Reviewer's report

Title: Mucopolysaccharidosis Type VI: Case Report with First Neonatal Presentation with Ascites Fetalis and Rapidly Progressive Cardiac Manifestation

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Reviewer: Eirini Manoli

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The manuscript by Rachel Sayuri Honjo et al, "Mucopolysaccharidosis type VI: Case report with first neonatal presentation with ascites and rapidly progressive cardiac manifestation" describes a rare presentation of prenatal fetal hydrops in MPS type VI associated with rapidly progressive mitral valve insufficiency and congestive heart failure by 6-7 months of age necessitating valve replacement at age 1yr. Successful resolution of the cardiac failure and improved growth and only mild motor delays are reported at age 2.5yrs with enzyme replacement therapy initiated after the cardiac surgery. The case is novel and expands the spectrum of MPS disorders that can present with non-immune fetal hydrops, highlighting the need for LSD work-up in "idiopathic" cases to facilitate early diagnosis, genetic counseling and referral for early intervention/enzyme replacement.

Infantile onset mitral valve insufficiency cardiomyopathy have been previously described in MPS VI patients. It would be helpful to the readers and more directly relevant with this case report if these cases were discussed in more detail and contrasted to the current case. They could be described in a separate table on the early onset cardiomyopathy in MPS VI, and include the case by Fong L.V. et al, 1987 (PMID: 3109796), presenting as endocardial fibroelastosis without valve involvement. Given all previous reports precede molecular testing, the current manuscript is also important for facilitating possible future genotype-phenotype associations.

Addressing the following comments would add to the clarity of the report:

* Clarify the fetal hydrops monitoring and resolution during pregnancy. Did it resolve spontaneously, was there any follow up of hydrocephalus or echocardiogram after birth?

* Was there hepatosplenomegaly, macrocephaly at birth/ the first few months? Why was a skeletal survey performed at 1 month of age?

* Provide more details on LV shortening fraction at 7, 9 and 10 months, and response to therapy and comment on any cardiac conduction anomalies. A normal ejection fraction is described in Fig 4, with no details on the age of the patient

* If available, provide glucosaminoglycans at diagnosis (only values after enzyme replacement are mentioned).
* Comment more on need for earlier detection and enzyme replacement.

* Provide the change at the protein level and discuss genotype-phenotype associations of cardiac variants.


**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.

No

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

Yes

**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

**Quality of written English**
Please indicate the quality of language in the manuscript:

Acceptable

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