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Clinical report

Turner syndrome: Study of 42 cases☆

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ABSTRACT

Background and objective: Turner syndrome (TS) is characterized by short stature, gonadal dysgenesis, and total or partial loss of X chromosome.
Patients and methods: A historical cohorts study of patients with TS ≤ 18 years old followed up in public hospitals in Castilla and Leon was undertaken.
Results: Forty-two female patients were included (prenatal diagnosis 11.9%, neonatal diagnosis 14.3%) with current median age 11.9 ± 4.2 years. Short stature was the reason for consultation in 87.1%. Total monosomy of X chromosome was present in 40.5%. The most frequently associated comorbidity was opthalmological (50%), with heart defects in 23.8%. Ninety-three percent were treated with growth hormone (GH), mean age at the beginning of treatment was 7.43 ± 3.4 years and mean height standard deviation was −2.84 ± 1.08. Final height was reached in 10 patients only (mean final height 151.47 ± 6.09 cm). Chronological age of puberty induction was 13.2 ± 0.94 years (bone age 12.47 ± 1.17 years).
Conclusions: Short stature was an important clinical sign for the diagnosis of TS, accompanied in some cases by other findings, with good response to GH treatment.

Síndrome de Turner: análisis de 42 casos

Palabras clave:
Síndrome de Turner
Talla baja
Hormona de crecimiento

RESUMEN

Antecedentes y objetivo: El síndrome de Turner (ST) se asocia con talla baja, disgenesia gonadal y monosomía parcial o total del cromosoma X.
Pacientes y métodos: Se realizó un estudio de cohortes histórico de las pacientes con ST ≤ 18 años seguidas en los hospitales públicos de Castilla y León.
Resultados: Se registraron 42 pacientes (diagnóstico prenatal 11,9%, neonatal 14,3%) con una edad media actual de 11,9 ± 4,2 años. La talla baja fue el motivo de consulta en el 87,1%. El 40,5% presentaban monosomía total del cromosoma X. La enfermedad asociada más frecuente fue la oftalmológica (50%), con problemas cardiacos en el 23,8%. El 93% reciben tratamiento con *growth hormone* (GH, «hormona de crecimiento»), con una edad media al inicio de 7,43 ± 3,4 años y una DE media de talla de −2,84 ± 1,08. Solamente 10 pacientes han alcanzado talla final (talla media 151,47 ± 6,09 cm). La edad cronológica media de inducción puberal fue 13,2 años ± 0,94 años (edad ósea 12,47 ± 1,17).
Conclusiones: Uno de los datos clave para el diagnóstico fue la talla baja acompañada en algunos casos de otros hallazgos, siendo el tratamiento con GH efectivo.

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◊ The names of the Pediatric Endocrinology Group components of Castille and Leon are available in the Annex.

Introduction

Turner syndrome (TS) is a genetic disorder caused by the complete or partial absence of an X chromosome, with or without mosaicism, which affects about 1/1500–2500 live births.[1,2] Among the most frequent clinical manifestations is short stature, this may appear alone or associated with other phenotypic alterations. Other manifestations frequently present in patients with TS are gonadal dysfunction and heart malformations. Treatment with *growth hormone*(GH) is the standard in patients with TS today, and an early start is crucial.[3] Although gonadal function is impaired in most such patients, requiring hormone replacement therapy (HRT), there are some who have spontaneous puberty.[2]

The aim of this paper is to analyse the clinical characteristics and treatments of a series of 42 girls with TS in Castille and Leon.

Patients and method

Data from 42 girls of ≤18 years of age with TS who are undergoing follow-up in the various public hospitals in Castille and Leon on 31.10.2015 were collected through the review of the medical records of each patient by professionals who perform their monitoring and in compliance with the ethical requirements of each centre. For some results, the sample was divided into 2 groups: one group with karyotype 45X0 patients and another group with the rest of karyotypes. Quantitative variables are presented as mean and standard deviation (SD), and qualitative variables according to their frequency distribution. The association of qualitative variables was analysed through Pearson's Chi-square test. Fisher's exact test or the likelihood ratio test for variables with more than 2 categories was used if the number of cells with expected values under 5 was greater than 20%. Comparisons of quantitative values were performed using the nonparametric Mann–Whitney *U* test. Data were analysed with IBM® SPSS® Statistics, version 20.0 for Windows®. *p* values <0.05 were considered statistically significant.

Results

A total of 42 patients with TS were recorded, half of the cases were found between Valladolid and Leon (13 in Valladolid, 9 in Leon, 6 in Burgos 5 in Salamanca, 3 in Avila, 2 in Palencia, 2 in Segovia, one in Soria and another one in Zamora). 40.5% had karyotype 45X0, the rest had mosaicism or X chromosome structural abnormalities (Table 1). The mean age of patients was 11.9 ± 4.2 years (range 5 months to 18 years). 11.9% were diagnosed prenatally (n = 5) and 14.3% (n = 6) in the neonatal period. Patients diagnosed in the neonatal period corresponded mostly to karyotype 45X0 (n = 4), and the guide symptom was the presence of oedema on the backs of the hands and feet. The mean diagnosis age of patients was 6.64 ± 4.44 years (excluding prenatal diagnosis), with younger diagnosis age in patients with karyotype 45X0, although it was not significant (Table 2). In patients diagnosed after the neonatal period, the most frequent reason for consultation was a short stature (87.1%), with other abnormalities associated in a significant percentage of cases (28.6% webbed neck, shield chest 30.9%, cubitus valgus 35.1%). Birth size was less than −2 SD in 21.4% of the sample, with no significant differences depending on the type of karyotype (Table 2). Regarding associated processes, heart problems were only present in 23.8% of patients (n = 10) aortic coarctation being the most common (n = 6), followed by bicuspid aorta and aortic insufficiency, all patients presenting normal blood pressure (a complete cardiological study was conducted in all of them, with echocardiogram included). Not all patients with heart disease had karyotype 45X0; only 3 of them. Two patients had celiac disease, diagnosis being prior to TS in one of them. None of the patients had liver disease. Thyroid processes (5 had positive thyroid autoimmunity and 6 hypothyroidism) were reported in 26.2% of the series (n = 11), only 3 of them with karyotype 45X0. 26.2% of the sample (n = 11) reported ENT problems, mostly regarding repeat serous otitis media, 4 patients associated hearing loss (all had karyotype 45X0 except one). Kidney malformations (horseshoe kidney) appeared in 3 patients, 2 of them 45X0. Ophthalmological processes were the most common, affecting 50% of the sample (refractive errors, strabismus, etc.). Blepharoptosis as isolated ophthalmological manifestation appeared in 3 patients (all karyotype 45X0). Regarding height, the mean SD of this regarding diagnosis (postneonatal diagnoses) was −2.46 ± 0.85, with greater height compromise in karyotypes 45X0, although not being significant (Table 2). 92.9% of patients are receiving or have received GH, the mean age at baseline being 7.43 ± 3.4 years. The mean height at the start of treatment was −2.84 ± 1.08, without significant differences between karyotypes (Table 2).

During the first year of treatment a significant height increase was observed ($p < 0.01$), improving it from a mean SD of −2.84 ± 1.08 up to −1.9 ± 1.7. If we compare the height SD at one year of starting treatment with GH with the height of the last recorded follow-up, no increase is observed ($p = 0.997$), presenting a mean height SD of −1.9 ± 1.3, with no differences between karyotypes. Only 10 patients reached adult height, with a mean of 151.47 ± 6.09 cm, with no significant difference related to the

Table 1
Patients' karyotypes.

Karyotype	Number of patients
45X0	17
46X,del(X)(p21)	2
Isochromosome X	4
46XX/45X0	10
46X,der(X)del(X)(p22.1)dup(X)(q26)	1
45X,delXp11.4 pter	1
45X0/47XXX	3
45X0/46XX/47XXX	1
46XX,add(X)(p22.1)	1
46X,i(Xq)/47,X,i(Xq),i(Xq)	1
46XX,del(X)(q21-ter)	1

Table 2
Patient characteristics depending on karyotype.

	45X0	Other karyotypes	*p*
Number of patients	17	25	
Current age	12.88 ± 3.71	11.27 ± 4.53	0.330
SD target height	−0.57 ± 0.82	−0.58 ± 0.83	0.957
Mean age at diagnosis	5.59 ± 4.83	7.35 ± 4.13	0.292
Prenatal diagnosis	2 (11.8)	3 (12)	1
Neonatal diagnosis	4 (23.5)	2 (8)	0.368
Postnatal diagnosis	15 (88.2)	22 (88)	1
Mean size SD at birth	−1.49 ± 1.26	−0.94 ± 1.79	0.067
Mean height SD at diagnosis	−2.67 ± 0.78	−2.35 ± 0.89	0.436
Heart disease	3 (17.6)	7 (28)	0.490
ENT disease	8 (47.1)	3 (12)	0.029
Renal disease	3 (17.6)	1 (4)	0.2886
Ophthalmological disease	7 (41.2)	12 (48)	0.663
Webbed neck	7 (41.2)	5 (20)	0.174
Cubitus valgus	5 (29.4)	10 (40)	0.482
Shield chest	6 (35.3)	7 (28)	0.616
Widely spaced nipples	9 (52.9)	8 (32)	0.175
GH treatment			
Start mean age	7.16 ± 3.07	7.64 ± 3.73	0.690
Start mean SD	−3.08 ± 1.12	−2.68 ± 1.05	0.060
First year of treatment SD	−2.42 ± 1.77	−1.55 ± 1.72	0.071
Menarche age	15.06 ± 0.65	13.70 ± 1.47	0.142
Mean adult height	148.40 ± 8.45	153.52 ± 3.39	0.286

Data are expressed as n (%) or mean ± standard deviation.