CASE REPORT

Turner Syndrome: Fifteen Years' Experience in India

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Introduction

Turner Syndrome (TS) is the commonest chromosomal abnormality in females, estimated to affect ~3 % of all female fetuses. Only 1 % of affected fetuses survive to term, leading to an incidence of ~1 TS patient per 2,500 live female births [1]. Data regarding clinical course and cytogenetics of Indian patients with TS were scarce. We found 2 clinical series with 45 and 24 patients [2, 3] and one article [4] dealt with the results of growth hormone treatment on Indian TS patients. In view of this paucity of Indian data, we searched our database from 1996 to 2010 and came up with 35 patients of TS, whose results are incorporated in this presentation.

Materials and Methods

Thirty-five patients with TS patients presenting to this referral endocrinology clinic—The Park Clinic, Kolkata, India—between 1996 and 2010 were included in this study.

Diagnosis of TS was done by karyotyping, involving a study of at least 50 metaphases and including G banding. A retrospective chart review of these patients formed the basis of this study. Simple descriptive statistical methods were used and percentages calculated wherever appropriate. The study protocol was presented before the Institute's Ethics Committee which approved the study and felt that the requirement of informed consent could be waived.

Results

Thirty-five patients with TS karyotype were seen, and the findings have been presented in Table 1. The mean age at diagnosis was 11.7 ± 5.2 years; the median age was 12 years (range 2–23 years). Patients with classic TS and those with cardiac or renal stigmata were diagnosed early. The commonest presenting features were delayed puberty and short stature. The oldest patient had mosaic TS and presented with premature ovarian failure.

Cytogenetic analysis of our patients showed that 14 patients (40 %) had classical TS karyotype 45 X0. Sixteen (45.7 %) patients had varying degrees of mosaicisms. One patient (2.9 %) had ring X chromosome 46X, r(X); 1 patient (2.9 %) had isochromosome X 46X, i(Xq); and three patients (8.6 %) had deletions 46X, del (X).

Spontaneous menarche occurred in nine patients, all of whom had either deletions or mosaic patterns in their karyotype. Seven patients had primary hypothyroidism with positive Hashimoto antibodies. One patient each had

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Table 1 Clinical characteristics of the TS Patients

Clinical characteristics	Percentage (number) of patients
Psoriasis	2.9 (<i>n</i> = 1)
Mentally challenged	8.6 (<i>n</i> = 3)
Hearing loss	2.9 (<i>n</i> = 1)
Spontaneous menarche	25.7 (<i>n</i> = 9)
Primary hypothyroidism	20 (<i>n</i> = 7)
Type 1 DM	2.9 (<i>n</i> = 1)
Type 2 DM	2.9 (<i>n</i> = 1)
Cardiac anomalies	22.9 (<i>n</i> = 8)
Renal abnormalities	2.9 (<i>n</i> = 1)

psoriasis, type 1 diabetes, and type 2 diabetes. One patient had documented sensori-neural hearing loss and one had surgery for hydronephrosis.

Two patients had cardiac surgery, one for total correction of Tetralogy of Fallot and another for congenital aortic stenosis. One patient had a prolapsed mitral valve, one had aortic coarctation, one had unexplained cardiomegaly and was lost to follow-up, one patient had spontaneous closure of VSD, and two patients had essential hypertension.

One patient had cerebral atrophy and needed special schooling. Two failed their Class 10 examinations, one needed counseling off and on and the other patient needed treatment with antidepressants. The patient with the ring chromosome had completed college and had normal educational attainments according to her family. Individual patients' IQs were not tested.

All patients and their parents received age-appropriate counseling. However, only 16 out of 35 patients revisited the clinic. The follow-up duration varied from 18 months to 6 years.

Puberty was initiated in 14 of the 16 patients on regular follow-up. One patient was underage and another had been initiated on a low dose of oral testosterone undecanoate elsewhere and requested a change to estrogens. Initiation of treatment with a non-aromatizable or weak androgen was not acceptable to 13 of the 14 families. In one case, where the father was a doctor, treatment was initiated with oxymetholone for 6 months. Conjugated equine estrogen was started in 6 out of 15 patients, while ethinyl estradiol was chosen by the remainder due to cost considerations.

Six patients requested and received advice for GH treatment in a dose of 1 unit per kg per week or 0.1 mg/kg/day. Two patients had the treatment for 3 and 4 months, two had it for 1–2 years, and another two are still continuing at 4 and 6 years. Of the latter two patients, one deferred the initiation of puberty to age 16.5 years and the other had spontaneous menarche at age 14 years. The growth of these 2 patients is shown in Fig. 1.

Fig. 1 Turner syndrome growth chart showing the growth of the 2 patients during the duration of their growth hormone treatment. A Growth curve for the patient with mosaicism B Growth curve for the patient with Xp deletion

Discussion

Given India's birthrate of 22,000 and an incidence of TS of 1 in 2,500 female births, ~5,200 TS girls are born in India each year. The paucity of Indian literature on the subject and the fact that this referral clinic saw merely two patients per year, suggested that a large number of TS patients go undetected. In Denmark, the median age of diagnosis for TS was 15 years which compared favorably with our data where the median age at diagnosis was 12 years. In Denmark, the number of diagnosed TS patients was 50 % of the number estimated to exist, suggesting underdiagnosis of the condition [5].

Unlike the findings of Bharath et al. [3], we found no clinically meaningful differences between classic TS karyotype patients and others. This underscored the need for further research to elucidate phenotype–genotype correlations.

Lack of follow-up, with 54 % (*n* = 19) of the patients in this series not revisiting, bedeviled our best efforts in treating TS. It also underscored the need for non-medical

counselors to keep in touch with patients and families. Patients' responses to puberty were sharply individual. Almost all rejected androgen pretreatment to enhance final height. One patient on GH persistently refused estrogen treatment till age 16.5 years on the grounds that it could diminish final height.

Mortality in TS under the age of 15 years has been found to be 4 times the background mortality, mainly due to cardiovascular disease. There were no reported deaths in this series. In an earlier series, even when congenital cardiac disease was factored out, life expectancy at 40 years was reduced by 10 years [6].

There is insufficient information in this series on GH treatment in TS. Two patients had GH for a substantial length of time and in the lowest recommended dose. The patient who is continuing with the GH treatment for 4 years now has Xp deletion, while the other patient who is being treated for 6 years now has mosaicism with 10 % of lymphocytes being 45 X0. It was worth noting that the lowest recommended doses of GH produced a marked height increase in the two patients.

Conclusion

A vast number of TS patients in India appear to be undiagnosed. Diagnosed patients were often lost to follow-up.

The patients who remained posed a challenge in that they could not be treated according to Western standards due to lack of financial and social support.

Conflict of interest None.

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