Author's response to reviews

**Title:** Myocardial fibrosis as the first sign of cardiac involvement in a male patient with Fabry disease. Report of a clinical case and discussion on the utility of the magnetic resonance in Fabry pathology.

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**Author's response to reviews:** see over
Reviewer 1

We thank the reviewer for his/her supportive comments and helpful suggestions.

1. Recently, Thompson et al. (Circ Cardiovasc Imaging 2013) published T1-mapping results in patients with Fabry disease. Amongst others, these authors stated that “sex differences in non-contrast T1 and ECV were independent of wall thickness” and concluded that “reduced non-contrast myocardial T1 values are the most sensitive and specific cardiovascular MRI parameter in patients with Fabry disease irrespective of sex and LV morphology and function”. Hence, Sechi et al. are right when arguing that “presence of LGE” (!) does not require myocardial hypertrophy in “both” (!) male and female patients with Fabry disease. However, this finding does not disprove the notion that there are some sex differences in the development/pattern of cardiomyopathy in patients with Fabry disease. The authors should address this important issue and the study of Thompson et al.

Answer: as suggested, we addressed the study of Thompson et al. in our discussion.

2. If possible, the authors should show comparative CMR images (cine as well as LGE images) of this patient prior to and post ERT.

Answer: As suggested, we added a new figure (Figure 3) showing cine CMR and LGE images acquired after 12 months of ERT.

3. There are some minor typos that should be corrected throughout the manuscript.

Answer: we corrected the minor typos.

Reviewer 2

We thank the reviewer for his/her supportive comments and helpful suggestions.

1. It would be helpful to demonstrate a corresponding slice of T2-imaging in figure 1.

Answer: As suggested, we added corresponding slices of T2-imaging in Figure 1.
2. Differential diagnosis of the LGE, i.e. myocarditis in the history of the Patient. Without the knowledge of molecular screening this diagnosis would be possible, too.

**Answer:** We agree with the Reviewer. The observed pattern of LGE may also be suggestive of previous myocarditis; however, in our patient, history of symptoms suggestive of remote myocarditis was negative. This has been acknowledged in the final version of the paper.

3. How do you explain the difference between the normal wall movement in the cine sequences / echocardiography and the feature-tracking Analysis.

**Answer:** We appreciate this important comment from the Reviewer. Non-invasive imaging modalities assessing myocardial deformation and strain (including speckle-tracking echocardiography, tagged-MRI and feature-tracking MRI) permit indeed a quantitative and objective measure of myocardial contraction. By using these techniques, selective analysis of longitudinal, circumferential and radial mechanics (which reflect forces of deformation of the left ventricle arising at different transmural level) is possible, thereby allowing identification of subtle changes of myocardial function which cannot be detected with conventional measures such as qualitative wall motion assessment.