A Case With Short Stature, Growth Hormone Deficiency and 46, XX, Xq27-qter Deletion

Şule Yıldırım[1], Naci Topaloğlu[1], Mustafa Tekin[1], and Fatma Sılan[2]

[1] Department of Pediatrics, School of Medicine, Çanakkale Onsekiz Mart University, Çanakkale, Turkey

[2] Department of Medical Genetics, School of Medicine, Çanakkale Onsekiz Mart University, Çanakkale, Turkey

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Abstract- We report a case of 11-year-old girl with growth retardation and 46, XX, Xq27-qter deletion. The endocrinologic evaluation revealed growth hormone deficiency. In karyotype analysis 46, XX, Xq27-qter deletion was determined. The deletion of terminal region of chromosome 27 is most commonly being detected during the evaluation of infertility, premature ovarian insufficiency or in screening for fragile X carrier status. To our knowledge, this is the first reported case with 46, XX, Xq27-qter deletion and growth hormone deficiency. Furthermore, this case might facilitate future search for candidate genes involved in growth hormone deficiency

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Introduction

Short stature in childhood is a relatively frequent reason of admissions to pediatric clinics. In terms of clinicians, a diagnostic workup that will detect as many as possible causes whereas preventing unnecessary procedures for the patient should be performed. After a thorough medical history, physical examination, necessary laboratory and radiologic examination; genetic testing can be the next procedure.

Although most cases are sporadic in growth hormone deficiency (GHD), in 3-30% underlying genetic etiology is suggested (1). Therefore, chromosome, as well as molecular analysis, are requisite diagnostic investigations in children with short stature although there is GHD.

We know that most common cause of short stature due to X chromosome is loss of genetic material from the chromosome, that is Turner syndrome. Less frequently, Xq duplications may be found by karyotyping in manifesting females studied because of mental retardation. The most frequent manifestations found in these patients are short stature, developmental delay, facial dysmorphism and gonadal dysgenesis (2-3). Herein, we presented a girl with short stature and Xq27-qter deletion. Chromosome analysis from peripheral blood was performed after short-term phytohaemagglutinin stimulated lymphocyte culture and GTG banding. High-resolution prometaphase banding showed an X chromosome deletion; her karyotype was designated 46, X, del(X)(q27-qter).

Case Report

An 11-year-old girl presented to our unit due to slow growing. She was the second child of unrelated parents. She was born at term by normal spontaneous delivery after an uneventful pregnancy. Her birth weight was 3750 g, and birth length was 50 cm. There is no medication history. Her neurodevelopmental development was normal. At conception, her mother was 28 years, and her father was 29 years. Before or during pregnancy there was no history of drug or disease.

Her mother and father had a height of 162 cm and 168 cm, respectively. Both of them are healthy.

The girl was 127 cm (<3rd percentile for normal population) with a weight of 24 kg (<3rd percentile for normal population). Her body mass index (BMI) was 14.9 (BMI SD score -1,61), and head circumference was 52 cm. Her genitalia was of the normal female phenotype. No other abnormal features were noted. Her mental-motor development was normal.

Laboratory tests showed normal hemogram and

Corresponding Author: Ş. Yıldırım
Department of Pediatrics, School of Medicine, Çanakkale Onsekiz Mart University, Çanakkale, Turkey
Tel: +902862635951-1434, Fax: 902862635951-1434, E-mail address: sule.yildirim@com.edu.tr

biochemical parameters including liver and kidney function, blood glucose, cortisol, thyroid function, insulin. Her urine analysis was normal, and her urine culture was sterile. Her stool examinations were normal. Her hormone tests were as follows: FSH 6,53 mIU/ml, LH 4,2 mIU/ml, estradiol 18,25 pg. Growth evaluation revealed low GH basal level and reduced response to GH stimulation testing.

Bone radiographic imaging of the left hand was compatible with 9 years. Her ultrasound examination of uterus, ovary and urinary system were normal. Cranial and hypophysial MRI were also normal.

Chromosome analysis demonstrated a 46,XX, Xq27-qter deletion(Figure 1). In the family chromosome analysis, her mother has balanced translocation.

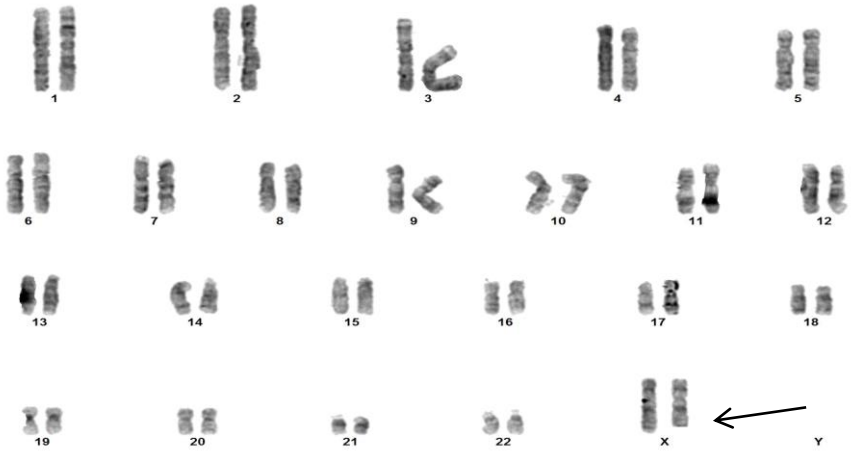

Figure 1. Karyotype of our patient

Discussion

We have characterized a mutation associated with short stature and GHD. The association Xq27-qter deletions with short stature and GHD is not well established. X chromosome-associated disease conditions form a large number of disease conditions. The X chromosome contains approximately 1,100 genes and is associated with over 300 Mendelian conditions (3-4). X-linked mental retardation is a common cause of inherited intellectual disability with an estimated prevalence of about 1/1,000 males (5). Besides the *FMR1* gene responsible for the fragile X mental retardation syndrome, the chromosomal region Xq27.3-qter harbors several genes that have been shown to be responsible for syndromic and non-syndromic forms of X-linked mental retardation (6). This region is at high risk for genomic instability, and several of these genes are implicated in genomic disorders (7). We describe a new patient with a short stature and Xq27-qter deletion resulting from an inherited maternal balanced translocation. The Xq deletions are likely to be lethal in males because of the many essential genes contained within the deleted regions. However, Schmidt *et al*., [1990] reported a 5-year-old girl with del Xq27.1-q27.3 who was phenotypically normal but developmentally delayed (8). Probst *et al*., [2007] reported a 6-year-old girl with intellectual disabilities and mild dysmorphic features and a 2.7 Mb microdeletion of Xq 27.3 and the FMR1, whose peripheral leukocytes showed random X inactivation (9). These clinical findings associated with the deletion are absent in our patient.

In 1996 Hamel *et al*., described a family in which mental retardation and isolated GHD cosegregated as an X-linked trait (10). In 1998 Raynaud *et al*., described another family in which mental retardation with isolated GHD is mapped to Xq22–Xq27.2 (11). In our patient there was no mental retardation or dysmorphic findings but sever short stature.

Consequences of deletion of X-linked genes are not well known. Clinical findings of our patient are not similar phenotypically with the other cases described in the literature except short stature. And also the deletion of X chromosome region “del(X)(q27-qter)” is different from the ones reported in the literature.

In conclusion, screening of patients should be considered in children with severe growth failure (height SDS <–2) although associated with GHD. We reported a

new case of 46, XX, Xq27-qter deletion associated with short stature and GHD. In the case of short stature, we should be aware of new karyotype anomalies. Further studies are required to understand the relation between short stature, GHD, and the Xq deletions.

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