Responses to the reviewer's comment

We appreciate the reviewer's constructive comments. Following changes were made according to your suggestions.

Manuscript NO: 63303

Title: Anderson-Fabry disease presenting with atrial fibrillation as earlier sign in a young patient: A case report and review of literature

Reviewer's comments

Reviewer #1

1. In the Abstract section, several abbreviations that occur for the first time should be provided with the full names, for instance, LVH and GLA.

Thank you for your kind comments. We corrected the abbreviations in the revised manuscript.

In the abstract section, we corrected the LVH and GLA, and electrocardiogram (ECG) was newly used. We revised abbreviations of the whole manuscript.

2. The microalbuminuria of the patient was 17.6 mg/day (normal range 0-2.0 mg/day). If this factor is correlated with AFD? Necessary discussion of the elevated microalbuminuria should be added into the part of discussion.

We thought it could lead to being misunderstandings in the contents, so we have modified the content according to your comments, and the normal range was incorrectly marked and corrected. We have written details in the discussion section regarding the possibility of earlier renal change. (page 7 / lines 5-6 in the laboratory examinations and page 10 in discussion)

An earlier renal biopsy would play a vital role in the confirmative diagnosis of AFD. Gubler M-C et al. analyzed earlier renal change for patients with AFD using light and electron microscopy[14]. They revealed that endothelial deposit of GL3 and glomerular sclerosis could be confirmed in most cases even though the young patients with AFD had 30mg or less per day of proteinuria. Therefore, renal involvement of AFD cannot be excluded, even not compatible with a range of proteinuria (<30 mg/24h). In this case, the amount of albuminuria for 24 hours was 17.6 mg. According to the KDIGO 2012 guidelines [15], the persistent proteinuria was categorized A1, A2, and A3, and this patient belongs to the A1 category (normal to mildly increased from less than 30 mg/24 hours per day). However, there was no study on the usefulness and safety of earlier renal biopsy in patients with AFD in the A1 category of proteinuria, and Ortiz A et al.[16] recommended that if baseline albuminuria >30mg/24h is shown, it can be considered as an indication of ERT. We thought that renal manifestation in this patient was started, and renal biopsy was not needed in the aspect of the decision of diagnosis and starting treatment because other organ involvement signs were definite.

Finally, we added additional references.

14. Gubler M-C, Lenoir G, Grünfeld J-P, Ulmann A, Droz D, Habib R. Early renal changes in hemizygous and heterozygous patients with Fabry's disease. Kidney Int. 1978 Mar;13(3):223-35. [PMID: 418264, DOI: 10.1038/ki.1978.32]

16. Ortiz A, Oliveira JP, Wanner C, Brenner BM, Waldek S, Warnock DG. Recommendations and guidelines for the diagnosis and treatment of Fabry nephropathy in adults. Nat Clin Pract Nephrol. 2008 Jun;4(6):327-36. [PMID: 18431378, DOI: 10.1038/ncpneph0806]