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REVIEW ARTICLE

Clinical and genetic aspects of Turner's syndrome

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Abstract Turner's syndrome, or monosomy X, is defined as the total or partial loss of the second sex chromosome. The clinical phenotype is highly variable and includes short stature, gonadal dysgenesis, *pterygium colli*, *cubitus valgus* and low hairline. The variable expressivity of height and other physical features may be only partially related to the chromosomal formula. Currently, the delay in the diagnosis of Turner's syndrome remains a problem, as only 15–30% of patients are diagnosed during their first year of life. Understanding its complex etiology and learning more about its clinical variability and complications will allow us to advance the therapeutic and management approach of such patients. This review summarizes the clinical characteristics of, and diagnostic tests for, Turner's syndrome and the advances in the study of its underlying genetic factors.

Introduction

Turner's syndrome, or monosomy X, is defined as the total or partial loss of the second sex chromosome, either X or Y.[1] Clinical phenotype is highly variable and includes short stature, gonadal dysgenesis, *pterygium coli*, *cubitus valgus* and low hairline.[2,3] It was first described by Ullrich in Germany in 1930.[4] In 1938, Turner's described a group of seven women, ages between 15 and 23, who presented a series of physical alterations, mainly characterized by a short size and gonadal dysgenesis.[5] In 1959, Ford et al. recognized the syndrome's chromosomic base, they found that patients presented 45 chromosomes with a single X chromosome.[6]

Turner's syndrome occurs in 1 every 2500–3000 live births and it is the only full monosomy which is compatible with life.[2–4] Advances in the study of underlying genetic advances allows for a greater understanding of associated co-morbidities. Since just 30% of TS cases are diagnosed early, a proper and timely management, with a subsequent improvement in quality of life, is not accomplished in most patients. This paper reviews the main clinical characteristics, diagnostic tools and advances in the study of its underlying genetic factors.

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Chart 1 Clinical characteristics of patients with Turner syndrome.

Clinical charactertistics	Frequency (%)
Low height	99
Short neck	50
Cubitus valgus	70
Pterigium colli	25
Low hair line	80
Edema of the hands and feet	80
Hyperconvex and/or deep nails	70
Characteristic dermatoglyphs	35
Gonadal dysgenesis	96
Cardiovascular disorders	50
Kidney malformations	40
Pigmented nevi	50
Eyelid ptosis	11
Hearing impairment	50
Hashimoto's thyroiditis	30
Carbohydrate intolerance	40

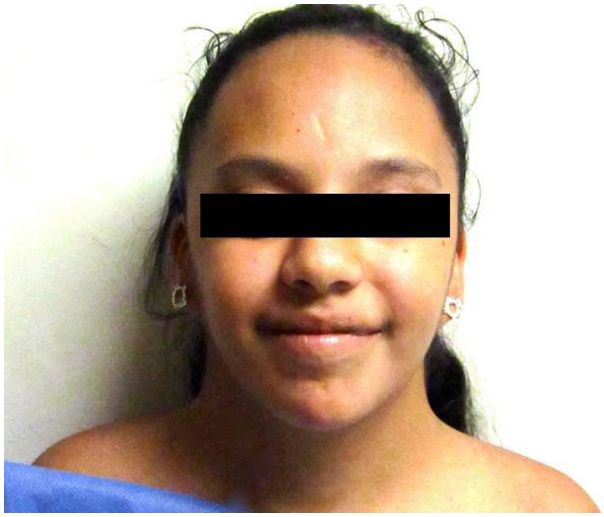

Figure 1 Craniofacial dysmorphias in a patient with TS. Downslanting eyelid openings, ptosis, low-set pinnae and a wide and short neck can be observed.

Clinical characteristics

The variable expressivity of height and other physical features may be only partially related to the chromosomal formula, even when most recent studies do not show a clear genotype-phenotype correlation. Sometimes the phenotype may be practically normal, which occurs more frequently in cases due to partial monosomy or mosaicism.[2] The frequency of structural and functional malformations are described in Chart 1.

Clinical phenotype

Short stature is the most constant data, it is present in over 90% of cases,[2,4] it varies depending on country of origin and it is usually 20–22 cm under the average population.[7] TS's spontaneous growth is characterized by a moderate intrauterine growth delay, slow growth from childhood, with a progressive separation from the average population's size, absence of puberty development and bone maturation delay.

A characteristic sign is a relative widening of the thorax ''shield chest'', sometimes linked to *pectum excavatum*. Extremity alterations are frequent, *cubitus valgus* and shortened metacarpal IV are both classic, more constant signs. Less frequent, however more suggesting is Madelung wrist deformity, observed from 5 to 6 years of age and characterized by a lower growth of the radius with respect to the ulna, generating a progressive dorsal deformity of the radial ulnar joint or the ''Dinner fork sign''. Regarding the lower limbs, *genu varum* and metatarsal shortening may be found.

Some anomalies in facial bone development contribute to the configuration of the ''sphynx'' face. These include microrethrognatia and an underdeveloped superior maxilla, which result in an ogival palate and dental malocclusion. Other frequent facial features include palpebral ptosis, strabismus, oblique palpebral openings from top to bottom, a thin upper lip with downward commissures and a long filtrum, epicanthal folds and ear implantation with posterior rotation as a consequence of the abnormal development of the bones at the base of the cranium (Fig. 1). These bone anomalies predispose a greater risk of presenting otitis media.

One of the most typical findings during the neonatal period is lymphedema in the feet and hands, which is a result of a drainage deficit due to hypoplasia of the lymphatic vessels and is usually transitory, yet it leaves as a sequelae hypoplastic, narrow and convex nails. Said abnormal drainage has visible and persistent consequences in the neck, where *pterigium colli* or webbed neck, secondary to nuchal hygroma during fetal life, as well as skin folds and a low hair line and ear implantation are attributed to hygrome absorption. Pigmentary nevus are frequent, along with telangectasias and keloid scars.

Cardiovascular features

Congenital structural heart diseases affect approximately 40% of TS patients and are an important cause of early mortality.[8] These anomalies include narrowing of the aorta, a bicuspid aortic valve and abnormal pulmonary venous returns. Aortic dilatation occurs in 15–30% of girls with TS[1] and depending on the size, carries a significant risk of dissection. Aortic dissection incidence in TS is estimated at 0.6–1.4% with a median age of 30–35 years of age.[9]

Adult patients with TS frequently show electrocardiographic abnormalities, including axis deviation to the right, T-wave abnormalities, accelerated AV conduction and prolongation of the QT-interval, often independent from structural defects.[10] Essential hypertension affects up to a 25% of adolescents and 50% of adult patients.

Endocrine and reproductive features

A greater susceptibility to endocrine and autoimmune diseases is well-documented in these patients.[11] Thyroid disease has been reported in up to 30%, with hypothyroidism