Reviewer's report

Title: Novel Unbalanced 16p;13q Translocation in a Patient with Factor VII Deficiency and Developmental Abnormalities: Case Report

Version: 2 Date: 15 July 2005

Reviewer: Felicitas Lacbawan

Reviewer’s report:

General
An interesting case that demonstrates the need for specialists to be wary and sensitive that multi-systemic involvement can mean chromosomal abnormality especially in a child with developmental delay and dysmorphic features. It also depicts the evolving practice of clinical genetics and the wealth of genetic and clinical information that patients with chromosomal abnormality can teach practitioners.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

1) A table summarizing the clinical characteristic of previous patients in comparison to the current patient provides a brief and concise review that readers will appreciate.

2) An ideogram demonstrating the breakpoints and showing the important monosomic genes and trisomic genes will give a comprehensive visual aid for quick reference. Enumeration of genes located within the chromosomal region of interest and a review/assessment of the candidate developmental genes aside from ZIC2 might explain the phenotype in this patient. Check MIM Gene map for the genes since NTN2L(Nextrin 2), SOLH (small optic lobes), few zinc finger proteins and transcription factor are in Chromosome 16p13.

3) I am not clear on what the “long-range genomic regulation of ZIC2 “ means in this paper. If the ZIC2 is intact as demonstrated by FISH, although there is still the remote possibility of a ZIC2 mutation, the midline abnormalities in this patient is most likely due to some developmental genes besides ZIC2. It is our observation that patients with ZIC2 mutations have milder facial features of holoprosencephaly like hypotelorism without cleft lip/palate but with brain findings of holoprosencephaly or variant and diabetes insipidus.

4) On the paragraph on Chromosome 16p trisomy, the authors must have meant “16” not “16p” – “the most frequent autosomal anomaly found in miscarriages”.

5) On the last paragraph of the Conclusion, other gene regulatory mechanisms like uniparental disomy and parental origin are to be considered given that there is a deletion-duplication of genes in this chromosomal abnormality.

6) It was not stated in the write-up when the patient’s peripheral blood karyotype was done in relation to the time that the FVII deficiency was found. This is relevant since the mapping of genes had accelerated in the past several years. Today, there is more molecular information available from knowing the chromosomal breakpoints that may guide the geneticist in pursuing pertinent clinical work-up.

7) This case demonstrate the evolving practice of clinical genetics and the need for specialists to be wary and sensitive that multi-systemic involvement can mean chromosomal abnormality especially
in a child with developmental delay and dysmorphic features.

8) Modify Background and Conclusions to include the suggested points above.

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the
author can be trusted to correct)

1) Please change the word “subject” to “patient”.
2) Statement of development, delete “somewhat”. There is definite delay in development.
3) Consistent tense on sentences in the paragraph on physical examination, use present tense throughout.
4) Additional description of nose and mouth –“ hypoplastic alae nasi with prominent columella.; thin
upper lip with downturned corners of the mouth”.
5) Include measurements of total hand length, palmar length and middle finger length since picture
at first glance does not clearly demonstrate brachydactyly.
6) Use “palmar” instead of “hand” creases.
7) On the last paragraph under Conclusions: use “and” not “&” and “,” not “;”. Description of the
 palate, “high arched” was use in the case presentation and this is not the same as “narrow”.
8) On figures, label “clinodactyly” as “fifth finger clinodactyly”

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Discretionary Revisions (which the author can choose to ignore)

1) The multiple miscarriages that the mother had is an important clue to a possible familial
chromosomal translocation. I wonder if the mother was counseled as to the utmost importance of
having the parental karyotypes. This could also resolve the issue on whether this is de novo or
familial occurrence.

2) Definition of the molecular breakpoints will be a refinement of the data and will be more
meaningful in the phenotypic correlation.

What next?: Unable to decide on acceptance or rejection until the authors have responded to the
major compulsory revisions

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:

I declare that I have no competing interests.