Original

Short Stature and Turner Skeletal Features in an 11-Year-Old Boy with a Ring Y Chromosome Missing the Short Stature Homeobox Containing Gene

Masayuki Tanaka and Yoshikazu Ohmizono
Department of Pediatrics, Shiga National Hospital, Shiga, Japan

Abstract. We report on an 11-yr-old boy with short stature and Turner skeletal features. Chromosome analysis revealed a 46,X,r(Y)(p11.3q11.2) karyotype, and FISH analysis showed loss of the Short stature homeobox containing gene (SHOX) from the ring Y chromosome. The results are consistent with the association of SHOX haploinsufficiency with short stature and Turner skeletal features, and suggest the importance of SHOX analysis in boys with Turner-like skeletal phenotype.

Key words: ring Y, SHOX, short stature, Turner skeletal features, Madelung deformity

Introduction

In 1997, the Short stature homeobox containing gene (SHOX) was cloned from the pseudoautosomal region of the short arm of the X and the Y chromosome (PAR1) (1). Subsequent studies have shown that SHOX haploinsufficiency leads to short stature, Turner skeletal features, and Leri-Weill dyschondrosteosis (LWD) characterized by mesomelic limb shortening and Madelung deformity (2–4). Here, we report a boy with short stature, Turner skeletal feature, and a ring Y chromosome missing SHOX.

Case Report

The boy was the first child born to non-

Received: May 18, 2005
Accepted: May 31, 2005
Correspondence: Dr. Masayuki Tanaka, Department of Pediatrics, Shiga National Hospital, 255 Gochi-Cho, Higashiohmi-City, Shiga 527-8505, Japan
E-mail: iky01@shiga-hp.jp
the ring Y chromosome (Fig. 3). FISH was also performed with an SRY probe, confirming the presence of SRY.

Discussion

SHOX haploinsufficiency resulting from a ring Y chromosome was identified in a boy with short stature, cubitus valgus, and mild Turner skeletal features (2–4). The results are consistent with the
association of SHOX haploinsufficiency with short stature and Turner skeletal features. In addition, the mild skeletal manifestation in this prepubertal boy is compatible with the previous notion that skeletal maturing effects of gonadal estrogens induce the growth failure and skeletal anomalies in patients with SHOX haploinsufficiency (4). Indeed, severe phenotype in SHOX haploinsufficiency has usually been observed in pubertal to adult females with normal ovarian function (4, 5).

In this study, it is notable that SHOX haploinsufficiency was found in a prepubertal boy. Chromosome analysis is usually performed on girls with short stature because of the possibility of Turner syndrome, and SHOX analysis is frequently carried out on pubertal to adult females because of obvious skeletal manifestations. By contrast, such analyses remain rare for prepubertal boys primarily due to male sex development and mild skeletal phenotype. We recommend such analyses for boys with short stature and Turner-like skeletal features. Identification of SHOX haploinsufficiency will permit application of GnRH analog (6) therapy and appropriate genetic counseling.

References

1. Rao E, Weiss B, Fukiai M, Rump A, Niesler B, Mertz A, et al. Pseudoautosomal deletions encasing a novel homeobox gene cause growth failure in idiopathic short stature and Turner syndrome. Nat Genet 1997;16:54–63.
2. Belin V, Cusin V, Viol G, Girlich D, Toutain A, Moncla A, et al. SHOX mutations in dyschondrostenosis (Leri-Weill syndrome). Nat Genet 1998;19:67–9.
3. Shears DJ, Vassal HJ, Goodman FR, Palmer RW, Reardon W, Superti-Furga A, et al. Mutation and deletion of the pseudoautosomal gene SHOX cause Leri-Weill dyschondrostenosis. Nat Genet 1998;19:70–3.
4. Ogata T. SHOX haploinsufficiency and its modifying factors. J Pediatr Endocrinol Metab 2002;15:1289–94.
5. Kosho T, Nagai MK, Fujimoto M, Yokoya S, Sakamoto H, Hirano T, et al. Skeletal features and growth patterns in 14 patients with haploinsufficiency of SHOX: implications for the development of Turner syndrome. J Clin Endocrinol Metab 1999;84:4613–21.
6. Ogata T, Onigata K, Hotsubo T, Matsuo N, Rappold GA. Growth hormone and gonadotropin-releasing hormone analog therapy in haploinsufficiency of SHOX. Endocr J 2001;48:317–22.