Reviewer’s report

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

Version: 1 Date: 23 October 2012

Reviewer: Francesco Brancati

Reviewer’s report:

Re: review of the manuscript entitled “Dystonia, facial dysmorphism, intellectual disability and breast cancer associated with a chromosome 13q34 duplication and overexpression of TFDP1: Case report”

The authors report on the identification of a genomic duplication spanning about 218,000 bp in a girl with syndromic dystonia (psychomotor delay, breast cancer, tall stature, facial dysmorphism) and speculated whether the genes involved in this rearrangement might have a role especially in the pathogenesis of dystonia. The father is also a carrier of the same rearrangement. Indeed, they verified that leucocyte expression of these transcripts was abnormally high (more than an additional 0.5x) for one of these genes (TFDP1) in the proband but not in her father. The authors provided a nice presentation of this gene as a candidate for dystonia, while the possible explanation of its differential expression among the father and his daughter is weak (“…could be gender dependent due to differential hormonal effects on gene regulation in either cis or trans”).

This is an interesting and well-written case report. It is true that there are very few patients with chromosomal imbalances manifesting primary dystonia. Also, the authors nicely cloned the duplication breakpoints, where a 69 bp fragment showing 100% identity to a long terminal repeat of the endogenous retrovirus family K was inserted, further highlighting how these rearrangements might be complex.

This work may benefit from revision with respect to the point mentioned below:

In this reviewer’s opinion, the manuscript should be significantly shortened and presented as a case report since there are no definite evidences supporting a pathogenic role of this duplication in the phenotype (and specifically in dystonia).

Other points to improve:

Major:

Please clarify which databases have been interrogated (or whether the authors have run a number control samples) to verify if the identified duplication might be a CNV.

Please clarify if even broader constitutional (not somatic) deletion/duplications comprising this segment at 13q34 have been previously reported in the literature and if patients displayed any of the features observed in your patient.
Minor:

Abstract: it is unclear whether the duplication is de novo or not.

It is stated “Karyotype analysis exposed a chromosome 13q34 duplication”. Please verify this statement considering that the estimated size of the duplication is about 225 kb as assessed by SNP-array.

I would move Table 1 (Primers) to supplementary file/online methods or make it available on request. Same for Table 2 (qPCR results to confirm the duplication on genomic DNA).

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 reply NO to all above-mentioned questions. Hence, I declare that I have no competing interests.