Reviewer's report

Title: Long-term auxological and endocrinological evaluation of patients with 9p trisomy: a focus on growth hormone-insulin-like growth factor-I axis.

Version: 2 Date: 22 August 2013

Reviewer: Rachel Crowley

Reviewer's report:

The authors present their findings in a study of growth hormone deficiency in the rare condition of 9p trisomy. This will be of interest to clinical geneticists, paediatricians with an interest in growth disorders and endocrinologists.

The important clinical question is whether identification of growth hormone deficiency and replacement is of benefit for these patients. Within the limitations of small numbers of patients in a rare condition, the authors have attempted to address this.

Major Compulsory Revisions

1. As a general comment the manuscript would benefit from an English language review.

2. The authors should state that the parents have given permission for the publication of photographs.

3. Results para 3 - what statistic was applied to analyse the effect of parental age?

4. Clarify karyotype / ambiguous genitalia for Case 4 - female XY?

5. The most important question here is the benefit of GH. Case 4 is still young. Case 3 appears to be still growing (assuming Case 3 = Figure 3, looks like growth is still >1cm/year). Therefore difference between growth on GH not clearly different from that on GH. This is mentioned in Results para 7 and should be developed in discussion. Also scoliosis in case 2 is mentioned in Discussion para 10 - this should be in results with more details, in order to evaluate the risks and benefits of GH.

6. The authors should describe how other causes of short stature were excluded (eg coeliac, feeding difficulties common in this disorder) and also how multiple hormone deficiencies were excluded (methods para 3). IGF1 is mentioned but not reported.

7. The discussion around the diagnosis of delayed puberty is confusing. The endocrine assessment of the hypothalamic-pituitary-gonadal axis should be described in methods and reported in results para 3. The authors should elaborate upon their point that subjects with normal gonadotrophins and GHD
may have delayed puberty; this is unclear.

Minor Essential Revisions
1. The figures are incorrectly labelled and hence the references to them in the text are incorrect.

2. Some non-standard abbreviations should be defined in the text.

Discretionary Revisions
1. In the table, GH peak appears to report baseline to peak, maybe an explanation here would be helpful, and specify which stimulation test was used.

2. The table is probably best presented as 2 separate tables.

3. The early part of the discussion contains a lot of material already presented in the introduction.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Not suitable for publication unless extensively edited

**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