Reviewer’s report

Title: A study of two Chinese patients with tetrasomy and pentasomy 15q11q13 including Prader-Willi/Angelman syndrome critical region present with developmental delays and mental impairment

Version: 1 Date: 16 October 2012

Reviewer: Luigi Boccuto

Reviewer’s report:

• Overall Comment

The paper by Yang et al. represents an interesting report of the first case of tetrasomy and pentasomy 15q11q13 in the Chinese population. The phenotypes caused by aneusomies of variable size are always subjected to some degree of variability and case reports from new ethnic backgrounds provide more information to better define such phenotype.

Moreover, the clinical presentation of the two patients includes some minor differences from the majority of cases with similar rearrangements reported in the literature.

For such reasons, I believe the paper constitutes an important contribution to the medical genetic field, even if the number of cases reported is just two. However, some minor adjustments are necessary: the authors should provide more detailed information about the behavioral and developmental evaluation of the patients. For example, they mention “autistic behavior” both in the abstract and the conclusions, but they only describe “outbursts”, “aggressive” behavior or “difficulty in interacting with peers”: were the patients ever evaluated for autism spectrum disorders?

• Major Compulsory Revisions

Abstract

1. Case presentation: “Both 15q11q13 aneusomies were resulted”, “were” must be canceled. Towards the end of the page and in other sections of the paper (pages 8 and 11) “mental impairment” or “mental deficits” should be replaced with “intellectual disability” (or disabilities). “Pentasomy patient was more severely affected than tetrasomy patient” should be replaced with “The patient with pentasomy 15q11q13 was more severely affected than the patient with tetrasomy of the same region”.

2. Conclusions: add “of” after “best”, replace “pentasomy 15q11q13 case” with “case of pentasomy 15q11q13”. Replace “pentasomy and tetrasomy 15q11q13 patients” with “patients with tetrasomy and pentasomy of chromosome 15q11q13”.

Background
3. Page 4, line 6: replace “particular, those that are maternally inherited” with “particularly on the maternal chromosome”.
4. Page 4, line 9: add reference(s) after “(SCM) in humans” to validate the statement.
5. Page 4, line 12: replace “underlining” with “underlying”.

Case Presentation

7. Clinical data. Page 5 line 10: after “non-consanguineous couple.” Add “Family history was unremarkable” and remove “Family history was insignificant” from page 6.
8. Page 5, lines 12-13: can the authors provide references in centiles for the birth parameters, related to the Chinese population? It appears the newborn was underweight for his length, but having a centile would give a better comparison with normal values. The same thing applies for patient 2.
9. Page 5, line 14: the authors should provide more details about the post-natal period, if possible. Was there a follow-up to the resuscitation? Any sign of asphyxia, jaundice, feeding problems, infections, or other post-natal problems?
10. Page 5, lines 16-17: can the authors document at what age the behavioral problems started to occur?
11. Page 5, last line: at what age was the Gesell Developmental Observation performed? Was it contemporary to the evaluation (5 years) or previous? It’s important to compare the output with the chronological age.
12. Page 7: all the markers should be in italics (i.e. D15S975).
13. Page 8, after line 4: there should be a “Discussion” header.
14. Page 8, line 6: replace “pentasome” with “pentasomy” and replace “ours is” with “the work presents the results of”.
15. Page 8, line 8: replace “overlapped” with “overlap”.
16. Page 8, line 9: after “West” the authors should list 3-4 features that are common to both the cases reported in the literature and the two patients in the manuscript and then close the sentence after “[2,4,6,10]”. Then replace “but some differences were also noted” with “However, some differences were noted”.
17. Page 8, lines 12-13: move “age of 5 and 6, respectively” from line 13 to line 12, after “examination”, then replace “had not been developed” with “were not observed”, and cancel “patients of” after “15q11q13”.
18. Page 8, line 15: cancel “no” before “vision deficits”, the sentence has already a negative in “Neither”.
19. Page 8, line 16: replace “mental deficits” with “intellectual disabilities” (see also note 1 of the abstract).
20. Page 8, line 18: replace “were” with “had”.
21. Page 8, line 20: remove the dot (“.”) after “age of 5”.
22. Page 9, line 1: replace “other tetrasomy 15q11q13 patients in the West” with “Western patients with the same aneusomy”.

23. Page 9, line 4-5: replace “that increases in copy number in high copy number 15q11q13 may not change” with “that the increase in copy number in 15q11q13 aneusomies may not change”.

24. Page 9, line 10: replace “clinical information available, and the presence of a normal cell line or a state of mosaicism” with “available clinical information, and the presence of mosaicism”.

25. Page 9, line 11: replace “to” with “for a”.

26. Page 9, lines 16-17: replace “present the patients described here” with “described in this report”.

27. Page 10, line 3: add “in” after “resulting”.

28. Page 10, line 6: the authors stated on page 6, line 17 that the array had an “average spatial distance between neighboring markers of 880 bases” but here they report “a precision of 1-kb intervals”. Which figure is correct?

29. Page 10, line 14: add “than” after “recombination”.

Conclusions

30. Page 11, line 6: replace “mental impairment” with “intellectual disability” (see also note 1 of the abstract and note 19 above).

Figures

Figures 1 and 2 need to be much larger. In Figure 1 the authors should use an arrow to point the preauricular fistula.

In the Figure 2 legend the authors should explain what is depicted in pink and what is in green, and use arrows to point the different probes.

For both Figure 3 and 4 the authors should clarify if the represented regions are from chromosome 15 or SCM 15, since they use “chromosome 15q11q13 in the legends, but “SCM 15” in the text.

Figure 3 legend: replace “Lower portion is array data from proximal chromosome 15q, and upper portion is enlarged part of affected 15q11q13” with “The lower portion of the figure shows array data from proximal chromosome 15q, and the upper portion represents the enlarged part of affected 15q11q13.

Figure 4 legend: add “the” before “upper”.

Table 1

For STS D15S1013 the proband has “2,2”: is this correct? It would imply no contribution from the mother (1,1).

• Minor Essential Revisions

Background

1. Page 4, line 14: the authors may add a coma “,” after “far”.
Genetic analysis
2. Page 6, line 17: the authors should explain what CEL stands for.
3. Page 10, line 17: the authors may replace “ones” with “cases”.

Conclusions
4. Page 11, line 7: the authors should add “the” after “with”.
5. Page 11, line 8: the authors should add “the” after “than”.

**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.