

## Case Report

# A rare cause of progressive gait abnormality in a case of Turner syndrome

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### ABSTRACT

Turner syndrome is a commonly encountered chromosomal disorder affecting females, while Duchenne muscular dystrophy is a severe X-linked recessive disorder affecting males. Although theoretically possible, very few cases of DMD associated with Turner syndrome have been reported. We report an 8 year old girl who presented with a rare association of Turner syndrome mosaicism (45X/46XringX) with Duchenne muscular dystrophy.

**Keywords:** Muscular dystrophy, Turner syndrome, Gait abnormality, Weakness, Pediatrics

## INTRODUCTION

Turner syndrome is a disorder caused by partial or complete absence of the second sex chromosome, with or without cell line mosaicism. Initially described by Henry Turner and later reported by Ullrich, it is characterized by phenotypic features like short stature, primary ovarian insufficiency along with other physical features arising from fetal lymphatic obstruction. The overall incidence is 1:2500 live born females.<sup>1</sup> Duchenne muscular dystrophy (DMD) is a severe X-linked recessive progressive myopathy with affected probands being only boys. It is caused by mutation in dystrophin gene located on Xp21.2. Among the DMD probands, 60% have deletions and 5-10% has duplication of exons with origin being the mother or de novo mutations.<sup>2</sup> The overall incidence is 1/4600 live born males.<sup>3</sup> The coexistence of Turner syndrome and X-linked recessive disorder is quite an unusual coincidence. Based on their incidences, both the disorders may coexist at a frequency of  $4 \times 10^{-8}$ . Previously, only a few cases of Turner syndrome with DMD have been reported, all with variable phenotypic and cytogenetic variations.

## CASE REPORT

Current study reports an 8 year old girl with Turner syndrome with progressive gait abnormality. The patient was the 1<sup>st</sup> living issue born to non-consanguineous parents at 36 weeks of gestation via cesarean section in view of breech presentation with birth weight of 1.85 kg. With rather uneventful antenatal and early childhood history, she was referred at 5 years of age for evaluation of short stature. Considering a case of a girl with unexplained short stature and supportive phenotypic features like short neck, low posterior hairline, strabismus, disproportionate short stocky appearance (increased upper: lower body ratio) and scoliosis (Figure 1), peripheral blood karyotype was done which revealed mosaic pattern Turner syndrome (45X/46XrX) (Figure 2). Fibrous streaks of ovaries could be visualized on ultrasonography. At 6 years of age, she was initially noted to have increasing difficulty in walking and climbing stairs with resultant frequent falls and difficulty in getting up from the floor. She was evaluated at the age of 8 years at which time her examination revealed proximal muscle weakness, waddling gait, valley sign, bilateral calf pseudohypertrophy along with a positive

Gowers' sign (Figure 3). Kocher-Debre-Semelaigne syndrome, a more plausible differential, was ruled out by normal thyroid function tests. Serum CPK levels done were raised (16012 IU/l).



Figure 1: Turner syndrome phenotype.

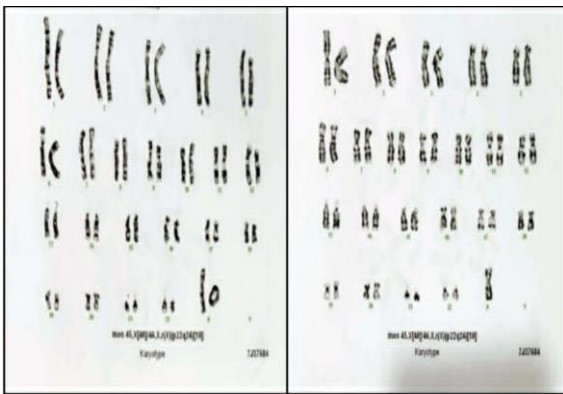


Figure 2: Turner syndrome karyotype.



Figure 3: Duchenne muscular dystrophy features

**Neuromuscular studies**

Electromyography of upper and lower limb muscles confirmed non-inflammatory (proximal>distal) myopathy.

**Genetic studies**

Multiple ligation probe amplification (MLPA) of the patient confirmed the diagnosis of DMD with homozygous out-of-frame mutation with deletion of 7 exons (exons 46-52).

**Treatment**

Following the diagnosis of Duchenne muscular dystrophy, the patient was started on deflazacort and rehabilitative physiotherapy.

**DISCUSSION**

Duchenne muscular dystrophy is a severe X-linked recessive disorder characterized by progressive proximal myopathy. It is known to affect males with females being the carriers. However, various genetic abnormalities in cases of female DMD have been documented previously: X-autosomal reciprocal translocation and a preferential inactivation of normal X chromosome; classical 45 XO Turner karyotype or Turner mosaicism; skewed X inactivation of a normal X chromosome of female DMD mutation carriers; uniparental disomy with DMD mutation in both X chromosomes; co-occurrence of mutation in both dystrophin and androgen-receptor genes; homozygous dystrophin mutation due to consanguinity.<sup>4</sup> Our case is similar to the case of Turner syndrome with dystrophin gene mutation in the remaining X chromosome. The available cohort of studies suggests that girls with classic Turner karyotype have a severe course of the DMD while those with mosaicism have a milder course as is seen in our case.<sup>5</sup> Existing literature shows few reported cases of DMD with Turner syndrome. However, most of them were based on clinical diagnosis of DMD as no molecular diagnosis was available at that time. Present cases as well as a few other case reported previously have documented cytogenetic evidence of DMD (Table 1).

**Table 1: Documented cytogenetic evidence of DMD.**

Author	Turner karyotype	DMD mutation
Walton (1957)	45X	Unavailable
Ferrier et al (1965)	45X/46XrX	Unavailable
Jalbert et al (1966)	45X/46XX/47XXX	Unavailable
Bortolini et al (1986)	45X/46XX/47XXX	Unavailable
Chelly et al (1986)	45X	Unavailable
Ou et al (2010)	46XisoXq	Deletion
Kaczorowska et al (2016)	45X	Point mutation
Verma et al (2017)	45X	Deletion
Kesavan et al (2019)	45X	Deletion
Present case	45X/46XrX	Deletion

Use of oral corticosteroids has been mentioned in only 1 of the mentioned cases.<sup>6</sup> In the current case too, Deflazacort was started to improve ambulatory and cardiovascular muscle function.

## CONCLUSION

The possibility of X linked recessive disorders such as dystrophinopathies should be considered in females with Turner syndrome presenting with myopathy. Available correlation between chromosomal abnormality and disease severity helps in guiding therapeutic interventions and prognostication. However, phenotypic affection due to various dystrophin gene mutations is an area which warrants further exploration.

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