Reviewer's report

Title: Streak ovaries in association with Aromatase deficiency due to a novel CYP19A1 mutation

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Reviewer: Arundhati Sharma

Reviewer's report:

In the paper entitled "Streak ovaries in association with Aromatase deficiency due to a novel CYP19A1 mutation". The authors have reported a novel duplication in CYP21 gene in a patient with aromatase deficiency. They have also tried to show the effect of this duplication on the alpha helix of the protein and how it would affect the binding.

The following points may be addressed by the authors ...........

Major revision.

The paper needs to be revised and presented in a concise manner. Since the authors have examined the patient at the age of 32 years and did not have a chance to review any of her previous records or slides, a short past clinical history may be presented without actually quoting any records.

The authors may emphasize on the clinical examination and hormonal investigations undertaken by them. The presence of streak gonads should not be over stressed as this might be misleading, especially for future research studies because the initial diagnosis of the patient was incorrect; diagnosis of Turner syndrome with 46, XX/ 45, X and Y chromosome mosaicism with an unusually tall stature is doubtful- that too at an age of 25 years. The streak gonads observed on USG might support the diagnosis of Turner syndrome but it may be little premature to conclude without any further evidence that aromatase deficiency led to streak gonads in this patient.

The title may be modified. ....for instance to “association of a novel CYP19A1 duplication mutation with Aromatase deficiency”

The authors may look up the exact way of reporting a mutation. The transcript reference etc. need not be mentioned in the results. This can be provided in supplementary material.

1) Abstract-

Background: Line 1: the line may be changed to about 24 case reports.
Line 4: this sentence may be changed to"We report a case of .............diagnosed at the age of ....years (age may be mentioned) due to a novel duplication..............gene.

Case presentation: The gene symbol of aromatase gene, MIM Number may be mentioned. Exon nomenclature may be in ...Arabic ...numerals. Mention first the
exon and then the duplicated region.

Conclusion: May be revised to make more precise. Sentences like “few cases of aromatase ……” and “this may reflect few adult case” are repetitive and may be omitted.

2) Main Manuscript-

Background: Paragraph 2 line 1: MIM nomenclature of CYP21 may be provided; coding exons should be numbered in Arabic numerals.

Line 10: Up until recently …..exons 3rd-6th, this sentence is not clear.

Line 13: ‘Recently a patient with...........in exon 10’. The single base pair change at position -41 may be specified. Is this a SNP? Has it been reported? Its role in reduction of aromatase levels may be mentioned.

Line 16: uniformity may be maintained in the style of writing mutations throughout the paper- either a three letter code like Asn 411Ser or N 411S may be adopted.

Paragraph 3, lines 30-33. ‘Many of the phenotypic......development does not add any new information and may be omitted.

Case presentation- paragraph2, line 3…..‘She disguised ....loose garments' this sentence may be omitted.

Paragraph 3, line 1...age 25 years to be added.

Line 6-12....the past reports may be just reported in a short concise way without “quoting”.

Paragraph 7, line 47-49: ‘Most individual ..........reported'. This sequence does not seem relevant here.

Were parents of the patient tested for the mutation? That would provide relevant information on the carrier status of the parents.

Paragraph 9, line 68 (reference may be given here)

Conclusion: May restrict to reporting just the novel duplication mutation. The associated clinical parameters observed by the authors are reported in other cases.

The Authors may reconsider inclusion of Figure 1

**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'