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Case Report

CLINICAL AND CYTOLOGICAL STUDY ON TURNER SYNDROME

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ABSTRACT

Turner syndrome (TS) is a common chromosomal disorder. TS also known as Ulrich-TS. Gonadal dysgenesis, 45X is a condition in which there is partly or completely missing X chromosome in a female. The main clinical features of TS are swollen hands and feet, wide, and webbed neck. A combination of the following symptoms may be seen in older females: Absent or incomplete development of puberty (sparse pubic hair and small breasts), broad and shield like chest, drooping eyelids. TS frequently seen in young infants. Our case is a 10-year-old girl with TS-specific clinical hallmarks, with the symptoms of short stature, wide shield like chest, drooping eyelids. She visited our hospital because of her neck swelling, pain on/off since 1 month. In our study, we report both clinical and cytogenetic investigations, which show that patient is suffering from TS. This type of syndrome is very rare in our region.

Keywords: Turner syndrome, Short stature, Chromosome analysis.

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INTRODUCTION

Turner syndrome (TS) is a common chromosomal disorder occurs due to loss of complete or partial X monosomy with a frequency rate of 1/2000 in female live births [1]. TS is not usually inherited from parents, while normal people have 46 chromosomes, people with TS usually have 45. The chromosomal abnormality may be present in some cells in which case it is known as TS with mosaicism. About 1-2% of all conceptions have an X monosomy, 99% of them end in spontaneous abortions, usually during the 1st trimester of pregnancy then the disorder affects only one in 1,800-5,000 live births in different populations. The reported prevalence in the world is 1:2,000-1:5,000 live new born females [2].

The most common cytogenetic presentation form of TS is 45X, however, about 50% of patients have a different chromosome formula. The 45X/46XY variety is rare and reported in about 5% of cases [3]. 45X/46XY mosaicism is an extremely rare disorder, its incidence in the general population varies between 1.5/10,000 and 1.7/10,000 depending on the series [4]. It is considered that detection of material corresponding to Y chromosome is growing due to more frequent use of techniques such as fluorescent *in situ* hybridization. This could mean that true incidence of this phenomenon among patients with TS may range from 10% to 15% [2].

The clinical phenotype of patients with 45X/46XY mosaicism is broad, ranging from women with or without TS stigmata to apparently normal males with intervening variable ambiguous phenotypes [2]. Gonadal histology associated with 45X/46 XY mosaicism is also variable with partial, complete, mixed or asymmetric gonadal dysgenesis [5,6].

Hence, we report a case of a female patient with clinical findings and cytological analysis of TS whose chromosome was 45X, this is one of the rare cases in North Karnataka.

CASE REPORT

A 10-year-old girl from a rural village area (Yadgiri) was admitted to pediatric outpatient department because of neck swelling with continuous pain from 1 month. The child was apparently allight 1 month back when she developed neck pain. It was associated with fever of moderate grade and also associated with restricted neck movements. Several such episodes have occurred in last 1 month. She is studying in 5th standard, and there is no family history of short stature (mother's height 150 cm and father's height 170 cm). On physical examination height: 119 cm, weight: 19 kg, bod

y mass index: 13.5 kg/m2, MPH: 153.5 cm, short neck, wide chest and drooping eyelids (Fig. 1).

Fig. 1 shows that child's weight is <3rd percentile and height is <3rd percentile, i.e. weight is 19 kg and height is 119 cm recorded during her admission to hospital [7].

Cytological study

Microscopic examination was carried out for barr body study, buccal smear taken. Microscopic observation showed moderate cellularity, comprising squamous cells around 200 squamous cells were counted, but no barr bodies seen. Karyotyping was performed to see any structural changes in the chromosomes.

About 1 ml of peripheral heparinized blood was taken from patient and then immediately transferred to Laboratory of Genetics. Standard procedures were performed on the TS karyotype. In this study, the Roswell Park Memorial Institute medium, 1640 medium containing 25% fetal bovine serum, antibiotics such as penicillin (300 mg/ml) and streptomycin (300 µg/ml) were used (products of GIBCO). Medium under the laminar air flow was prepared. For cultivation, 5 ml of cell culture medium in each tube, 100 µl phytohemagglutinin and 1 ml peripheral blood were added and incubated for 72 hr with 5% CO_2 at 37°C, respectively. Tubes containing those medium were gently shaken daily. After this, 50 µl of colcemid was added to each tube and after half an hour, harvesting steps were done. Tubes were placed for 15 minutes in the serologic bath. After centrifugation, at 1200 rpm for 10 minutes, cells isolated from the culture medium were impressed with the hypotonic solution (KCl; 0.75 M). After centrifugation, the cells were exposed to the fixative solution (methanol and acetic acid at

a ratio of 3:1), and they were centrifuged again. After several washing steps with fixative solution, a clear suspension of lymphocytes obtained. Drop shot technique was used with sterile Pasteur pipette, and several slides were prepared [8]. With the G-banding method, metaphase spreads were prepared on the slides [9]. First, metaphase spreads were exposed to trypsin for 15 seconds and then placed in Giemsa solution. After 10 minutes, the slides were washed with distilled water. Pictures were taken from slides of each patient and with karyotyping software, they were analyzed and descriptive statistics were diagnosed.

In the second Figure showed that 20 were metaphase, total 44 were autosomes these were observed under 450 band resolutions with the help of Geneasis Software. 45th stage shows only one X chromosome instead of 2 XX chromosomes, i.e. 45X, normal male and female having 46 XX and XY. This is the unique chromosomal structural change observed in our study. This result indicates that patient is suffering from TS (Fig. 2).

DISCUSSION

According to a review of literature around the world, many authors have reported with similar cases with 45X/46XY and female phenotype with TS. Few cases were reported in India. To the best of our knowledge, this is the first case to be reported in our region. The occurrence of only one X chromosome and the other X chromosome is missing, i.e. 45X.

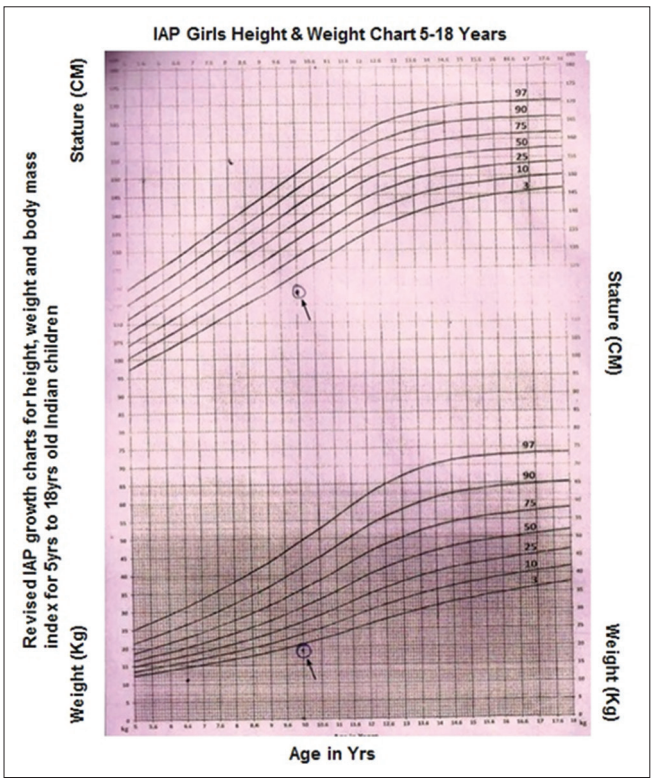

Fig. 1: IAP growth curve of patient

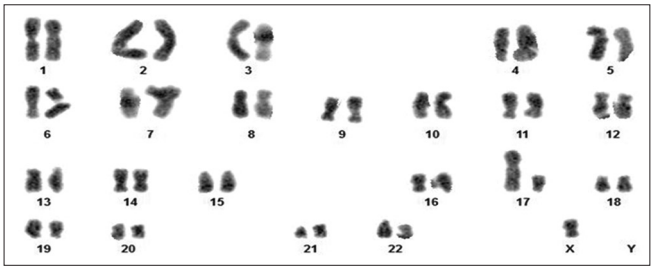

Fig. 2: Karyotype showing 45X chromosomes

For patients, we can observe structural changes in chromosomes, 45X/46XY. For patients with 45X/46XY mosaicism, they presumably reflect a wide variety of phenotypes observed in the different proportions of the 45X and 46XY chromosomal cell lines among the tissues in individuals [9,10]. In our report, there is no mosaicism type, phenotypic variation was not observed.

In TS, along with clinical signs both males and females with mosaicism and phenotype range from normal male development to individuals with incomplete sexual differentiation. About 60% of cases had sexual ambiguity. Less common categories of 45X/46XY patients present with bilaterally descended testes (11-12%) and normal female phenotype with TS stigmata (<5%) [11]. In our case study, patient had normal female phenotype with one X chromosome is missing, mosaicism types were not observed.

TS mechanism of genotype-phenotype correlation is to be understood. The genotype-phenotype correlation is not understood [12]. In TS, genetic polymorphisms are associated with clinical features [13]. TS 45X karyotype is most frequent, there is a loss of the paternal X or Y chromosome in meiosis or in early embryogenesis than by loss of the maternal X chromosome [14].

Approximately, 20% of the patients were diagnosed after 12 years of age in TS cases [15]. TS cases were detected in mid-childhood. At that time, most of the patients were failed to reach pubertal changes and growth hormone therapy, will result in short stature.

In our report, chromosomal analysis showed that one of her X chromosome is missing. In some cases, short arm deletion/long arm duplication presents in approximately 18% of all TS cases. This will result in short stature. Our report shows one of the chromosomes was conserved. Our case highlights short stature is a typical clinical feature of TS. Precocious puberty in patients with TS is less frequent, 5 cases have been reported, 4 of them showed mosaic TS [16]. One of the patients had variant TS, as was found in our previously reported patient [17]. When cells with X chromosomes containing duplicated long arms undergo dosage compensation, it allows normal ovarian function at that time which can be seen as precocious puberty in many girls with TS.

CONCLUSION

TS has clinical and structural changes in chromosomes like Y chromosome mosaicism. The chromosome study is essential for this type of genetic disorders, which will in turn help practitioners to diagnose it early. Other clinical tests like hormonal estimation (growth hormone) and sex steroids should be done as early as it will help the patient's future quality of life.

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