Reviewer’s report

Title: Premature ovarian insufficiency as a variable feature of blepharophimosis, ptosis, and epicanthus inversus syndrome associated with p.Leu75Phe FOXL2 mutation: a case report.

Version: 2 Date: 27 May 2019

Reviewer: Petra Liskova

Reviewer's report:

General comments

The manuscript has been improved but there are still issues that need to be corrected.

Overall the manuscript would profit from professional English editing.

Figures are slightly blurry, please correct- unless the size has been decreased on purpose prior to sending the files to reviewers.

Minor corrections.

1. Line 93 18 years old nulliparous woman (MP), line 121 The other three family members (MF, MS and MH) suspected.

I would recommend not to use these abbreviations at all. As it is highly suspicious of being initials of the patients (M seems to be surname of the family) which may have ethical implications as it could lead to their identification given the rarity of the disease and typical facial appearance. It is recommended to use indicator from pedigree figure, e.g. II:1 instead.

2. Line 153 FOXL2 variant has not been reported in GnomAD 153 (http://gnomad.broadinstitute.org) database nor in our own database including over 1,000 WES samples from the Polish population.

Line 155 In the proband no plausible rare variants (frequency <0.0001 both in gnomAD, and an in-house database of >1000 Polish exomes) in other genes were found.
Information about the 1000 Polish data is a bit repetitive, it could be reworded and the sentences merged. Moreover the authors need to be consistent in using WES or exome and GnomAD and gnomAD.

3. Line 163 proband had typical ophthalmic symptoms
Change symptoms for signs.

4. Line 167 However, in case of other described mutations (missense mutations or microdeletions), the genotype-phenotype correlation was not apparent.
Please add reference.

5. Line 170 The p(Leu75Phe) mutation
Typing error p. missing

6. Line 171 three women of two Chinese families
from two.. please change.

7. Line 183 premature ovarian insufficiency
Abbreviation POI has been introduced, please use it.

8. Line 218 ADS- Amplicon Deep Sequencing;
219 AFC: Atrial follicle count;
220 AMH- Anti-Müllerian hormone
Be consistent using only -

9. Table 2. Standard Synacthen (250 μg intravenously) Test
Legend of Table 2 is not self-explanatory. In addition, information in the text is not sufficient to understand the table and not all readers know what is this test about.

10. Figure 3 legend

Next-Generation Sequencing
Typing error Next-generation

11. Figure 3

The pedigree in figure 3 is disproportional vertically.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

Not relevant to this manuscript

Quality of written English
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published
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