all suggested changes.

I Responses to reviewer Phyllis Speiser

Comments to authors:

1. Abstract & Discussion:

This is a single case report of a boy followed for 3 years during growth hormone treatment for short stature in the setting of Dent disease.

The authors fail to acknowledge up front that at least one prior report describes the use of GH in Dent disease (Ref #10: J Pediatr Endocrinol Metab. 2008; 21:279-86). In that publication, partial GH deficiency is described. Of course it is widely understood among pediatric endocrinologists that ~75% of such arbitrarily termed GH deficiency is a temporary, functional state of inadequate GH production, rather than a true inborn error of somatotropin cell development. Thus, the question is not so much whether GH is deficient, but rather whether GH is therapeutic for growth and/or kidney function in the setting of Dent Disease. Clearly, one cannot answer that question based on a single case. It is worth noting, however, that the height SDS did improve during GH treatment and that renal function remained stable.

Response of authors:

We made corrections as you suggested. Confusion was about the interpretation of partial GH deficiency in Ref #10: J Pediatr Endocrinol Metab. 2008;21:279-86.
2. Quality of written English: language corrections before being Published
Response of authors:
We made the language corrections.

II Responses to reviewer Craig Langman
1. If other, please specify:
The abstract conclusion should be revised to be less negative, as the patient did well!
Response of authors:
We absolutely agree with you. We revised abstract conclusion.

2. Comments to authors:
The authors are congratulated on reporting on a rare disease and even rarer, reports of growth and development. They need to expand the discussion of the disorder, Dents Disease, to include the OCRL mutations that may be phenotypically similar to those of the CLCN5 gene mutations too.
The abstract conclusion is too negative, and should be revised to note the successful result in this case, but that more data are needed of course.
Response of authors:
Some patients with Dent’s disease have been observed to have extra-renal manifestations such as mild intellectual impairment, hypotonia and cataract, and such patients have been reported to share mutation in OCRL1 with the oculo-cerebrorenal syndrome of Lowe. The occurrence of these extra-renal manifestations with mutations relating to Lowe syndrome is referred as Dent disease 2. We expanded the discussion on CLCN5 gene mutation and gave the reference (11).

3. Quality of written English: Needs some language corrections before being published
Response of authors:
We made the language corrections.

III Responses to Associate Editor
A. General comments. This appears to be the third report of GH therapy in Dent’s disease, and so has merit.
Response:
We made correction as you suggested. Confusion was about interpretation of partial GH deficiency in Ref #10: J Pediatr Endocrinol Metab. 2008;21:279-86.

B. Specific comments.

1. The authors should state (end of text) that the patient's mother provided written informed consent; they should also state whether an institutional review board gave permission for this case report.

Response:
Corrected as you suggested. Patient's mother provided written informed consent and we have permission from institutional review board for this case report.

2. The indication for GH therapy age age 9 are given as short stature and CKD, which is generally meant as impaired GFR? but the creatinine clearance was normal. (The dipstick showed protein, but we are not told the level). This should be discussed and a reference provided supporting the indication for GH therapy. Further, the authors should discuss the extent of CKD at GH initiation in the case report of Sheffer-Babila.

Response:

Also, as you suggested, we discussed the extent of CKD at GH initiation in the case report of Sheffer-Babila.

3) At age 9, interventions initiated included calcitriol, phosphate, and citrate, together with GH. The authors should present their views on why the growth acceleration can be attributed exclusively to GH or alternatively present a more nuanced interpretation of the role of GH in improved linear growth.

Response:
Conventional treatment of children with Dent's disease and hypophosphatemic rickets with oral phosphate and calcitriol can heal rickets, but it does not always normalize linear growth. We started with the therapy simultaneously because of age of the patient. The IGF-1 levels were below normal range before treatment and increased to normal values after treatment. The acceleration in growth velocity could be attributed to the increased concentration of circulating IGF-1.

4. There is some confusion as to how GFR was assessed: P4, creatinine clearance; P5, glomerular filtration rate; estimated GFR. The authors should distinguish between measured creatinine clearance (24 hour urine collection) and eGFR, and for the latter should provide the equation (e.g. Schwartz) and the reference.
Response:
We assessed GFR as creatinin cirens.

5. The authors do not refer to their prior publication on a patient with Dent?s disease and partial GH deficiency (Ped Nephrol 2010).

Response:
We added new reference.

C Minor comments.

1. There a number of typographical errors which can be corrected by the journal copy editor (if available) or the authors.

Response:
We corrected typographical errors.

2. P6: In the discussion, sentences 3 and 4 seem to be in conflict about the association of the S244L mutation and rickets.

Response:
We revised sentences 3 and 4.

3. Table 2. A legend would be helpful, explaining the abbreviation ?SDS.? 

Answer:
We added legend for SDS.

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Best regards
Dr Mira Samardzic
Podgorica, Montenegro
Podgorica, 10.April 2011.