Author's response to reviews

Title: Clinical correlation between premature ovarian failure and chromosomal anomaly in a 22-year-old Caucasian woman: case report

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Author's response to reviews: see over
Dear Editor,

as you requested, we send you the corrected manuscript titled “CLINICAL CORRELATION BETWEEN PREMATURE OVARIAN FAILURE AND CHROMOSOMAL ANOMALY IN A 22-YEAR-OLD CAUCASIAN WOMAN: CASE REPORT (MS 1567559094743945)” . These corrections have been highlighted in the paper which is attached to this letter.

Authors’ contributions
DD analyzed and interpreted the patient data and wrote the manuscript. AT, EM, AM and EP worked up the clinical details and helped to prepare the manuscript. AAE, DL and ML studied the androgen receptor gene. OC and MR used the Fluorescent in situ hybridation. DD was a major contributor in writing the manuscript. All authors read and approved the final manuscript.

We answered to the reviewer’s questions

☐ A parental karyotype have been done? Why?
Page n.4 line 14-16. To assess whether the chromosomal abnormality was found segregating or de novo, we proceeded to the study of the karyotype of both parents. The karyotype of these was normal. From the above, the highlighted chromosomal abnormality was de novo.

☐ Do the authors consider that shewed inactivation may led to the expression of recessive X-linked genes in the rearranged chromosome? Why? If yes you could discuss this question in the paper.
Page n.4 line 17-18. Furthermore, the patient did not present clinical manifestations associated with diseases X-linked recessive.

☐ The discussion is the most important part of the article, and as currently written I do not understand it. It sounds as if they have evidence that the X chromosome that is not translocated is the one that is inactivated in all cells, and if this is the case they should provide additional references for this.
Page n.4 line 9-13. For the evaluation of the X-chromosome inactivation, we used the "HUMARA assay", which uses the locus of the androgen receptor (AR) in Xq11.2. In the first exon of the gene there is a trinucleotide repetition (CAG) highly polymorphic (~90%), next to the cleavage sites of restriction enzymes sensitive to methylation (HpaII or HhaI), methylated only on the X inactive. The assay demonstrated that the active X chromosome was translocated (X-autosome: X;14).

☐ I also recommend that they discuss specific genes on the X chromosome proposed to be involved in POF, and how they may be related to this case.
The genes involved in POF are given into the publications mentioned in the reference section:


☐ It is not necessary to explain the details of the MRI if it is normal. A statement describing that the brain MRI (including visualization of the pituitary gland) was normal would be sufficient.

Page n.3 line 27-31. From encephalon and hypophysis Magnetic Resonance Imaging (MRI) by means of paramagnetic contrast it was observed : sellar cavity regular in morphology and dimensions, without any structural alterations. Adenohypophysis within the rule limits for dimensions, without clear focal altered signal areas nor lack of impregnation after contrast means. The hypophyseal peduncle oriented normally.

Best Regards,
Dr. Domenico Dell'Edera

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