Reviewer's report

Title: Dystonia, facial dysmorphism, intellectual disability and breast cancer associated with a chromosome 13q34 duplication and overexpression of TFDP1: Case report

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Reviewer: Daniela Turchetti

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The authors describe the case of a 36 year-old woman with developmental delay and dysmorphic features, carrying a chromosome 13q34 duplication inherited from the healthy father. At age 30, she developed a psychiatric disturbance and was treated with antipsychotic drugs. After that, she manifested dystonia and at age 35 underwent right mastectomy for breast cancer.

Major Compulsory Revisions

Although the case is very interesting, the causal link between the CNV and the clinical phenotype remains largely undemonstrated. In particular, late manifestations such as dystonia and breast cancer look more likely to be secondary to the antipsychotic treatment.

To try to address this issue, the authors should provide the following information.

1) Segregation of the CNV in the family. The assessment of the CNV in other family members is needed to provide support in favour or against its causative role in the patient's phenotype. Since the proband is the fourth child and the siblings are reported as healthy, it would be crucial to test them, as well as other potential carriers in the paternal side of the family, for the presence of the CNV and the expression of the genes involved. This could also allow to test the hypothesis, raised by the authors, of a gender dependence of TFDP1 expression.

2) Breast cancer features. A more detailed description of the tumour is required to support a relationship between the genomic defect and the development of cancer. Indeed, amplification of genes in chromosome 13q34 (particularly TFDP1) in breast cancer has been associated with negative estrogen receptor immunoreaction, high histologic grade and unfavourable prognosis. Conversely, breast carcinomas arising in patients treated with neuroleptics, prolactin-releasing drugs, are reported to be more frequently estrogen receptor positive, rarer histologic types such as mucinous type have been described in these patients; moreover positive immunoreaction for prolactin receptor is very common (Fujita et al, 1994). The authors should report at least the biological features of the carcinoma that are routinely assessed for diagnostic purpose, such as grading, estrogen and progesterone receptors, proliferation index; if possible, prolactin receptor staining should be performed. In addition, they should
report if serum prolactin levels had been assessed in the patient. Finally, the possibility that breast cancer could have been favoured by the therapy should be discussed.

Discretionary Revisions

3) The clinical presentation is skewed toward neurological manifestations and treatment, with little description of the other features. The paper would benefit of a more balanced description; for instance, dysmorphic features should be described in more detail, and target stature given (to give a measure of how much the stature is abnormally tall in this patient).

4) Some comments on CNVs inherited from healthy parents, based on recent literature, would be useful in the discussion.

**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