June 20th 2022

Dear Editors of the World Journal Of Clinical Cases:

Thank you for giving us the opportunity to submit a revised draft of our manuscript titled **"A case report of unusual presentation of Loeys-Dietz syndrome; clinical findings and treatment challenges"** with manuscript ID **76804** to the *World Journal of Clinical Cases*. We appreciate the time and effort that you and the reviewers have dedicated to providing your valuable feedback on my manuscript. We are grateful to the reviewers for their insightful comments on our paper. We have been able to incorporate changes to reflect most of the suggestions provided by the reviewers. Because the template is auto generated, we have outlined here the changes:

Here is a point-by-point response to the reviewers' comments and concerns.

Response and Comments from Reviewer 1; code 04923165:

- We have updated the information and have included all the six subtypes of the Loeys-Dietz syndrome that you kindly pointed out. We also enlarged our only table categorizing all subtypes with their clinical findings to complement that section.

- We added that in LDS there aren't the typical marfanoid habitus and the lens displacement.

- We wrote differently the passage that was not very clear to make it more grammatically correct.

- We have added information about the mutation found in our patient. It is a heterozygous missense mutation in TGFB2 gene, variant c.439C>T p.(Prol47Ser) in Exon 3, categorized as uncertain significance mutation consistent of Loeyz-Dietz syndrome type 4. And she does not have any typical feature within her phenotype.

Response and Comments from Reviewer 2, code 00233953

- We have agreed to change the title as you kindly suggested. It is now called: A case report of unusual presentation of Loeys-Dietz syndrome; clinical findings and treatment challenges.

- We have added two more subtypes of the disease recently described. . We also enlarged our only table categorizing all subtypes with their clinical findings to complement that section.

- We now mention that differential diagnosis, clinical presentation and treatment options for this syndrome are discussed in this article.

- We included the days of hospitalization and follow up visits
- We have cut a part of the introduction and included it within the discussion, as you kindly suggested
- We added the report of a LDS late in life to the manuscript
- The normal treatment of these kind of patients depends on their individual clinical presentation and anatomic abnormality so we briefly mention our patient´s treatment, although it can vary among LDS patients depending on their vessel involvement.

Response and Comments from Reviewer 3, code 06139999:

- What's the origin of pulmonary embolism? The pulmonary embolism originated because of multiple thrombus accumulating throughout her abdominal venous system due to its tortuosity. We did perform a lower extremities doppler ultrasound but it was completely normal. We actually believe that the recent administration of hormonal contraceptives helped the emboli formation.
- When we found the pulmonary embolism the first time, we did administer enoxaparin to full therapeutic ranges; at 1 mg/kg subcutaneous twice daily. During the second time of her pulmonary embolism, the massive one, we initiated heparin so we can stop it at any given minute because of her bleeding problems.
- The thrombectomy was performed by our team of interventional radiology, they inserted a cathether through the femoral veins and removed the thrombus manually by AngioJet.
- The genetic testing confirmed a heterozygous missense mutation in TGFB2 gene, variant c.439C>T p.(Prol47Ser) in Exon 3, categorized as uncertain significance mutation consistent of Loeyz-Dietz syndrome type 4. We have added it to the manuscript.

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