Author’s response to reviews

Title: Atrial septal defect (ASD) in a patient with congenital disorder of glycosylation type 1a (CDG-1a): a case report

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Version: 1 Date: 21 Sep 2017

Author’s response to reviews:

Reviewer #1:

Comments:

1. Few clinical findings and 2D-Echocardiography parameters are missing.

2. Improvement in language is required. Certain sentences confuse the readers instead of providing a clear insight into the condition.

3. Overall its a well evaluated case, but major changes in the quality of English are required. References have to be written in Vancouver style.

Responses:
1. Considering that the sign of lipodystrophy in our patient is too slight (almost normal) to observe and hardly to capture by camera (he cannot sit with support for a long time cause of hyponia), so we delete this image and focus on the obvious and typical signs in our patient such as alternating squint and inverted nipples and make a comparison of those signs before and after treatment and observation in order to understand the progression of CDG-1a.

As your advices, we add the Qp/Qs ratio as 2D-Echocardiography parameters and make a comparison of changes in Qp/Qs ratio before and after treatment and observation in order to understand the changes in blood shunt of ASD.

2. We have improved the English language in the manuscript to the best of our ability and rewritten those confused sentences.

3. As your advices, we have rewritten the References in Vancouver style.

Reviewer #2:

Comments:

1. While I believe the authors have followed rigorous genetic testing protocols to confirm CDG 1 mutation along with enzymatic changes of PMM2 activity, I am not convinced the ASD can be ascribed to CDG1. ASD is a fairly common congenital cardiac disorder with close to 5-6 cases per 100,000 live births. In such a scenario can it not be a possible that both these conditions co-existed in the presented patient? I would be weary of rushing to causality and association in this situation. I feel the authors should tone down their conclusions about this being the first ever reported case of CDG1 leading to ASD.

2. More detailed description of treatment, especially for the ASD should be provided. Also, follow up echocardiograms if any should be mentioned with timeline.

3. It is no doubt an interesting case. However, as mentioned above I think the conclusion that ASD is a result of genetic mutations may be farfetched in this case. Moreover, the authors themselves concede that the mutations known to be associated with ASD were in fact absent in this patient.

Responses:

1. As you say, it is hard to tell whether ASD in our patient is ascribed to CDG-1a or just a co-existed abnormalities, so we abandoned this controversial view and focused on making clear to the affect of CDG-1a to the existed ASD by following up our patient to 3 years old. Through the comparison of changes in defect size and blood shunt of ASD before and after
treatment and excluding the possibility that the exacerbation of ASD is caused by intrinsic cardiac factors directly, we assume CDG-1a can worsen the situation of existed ASD to some extent.

2. Considering that our patient has low levels of antithrombin III and takes more risk when performing interventional operation even administration of exogenous antithrombin III concentrate, so we just follow up echocardiograms until now and do not administrate any specific therapy for ASD yet. Besides, his parents disagrees the administration of interventional operation yet, but with the exacerbation of ASD, we believe that it is necessary to perform interventional operation to cure ASD, so we are still trying to persuade his parents to give their consent for performing interventional operation.

3. According to your comments, we have performed CHD-associated genes sequencing in our patient and his family additionally, we found our patient and his parents have no pathogenic or susceptible mutations in those genes, which suggest ASD in our patient may be sporadic with no specific cause.