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LETTER TO THE EDITOR

Klinefelter syndrome and short stature: an unusual combination

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Abstract Klinefelter syndrome is not easy to diagnose in childhood because of the absence of significant manifestations before puberty. Three main clinical signs should suggest the diagnosis in a child: small testes, tall stature, and mental retardation or learning problems. We present a patient with Klinefelter syndrome and short stature due to growth hormone deficiency. His height was below the third percentile for age and his bone age delayed. Maximal serum GH levels after insulin-induced hypoglycemia and clonidine were low, demonstrating GH deficiency. He received growth hormone treatment with good response. The diagnosis of Klinefelter syndrome was made at puberty, because the patient did not present a normal progression of testicular development and puberty. At that moment, a karyotype was made confirming the suspected diagnosis. We wish to emphasize the rare association between Klinefelter syndrome and growth hormone deficiency.

Klinefelter syndrome is the most common cause of hypergonadotropic hypogonadism in males. It was first described in 1942 as a syndrome characterized by hypergonadotropic hypogonadism, small testes, and gynecomastia; and has a high prevalence, more than expected: 1/600–1000 male births [1, 2]. One of the most characteristic features is tall stature.

We report an 8 years boy, who was referred by his pediatrician for short stature. He came from a twin pregnancy (his sibling died in uterus) and was born at term with normal length and weight. The neonatal period was uneventful. Height gain was normal in the first 2 years of life with slowing growth rate in subsequent years. His height at first visit was 118 cm (−2.58 SD) with BMI 17.48 kg/m^2 (−0.21 SD). He had hypertelorism without another dysmorphic features, normal testes (2 ml), and penis. Bone age was retarded 2 years (TWRUS-II method). Routine blood, urine test, and thyroid hormones were normal. Celiac disease was excluded. IGFBP3 and IGF-1 values were 2.25 mcg/ml (1.7–3.52) and 68 ng/ml (76–499), respectively. Maximal serum GH levels after insulin-induced hypoglycemia and clonidine were low (4.36 and 3.30 ng/ml, respectively) demonstrating GH deficiency. Brain magnetic cranial resonance was normal. In the next years, he presented difficulties in school efficiency, and an intellectual coefficient was performed with a value of 66. The growth rate was slowing down gradually maintaining bone age delay. Growth hormone treatment was started at 12 years of age. After treatment, IGF-1 values and growth rate were normalized with appropriate catch-up growth. He started puberty at 14 years (bone age 13) with adequate progression. A testicular volume of 10 ml was reached at 16 years, with pubic hair and external genitalia at stage IV (Tanner). At 17 years, testicular volume was reduced to 3 ml, maintaining pubic hair and penis development. At that moment, total testosterone was 1.78 ng/ml (1.81–18) and basal follicle stimulating hormone and luteinizing hormone were increased (38.60 and 21.10 mUI/ml, respectively). A karyotype was made showing a chromosomal pattern of 47 XXY. The diagnosis of Klinefelter syndrome was then made.

Although one of the most characteristic features of Klinefelter syndrome is tall stature, some uncommon variants are associated with short stature (49 XXXXY,

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isochromosome Xq) [3–5]. To the knowledge, there are few reported cases of Klinefelter syndrome and short stature secondary to growth hormone deficiency [1, 4]. Rossodivita et al. in 1994 [1], reported an 8-year-old boy with Klinefelter syndrome and short stature. Complementary studies showed a partial growth hormone deficiency. Their patient started growth hormone treatment at 5 years and the results were successful in the first year of treatment, but they did not report more data. Tori et al. [4] reported a 13-year-old boy with short stature, Klinefelter syndrome, and partial growth hormone deficiency but the patient did not receive growth hormone treatment.

We report a case of difficult diagnosis of Klinefelter syndrome, due to the presence of short stature and the absence of other symptoms.

Conflict of interest The authors declare no conflict of interest.

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