8-1-2012

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LETTER TO THE EDITOR

Diagnosis of Variant Klinefelter Syndrome in a 21-Year-Old Male Who Presented with Sparse Facial Hair

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Dear editor:

Klinefelter syndrome (KS) describes a sex chromosomal aneuploidy caused by the addition of at least one extra X chromosome to normal male karyotype, XY. It is the most common disorder of sex chromosomes with a prevalence of one in 600 males[1]. Variants of KS are characterized by the addition of an extra X or Y chromosome to classic karyotype 47,XXY. Although somatic malformations and mental retardation are more severe in these variants, most cases remain undiagnosed till puberty when the symptoms of androgen deficiency are recognized[2,3].

A 21-year-old male presented with sparse facial hair since the onset of puberty. His medical history revealed cryptorchidism, delayed neuromotor development, and mild mental retardation recognized in early childhood. His parents were nonconsanguineous, and there was no history of a genetic disease in the family. On physical examination, the facial (Fig. 1A) and axillary hair (Fig. 1B) were sparse whereas other body hair was in normal density. His height and weight were 193 cm and 103 kg, respectively, and the feminine distribution of the adipose tissue was striking on examination (Fig. 1C). He had dysmorphic features consisting of hypodontia, hypoplastic teeth, prognatism, short filtrum (Fig. 1A), gynecomastia (Fig. 1C), clinodactily, and fusiform shaped fingers. Chromosome analysis of a peripheral blood sample disclosed a 48,XXXY karyotype, compatible with the diagnosis of variant KS.

Detailed hormonal profile analysis revealed a hypergonadotropic hypogonadism, and mild hypothyroidism. Furthermore, scrotal ultrasonography showed small sized testicles. Accordingly, the patient was started on testosterone treatment.

Patients with KS may present with a variety of subtle clinical signs of endocrinological, psychological and orthopedic problems. Thus the diagnosis may be quite challenging after birth. In infancy, hypospadias, cryptorchidism or small phallus may be helpful for the diagnosis, while during childhood, speech and language deficits, behavioral and cognitive problems may serve as diagnostic clues[1]. After puberty, a relative testosterone deficiency becomes evident, and suspicion arises when the development of secondary sexual characteristics is not completed[4]. The typical male with KS is characterized by eunuchoid body proportions, abnormally long legs and arm span, feminine distribution of adipose tissue, absent or sparse facial, body and sexual hair, small testes and penis. The syndrome may later be diagnosed among adults with azoospermia visiting infertility clinics[2]. Correct diagnosis needs careful attention as the syndrome is mostly overlooked. One study showed that 10% of the cases were recognized prenatally while 26% were diagnosed in childhood or adult life, leaving 64% of the cases undiagnosed[2].

The existence of every extra chromosome in KS worsens the clinical manifestation. An average to tall stature, ocular hypertelorism, flat nasal bridge, epicanthic folds, low set ears, prognathism, kyfosis, scoliosis, radioulnar synostosis and clinodactily are common findings of 48,XXXY variant of KS[1,3]. Prevalence of this disorder is approximately 1 : 50,000[1,3]. The rarity of reports may be due to a phenotype identical to the 47,XXY phenotype[3].

Received June 14, 2011, Revised September 17, 2011, Accepted for publication September 19, 2011

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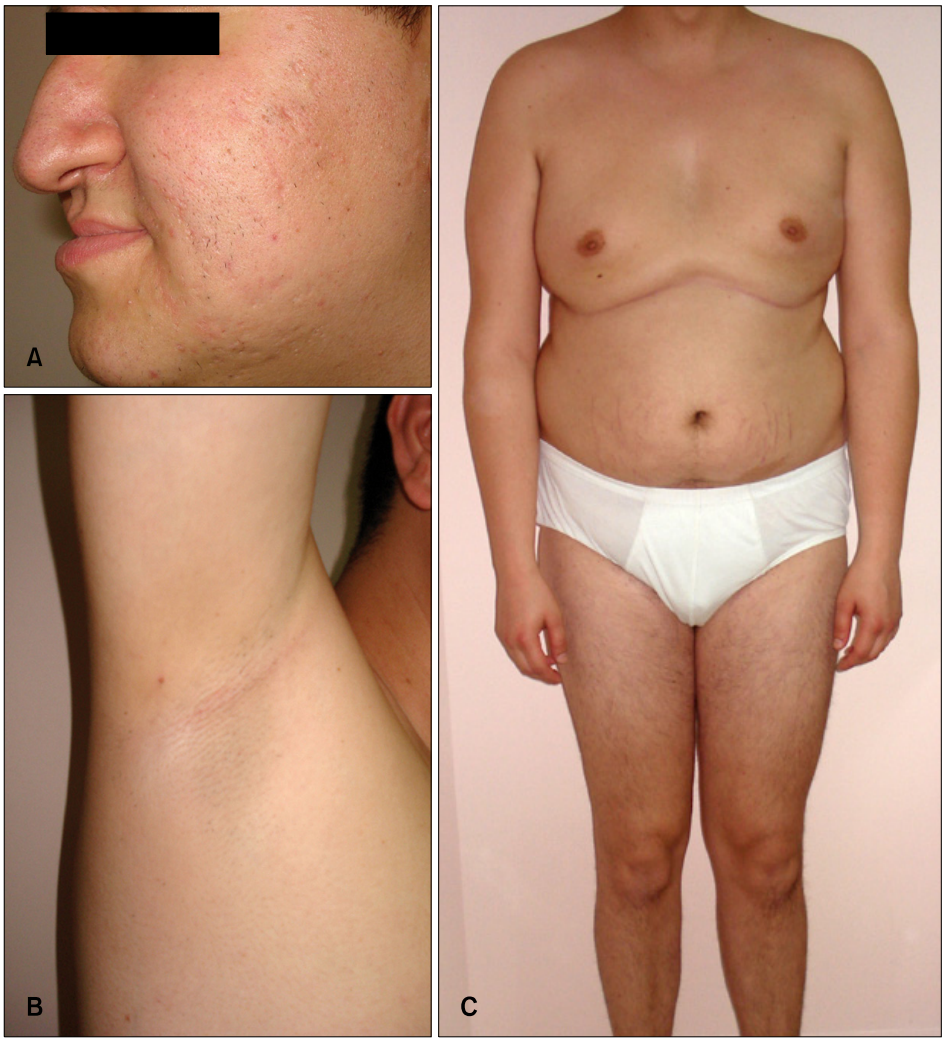

Fig. 1. (A) Sparse facial hair, prognatism and short filtrum. (B) Sparse axillary hair. (C) Gynecomastia and feminine distribution of adipose tissue.

Thus, in the literature, the data for 48,XXXY variants is limited, especially regarding the age of diagnosis and congenital malformations[5].

Clinicians should pay more attention to this easily overlooked syndrome in order to diagnose more boys with KS at an earlier age. The finding of sparse facial and axillary hair, even though could be familial, is a typical symptom of hypogonadism. Among the most frequent causes of male hypogonadism, KS should come to mind in the presence of eunuchoid body proportions, cognitive or dysmorphic facial features. Unfortunately, our case was left undiagnosed till he visited our clinic with the complaint of sparse facial hair at the age of 21. When his dysmorphic features came to notice during the dermatologic examination, a chromosome analysis was performed and the patient was properly diagnosed as variant KS.

In conclusion, KS and its variants can be recognized by even very indefinite findings such as sparse facial hair when combined with a careful detailed physical examination. Thus, we would like to emphasize the importance of a thorough physical examination during dermatological evaluation of a patient that can disclose any underlying systemic illness.

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