Growth Hormone Deficiency in a patient with 4p16 Deletion: an infrequent association with Wolf-Hirschhorn syndrome

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BACKGROUND

Wolf Hirschhorn syndrome (WHS) is one of multiple malformation syndromes which affects 1 in 50000 live birth(1). It is caused by variably-sized deletion of the distal portion of the short arm of chromosome 4 involving 4p16. Typical craniofacial features are 'Greek warrior helmet appearance' of the nose, microcephaly with micrognathia, prominent grabella, ocular hypertelorism, epicanthus, and poorly formed ears(2). Almost all patients show mental retardation, seizures and growth delay(2,3).

We report on a patient carrying a 4p16 deletion and growth hormone (GH) deficiency treated with recombinant human GH (rhGH).

CASE REPORT

The patient is male, born at term (birth weight 2810gr, length 50cm) with normal perinatal events. His mother has type 1 diabetes mellitus on intensive insulin therapy. Developmental delay was evident since the first months of life.

At the age of 5years he referred to us due to short stature 87cm (-4, 99 SDS), (fig1a) delayed bone age 3 10/12 years and impaired growth velocity 3cm/year. On physical examination he had generalized hypotony, dysmorphic features (microcephaly, hyperthelorism, prominent nasal bridge and glabella, epicanthus, micrognathia, cleft palate) (fig1b) psychomotor development (IQ<30) and systolic murmur 3/6. Due to growth retardation GH reserve was investigated by both L-dopa and glucagon GH provocative tests (GH peak 6,29 and 8,06ng/ml, respectively). Both tests showed GH deficiency. He was on treatment with levothyroxine for two years. Thyroid ultrasound showed small shaped thyroid gland while heart and abdominal ultrasonographic evaluations were normal. Brain MRI showed small anterior pituitary gland.

A. B.

Fig1 The patient at 5 years old. A short stature, B.facial features

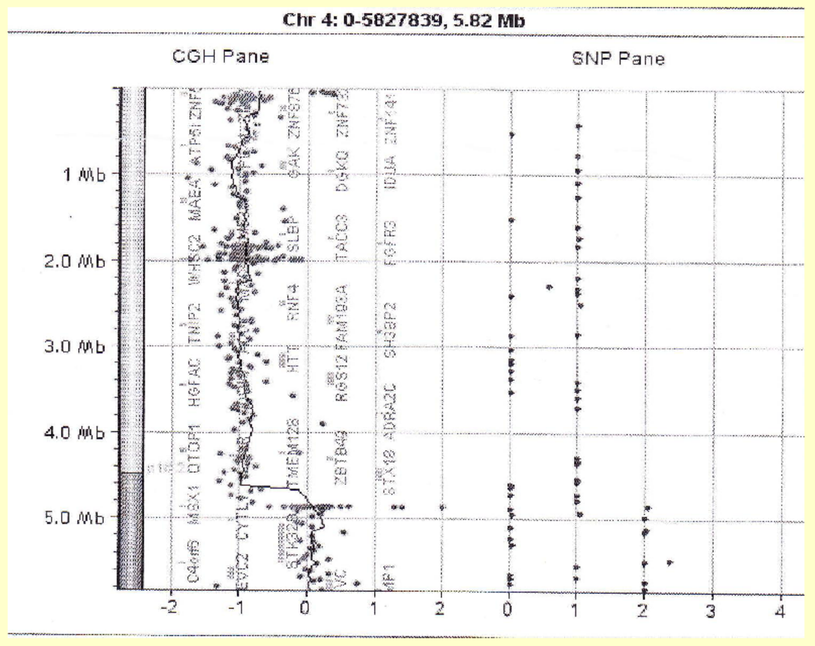

Fig 2 Array-CGH result

RESULTS

- Conventional chromosome analysis of peripheral blood lymphocytes showed a karyotype 46,XY.
- Due to congenital cardiopathy FISH was performed, in order to detect chromosome 22 deletion, which was negative.
- Array CGH was also performed showing deletion of chromosome 4 involving 4p16.3-p16.2, sized 4,7Mb (fig2) associated with WHS (5).
- RhGH treatment in a dose of 0,025 mg/kg/d was initiated. At the end of the first year of treatment, the patient's growth velocity reached 7,8 cm/year.

CONCLUSIONS

We describe the second case in the literature of a boy with WHS syndrome and GH deficiency and the first case reported treated with rGH. Although WHS associated with GH deficiency is extremely rare it should be included in the workout as GH replacement therapy may promote patients' growth.

References

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ESPE 2015 1043--P3

Growth

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DOI: 10.3252/pso.eu.54espe.2015

Poster presented at: ESPE 2015 BARCELONA

PosterSessionOnline.com