Reviewer’s report

Title: Short Stature as a Presenting Symptom of Attenuated Mucopolysaccharidosis Type I: Case Study and Clinical Insights

Version: 0 Date: 26 Sep 2018

Reviewer: Heather Church

Reviewer’s report:

This manuscript describes a case presentation of a patient with MPS I who experienced a significant delay in diagnosis of 11 years from onset of clinical symptoms. It illustrates how this patient was not investigated fully for the possibility of an MPS disorder despite showing clear clinical symptoms, and goes on to highlight the clinical features that should raise the suspicion of an MPS disorder.

Publication within this journal acts as a valuable educational case presentation with a target audience that may not familiar with lysosomal storage disorders. I recommend that the manuscript is accepted for publication. I have some minor recommendations that would add information:

1. Figure 3 describes a recommended diagnostic algorithm for MPS disorders. The urine GAG screen states that the urine analysis may be qualitative or quantitative. Quantitative analysis may be a full GAG analysis by TMS but may also purely be an assessment of total GAGs. It is well documented that total GAGs may not be raised in attenuated MPS patients and could give a false negative result if this test is performed in isolation. It is important to stress that a thorough urine MPS screen is required either by total GAGs and electrophoresis, or by TMS.

2. Figure 3 - Enzyme function test states DBS as source and screen for treatable MPS subtypes (MPS I, II, IV and VI). Please also consider MPS VII.

3. The manuscript states that variants in the IDUA gene have been identified but doesn't state what the genotype is. This is useful information.

4. General comment - the focus of this paper is MPS I but there is considerable clinical overlap with other MPS disorders. The discussion describes how MPS I should be part of a differential diagnosis in short stature but this is equally true of other MPS disorders, particularly MPS II, IV, VI and VII. The discussion would benefit from a broader angle to encourage the target audience to consider MPS disorders in general and not focus on MPS I.

These recommendations will not require significant alterations to the manuscript and should be easily addressed by the authors.
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?
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Yes

Are the conclusions drawn adequately supported by the data shown?
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Yes

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