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Concerning the Article by Ogata et al. [1]

Hypergonadotropic Hypogonadism in a 3-Year-Old Girl with Blepharophimosis, Ptosis, and Epicanthus inversus Syndrome

In the September issue of *Hormone Research*, Ogata et al. [1] describe a prepubertal patient with blepharophimosis, ptosis, and epicanthus inversus syndrome (type 1 BPES) with hypergonadotropic hypogonadism. Although the syndrome is subdivided into type 1 with infertility of affected females and type 2 with male and female autosomal dominant transmission, it is not known whether the two forms are allelic variants [2]. Both types are heterogeneous and have been linked to a 3q22–23 continuous gene deletion with larger deletions having more dysmorphic features, short stature, and mental retardation [2].

Other endocrine abnormalities are not frequent, although the single mesial maxillary tooth that is sometimes associated with growth hormone deficiency and the holoprosencephaly sequence were described by Karimi-Nejad et al. [3] – in that case computed tomography scans of the brain were normal. I here describe an 11.4-year-old male with type 2 BPES probably inherited from his father who presented with a height SD score of –1.52 as compared with a mid-parental height of +0.4. The TW2 bone age was 9.5 years. The peak growth hormone level to stimulation was 6.5 mIU/l; normal luteinizing hormone releasing hormone test (luteinizing hormone 0.3, 2.1, and 2.7 mIU/ml and follicle-stimulating hormone 2.6, 5.6, and 8.3 mIU/ml at 0, 20, and 60 min, respectively) with a normal thyrotrophin-releasing hormone, prolactin, and cortisol response. Karyotype normal and chromosome 3 normal to detailed banding studies. Magnetic

resonance imaging showed hypoplastic anterior pituitary with normal stalk.

Apparently isolated growth hormone deficiency was present in this case of BPES associated with a small pituitary gland and presumably only a small, undetected, gene deletion. Many genes are implicated in normal pituitary development and may be associated with midline facial and eye abnormalities [4]. It is possible that some cases of BPES may have pituitary abnormalities accounting for short stature and that chromosome 3 may be worth searching for further genes related to pituitary development.

References

- 1 Ogata T, Hasegawa T, Tamai S, Sato S, Hasegawa Y, Matsuo N: Hypergonadotropic hypogonadism in a 3-year-old girl with blepharophimosis, ptosis, and epicanthus inversus syndrome. *Horm Res* 1998;50:190–192.
- 2 On-line Mendelian Inheritance in Man (OMIM). <http://www.ncbi.nlm.nih.gov/Omim/>
- 3 Karimi-Nejad A, Karimi-Nejad R, Najafi H, Karimi-Nejad MH: Blepharophimosis syndrome (BPES) and additional abnormalities in a female with a balanced X:3 translocation. *Clin Dysmorphol* 1996;5:259–261.
- 4 Dattani MT, Martinez-Barbera J-P, Thomas PQ, Brickman JM, Gupta R, Mårtensson I-L, Toresson H, Fox M, Wales JKH, Hindmarsh PC, Krauss S, Beddington RSP, Robinson ICAF: Mutations in the homeobox gene HESX1/hesx1 associated with septooptic dysplasia in human and mouse. *Nat Genet* 1998; 19:125–133.