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:** 16 August 2013

**Reviewer:** Nigel Glynn

**Reviewer's report:**

I was pleased to review this manuscript in which the authors report the results of a case series of children with 9p trisomy. Detailed observations at diagnosis and follow-up of 4 children with this chromosomal abnormality are described. The study focuses on growth failure, assessment of the growth hormone (GH) axis and response to GH replacement. Essentially, the results show that GH deficiency is common among this cohort of patients and the response to GH replacement (n=2) is satisfactory.

The main merits of this paper are the detailed clinical and endocrine evaluation of the patients with a rare chromosomal disorder as well as the long follow up in most patients.

**Major compulsory revisions:**

Does this series describe all of the patients with 9p trisomy attending this single centre or are there other patients with this chromosomal abnormality who don’t have GH deficiency? This is important as it will give an indication of the prevalence of GH abnormalities with this condition.

The focus of the paper is abnormalities of the GH/IGF-1 axis and therefore the authors could provide more details about which provocation test was used in each patient. Why did they choose the clonidine, arginine and GHRH+arginine in preference to other stimulation tests? They could report the basal as well as the peak GH values during the test. In addition, more discussion about the GH cut-offs used would be helpful – the threshold levels described in the paper would appear to be adult levels.

While the authors provide clear data about the growth velocity during treatment with growth hormone, we are not provided with details of the GH dose used or IGF-1 values during follow-up.

**Was GH reserve re-assessed upon attainment of final height?**

**Minor essential revisions:**

What assay was used to measure GH and in particular IGF-1?

In the results section, the authors report that two of the patients had scoliosis and
state that in patient no. 2 “this problem appeared to be stressed with GH
treatment”. They should provide greater detail about the clinical course for this
patient

In Methods section the authors state that “pubertal stage was assessed
according to Marshal and Tanner” but don’t describe the results of this
assessment clearly.

Similarly, they state that “intracranial imaging was obtained by MRI” but do not
report the results.

Did any of the patients in the series have intra-uterine growth restriction or any
obvious abnormalities on antenatal ultrasound?

Discretionary revisions:
A more detailed description of the assessment of the adrenal and thyroid axis
could be provided.

Minor issues not for publication:
There is scope for improving the english grammar in the manuscript. For
example:

• Abstract – “Trisomy 9p is a no rare chromosome anomaly…..” should read
  “Trisomy 9p is an uncommon anomaly..”

• Results section, paragraph one – “Familiar history was uneventful” should read
  “Family history was unremarkable”

• Results section, paragraph one – “Three patients was the only child…..” Should
  read “Three patients were only children”

• Results section, paragraph three – “Apparently, there was no parental age
effect” should be replaced by “Parental age ranged from xx to xx years”.

• Results section, paragraph four – “Besides, two patients..” should read “In
  addition, two patients…”

• Discussion, last paragraph – “GH neurosecretory dysfunction may be frequently
  discovered…” should read “GHND may be diagnosed frequently…”

Also abbreviations are not well explained in the manuscript. A list should be
provided.

**Level of interest:** An article of importance in its field

**Quality of written English:** Needs some language corrections before being
published
**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.