Reviewer’s report

Title: An Atypical Variant of Anderson-Fabry Disease in a Female Patient with Renal and Cardiac Involvement and Transient Ischemic Attack: a Case Report

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Reviewer: Daniela Concolino

Reviewer’s report:

The manuscript presenting an interesting case of a patient with clinical features of FD due to a molecular variant. The association of intronic mutations in GLA gene has been reported. This case is useful to emphasize a phenotypic spectrum that is linked to the molecular anomaly. This paper provides a valuable contribution to the emerging literature on this condition.

There is an inconsistence in the title of the article “An Atypical Variant of Anderson-Fabry Disease in a Female Patient with Renal and Cardiac Involvement and Transient Ischemic Attack: a Case Report”. We can say that in this patient symptoms are not affecting a single, specific organ, like in the atypical forms of FD previously described, but the clinical manifestations are the expression of a multisystemic involvement that characterizes classical forms. The title of the manuscript could be modified. We suggest: “A classical phenotype of Anderson-Fabry Disease in a female patient with intronic mutations of GLA gene: case report”

Regarding the Abstract form, I would change:
- Case presentation: delete “proteinuria”
- Conclusions: 1) “symptoms” should be replaced by “features”; 2) The sentences “In our patient clinical picture showed a multisystemic involvement with early onset of symptoms, thus suggesting that these polymorphisms can be found even in patients with classical form of FD” could be added.

Regarding the Background section:
- Line 5 “damaging normal cellular functioning” should be replaced by “with consequent cellular damage”
- Line 10 the other cellular types in which Gb3 accumulation occurs could be added
- Line 17 “In the latter study, 86% had an intronic mutation, called c.936+919G>A, that is associated with an atypical form of FD which is characterized by residual enzyme activity that remains high enough to prevent organ damage in childhood and adolescence.” Add the reference
- Line 19 it’s not clear what does “severe skin involvement in the teen years” mean.
- Line 2 from bottom “In this patient the evidence of occasional…..” should be
replaced with “In this patient molecular evaluations confirmed the diagnosis of FD: we found four mutations in promoter and regulatory intronic regions of the GLA gene.”

Regarding Case presentation section:
- everything is clear and detailed, but I think that too much space is spent to describe renal biopsy and cardiac MRI study.
- What found in these instrumental exams, is obviously specific for FD, but not less important than other clinical manifestations. For this reason at line 49 I'd add: “As a result of the renal biopsy and cardiac MRI study findings, associated to the clinical history, suggesting FD, the patient underwent….”

Regardind Conclusions section:
- Line 1 I suggest to modified the first sentence in this way: “In this paper we reported the case of a female patient in which, clinical history and specific instrumental findings suggested the diagnosis of FD. A genetic survey….”
- Line 5 the sentences “These mutations have been observed in several patients with atypical variants of FD characterized by not severe clinical picture, with symptoms affecting a single, specific organ, and which manifests later in life because residual enzyme activity remains high enough to prevent organ damage in childhood and adolescence. In our patient multisystemic involvement and early onset of symptoms seems to suggest a classical form of FD, but without any mutation in coding region of GLA gene. Our results…” should be added
- Line 5 from bottom The sentences “We do……Variant of FD.” Should be replaced by “This can lead to confirm diagnosis of FD in a higher number of patients, thus providing a more realistic evaluation of the prevalence of FD in general population.”

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
'I declare that I have no competing interests'