

Clinical case

Turner's syndrome with mosaicism 45,X/46,XX/47,XXX associated with Klippel-Feil syndrome

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Abstract

Background: Turner's syndrome is due to the absence or anomaly of an X chromosome, resulting in short stature, gonadal dysgenesis and various physical characteristics. The association of this syndrome with other alterations such as autoimmune diseases has been described and, in rare cases, coexists with Klippel-Feil syndrome. We undertook this study to report the case of a female with Turner's syndrome with mosaicism (45,X/46,XX/47,XXX) with the coexistence of Klippel-Feil syndrome.

Case report. We present the case of a female patient with short stature and physical characteristics of Turner's syndrome. The patient presented with limitations of neck movement with a forced position to the right side of her skull. Karyotype showed a chromosomal complement (45,X/46,XX/47,XXX). Radiologically, fusion of the first and fifth cervical vertebrae and vertebral fusion of the seventh cervical vertebra with the first thoracic vertebra were observed.

Conclusions. This may represent the first case of Turner's syndrome associated with a cytogenetic variety of Klippel-Feil syndrome.

Key words: Turner's syndrome, Klippel-Feil syndrome, mosaicism, association between Turner's and Klippel-Feil syndromes.

Introduction

Turner's syndrome originates due to absence or structural anomaly of one of the X chromosomes and is characterized by short stature, gonadal dysgenesis, and physical stigmas.^{1,2} Turner, in 1938, on studying a group of postpubescent women, described the syndrome that carries his name. It is characterized by short stature, sexual immaturity, primary amenorrhea, webbed neck and cubitus valgus.² Ortiz et al. pointed out that it was Ford who, in 1959, first described the karyotype 45,X. They also point out that there are other cytogenetic variants, among which is mosaicism XO/XX.³ The association of this syndrome with inflammatory intestinal disease, rheumatoid arthritis, autoimmune thyroiditis and diabetes mellitus has been described.⁴

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Figure 1. Note the low-set ears with superoposterior rotation, micrognathia and short neck.



Figure 2. Flattened mid-face, short neck.

Klippel-Feil syndrome is characterized clinically by a short neck with limited mobility and low implantation of hair on the region of the back of the neck due to the merger of two or more cervical vertebrae.⁵ According to the etiology of this syndrome, environmental and genetic factors have been documented that cause a defect in embryonic development between 3 and 8 weeks of pregnancy, causing a lack of segmentation of cervical somites, giving rise to a lack of separation of vertebral bodies of the cervical spine.^{6,7} McKusick notes that this syndrome was first described in 1912 by Maurice Klippel and Andre Feil and, since then, associations with other skeletal abnormalities such as scoliosis and Sprengel's deformity and hearing loss, as well as cardiac and renal anomalies have been documented.^{5,6} In the past 30 years, two studies have been documented with the association of Turner's and Klippel-Feil syndromes (Hillemand et al. 1973 and Suchkova et al. 1987) Both publications refer to Turner's syndrome according to regular X monosomy (45,X).^{8,9} This study aims to report the case of a female with Turner syndrome mosaicism 45,X/46,XX/47,XXX

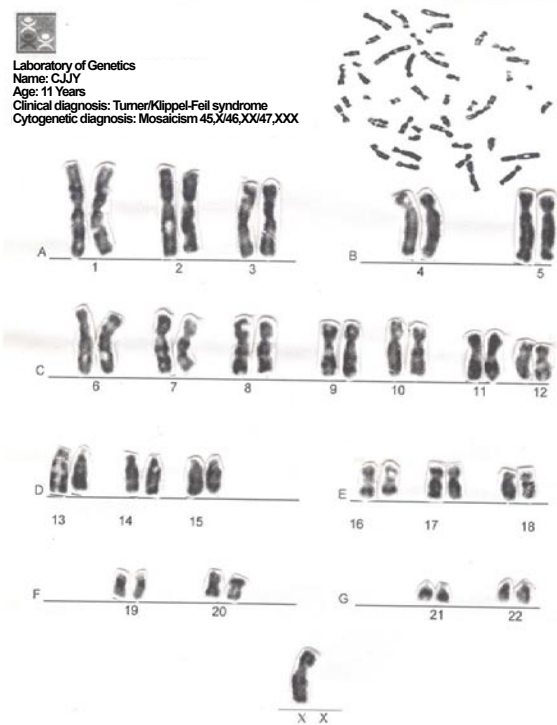


Figure 3. Chromosome complement 45,X.

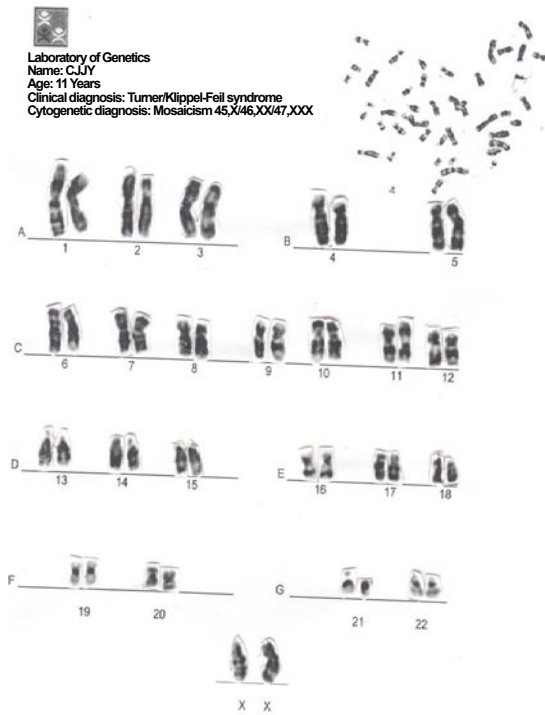


Figure 4. Chromosome complement 46,XX.

and in whom Klippel-Feil syndrome coexists.

Clinical Case

We present the case of an 11-year-old female who is a native of and resident of Amatan, Chiapas, Mexico. The patient is the product of the first gestation of the mother who experienced a normal pregnancy (no history of teratogenicity). At term, childbirth was apparently normal with labor at home. Neonatal period was uncomplicated and birth measurements are unknown. Neurological development in infancy was delayed with the following reported: sitting at 10 months, walking at 18 months and beginning of language with phrases at age 3 years. Parents were unrelated. The mother was 16 years old and the father 27 years old at the time of the patient's birth.

Physical examination revealed the following: weight 27 kg (10th percentile), height 101 cm (<3rd percentile). These cause the appearance of the patient to be younger than her age, slender, with flattened occiput skull, eyelashes of unusual length, horizontal palpebral fissures, narrow forehead, flattened nasal bridge, low-set ears rotated backwards, carp mouth, high-arched palate, and micrognathia. The neck is short and wide with low implantation of hair in the posterior region and limitation of neck rotation. She must assume a position of right lateral tilt of the skull

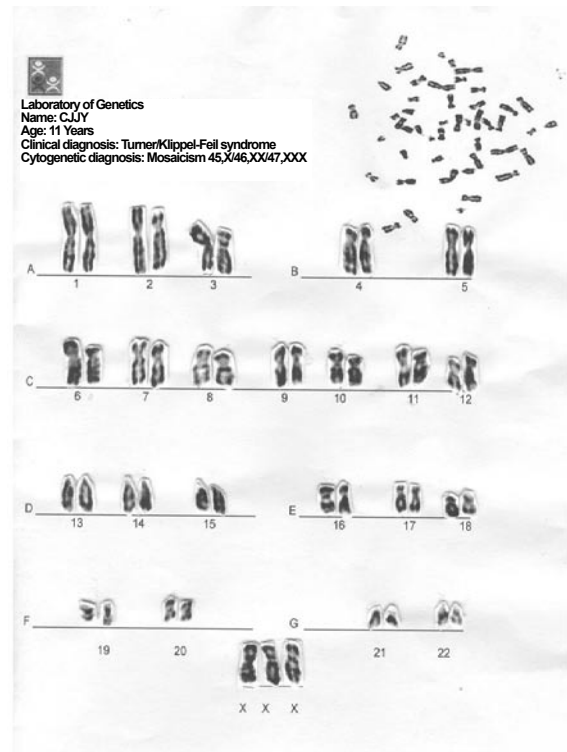


Figure 5. Chromosome complement 47,XXX.



Figure 6. Note the synostosis of the bodies of cervical vertebrae 1-5

(Figures 1 and 2). Routine studies consisting of blood count, blood chemistry and general urine examination were normal. Thyroid profile, T3, T4 levels and thyroid stimulating hormone (TSH) were normal. Cultivation of peripheral blood lymphocytes for chromosome analysis revealed the existence of three cell lines: 45,X/46,XX/47,XXX, at 64, 24 and 12% respectively (Figures 3-5). Echocardiography showed normal heart rate, and radiographic fusion was observed from first to fifth cervical vertebrae and intervertebral space narrowing 5-6 and 6-7, in addition to spinal fusion of the 7th cervical to 1st thoracic vertebrae (Figure 6).

Discussion

One of every 400-500 live newborns presents sexual chromosomal abnormalities.¹⁰ Turner's syndrome has an incidence of 1/2000 to 1/3000 live female newborns and is due to the absence or anomaly of an X chromosome with the consequence of low stature, gonadal dysgenesis and physical stigmas.¹ In 50% of the cases there is absence of an entire X chromosome, with a chromosomal complement 45,X being observed, whereas the remaining 50% present with multiple chromosomal anomalies such as mosaicisms, partial deletions or translocations.¹¹ Among the most common mosaicisms are 45,X/46,XX; 45,X/46,XXiq; and 45,X/46,XY.¹¹ The association of this syndrome with other alterations such as autoimmune diseases has been described, among which are intestinal inflammatory diseases, rheumatoid arthritis, autoimmune thyroiditis and diabetes mellitus.⁴ The phenotype of Klippel-Feil syndrome has a triad that presents itself in <50% of the cases and is characterized by low implantation of hair, short neck and limitation of neck mobility.¹² These characteristics are shared with Turner's syndrome, with the exception of neck mobility limitation. In 1973, Hillemand et al. described the case of a female with Turner's syndrome who also had co-existence of

Rokitnasky-Kuster-Hauser syndrome and Klippel-Feil syndrome.⁸ Later in 1987, Suchkova et al. reported another case of association of Turner's syndrome and Klippel-Feil syndrome.⁹ In both cases, Turner's syndrome corresponded to the cytogenic variety of regular monosomy X. Similarly, there are reports that point out the association of Klippel-Feil syndrome with structural type chromosomal aberrations. Clarke et al., in 1995, reported a familial Klippel-Feil-type syndrome in which they identified a paracentric inversion of the long arm of chromosome 8, inv(8) (q22.2 q22.3).¹³ These authors observed that those affected with this structural chromosomal aberration presented with congenital vertebral fusion.

The case reported here corresponds to an 11-year-old female with a chromosomal complement that includes three cellular lines: 45,X/46,XX/47,XXX, with clinical manifestations of Turner's syndrome and with limitations of movement of head turning. These correspond clinically, cytogenetically and radiologically to a case of mosaic Turner's syndrome associated with Klippel-Feil syndrome, possibly corresponding to the first case of Turner's syndrome with this cytological variety associated with that of Klippel-Feil syndrome.

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