Reviewer’s report

Title: Sustained endocrine profiles of a girl with WAGR syndrome

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Reviewer: Marta Corton

Reviewer's report:

This case report describes a Japanese child with WAGR syndrome associated with a large 14Mb deletion at 11p14-p12 being identified by karyotype and aCGH array and further validated by FISH and qPCR. Due to the fact that WAGR syndrome is a rare disease, this study sounds interesting since it provides new information about large CNVs linked to the disease. Besides, causative CNV was thoroughly investigated by different and appropriated molecular studies.

Although the phenotype associated with WAGR deletions is well known, the case here described carried one of the biggest deletions reported to date, involving 50 different genes. The clinical description is not exhaustively described and it is not clear if the patient suffered from developmental and/or intellectual delay at 5 years. I suggest that the authors include a table summarizing clinical symptoms of the patient observed at the examined ages. It could be interesting if the authors compare and discuss the phenotype of this case with the previously reported for other WAGR patients carrying this type of large deletion.

It is expected that some of the phenotypic manifestation of the patient could be due to other different genes that PAX6 (explains aniridia), WT (Wilms tumor) and BDNF (explains obesity). However, this possibility has not been discussed in this case report. In the CNV here described, PRRG4 is also involved and could also contribute to developmental delay, as previously reported by other authors (Yamamoto T, et al. Narrowing of the responsible region for severe developmental delay and autistic behaviors in WAGR syndrome down to 1.6 Mb including PAX6, WT1, and PRRG4. Am J Med Genet A. 2014)

In addition, RNA expression and methylation analysis for BDNF in lymphocytes was also determined, but they show normal values as compared with controls. It is not clear how this negative finding is really relevant to this disease if only one patient was studied. Thus, the conclusion in the abstract "We conclude that patients with WAGR syndrome manifest their growth phenotypes through distinct mechanisms from that of the other imprinting-associated disorders" is misleading. Seeing that this study was performed in only patient, the author cannot make this generalization and this conclusion has not been really demonstrated in this report.

This case report is quite interesting since increases the number of patients carrying this kind of CNVs, however it does not contain relevant elements of novelty with the data here included.
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
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No

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