International Journal of Contemporary Pediatrics
Sanadhya A et al. Int J Contemp Pediatr. 2021 Apr;8(4):770-772
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: https://dx.doi.org/10.18203/2349-3291.ijcp20211094

Case Report

Duchenne muscular dystrophy in a female with x-autosome translocation

Anuradha Sanadhya, Ritvika Jyani, Suresh Goyal, Neha Asora, Mukesh Kumar Gurjar*

Department of Pediatrics, RNT Medical College, Udaipur, Rajasthan, India

Received: 05 February 2021
Revised: 05 March 2021
Accepted: 06 March 2021

***Correspondence:**
Dr. Mukesh Kumar Gurjar,
E-mail: sbapna.1@gmail.com

ABSTRACT

Duchenne's muscular dystrophy is the most common hereditary neuromuscular disease, which affects all races. Its classical characteristic clinical features being progressive muscular weakness, intellectual impairment and hypertrophy of the calves with proliferation of connective tissue and progressive fibrosis in muscles. As the disease is inherited as an X-linked recessive trait, thus females not manifesting the disease and acting as carriers only, as second X chromosome prevents the manifestation of disease. We report a case of classical Duchenne muscular dystrophy in 10 year old female with no intellectual deficit and no family history of similar type of muscular dystrophy.

Keywords: Muscular dystrophy, X linked recessive, Translocation, Autosome

INTRODUCTION

Duchenne 's muscular dystrophy is a X-linked recessive single gene disorder, which usually manifests in males and females act as carriers in transmission of disease.[1] This is the most common dystrophinopathy caused by mutation in dystrophin gene and is very important differential diagnosis of progressive muscular weakness in male children. In extremely rare circumstances it does manifests in females, arousing the suspicion of underlying chromosomal disorder in affected females.[1]

CASE REPORT

A 10-year old female child, product of non-consanguineous marriage and 2nd in birth order, presented with difficulty in walking, recurrent falls and progressively increasing weakness of lower limbs since the age of 5 years. Age of her parents at the time of her birth was 22 and 26 years respectively. Her birth history was not significant and she achieved milestones at appropriate age. Her all other male and female siblings were normal with no history suggestive of muscle weakness. Her maternal uncles and cousins were also apparently healthy. She had abnormal gait initially followed by difficulty in standing from sitting position and climbing stairs. The disability is increasing over last 5 years. There is no apparent muscle weakness in upper limb musculature and neck and spine muscles. She could comfortably get up from lying down position and do routine household activities done by hands. There was no muscle weakness in facial muscles and other small muscles of the body.

On examination the weight of child was 19.2 kg(<3SD), height 110.5cm (<-3SD), US:LS (1.05:1). Her IQ was found to be normal with normal school performance. There was hypertrophy of both sided calf muscles (fig 1), thinning of thigh muscles, increased lumber lordosis with wide based waddling gait. Also there was hypertrophy of bilateral deltoid and infraspinatus muscles, though thinning of arm muscles was not very apparent. Gower's sign could be elicited comfortably suggestive of DMD. Examination of CNS, respiratory, cardiovascular and gastrointestinal system was normal. There was no dyspnoea on exertion suggestive of no cardiac involvement.

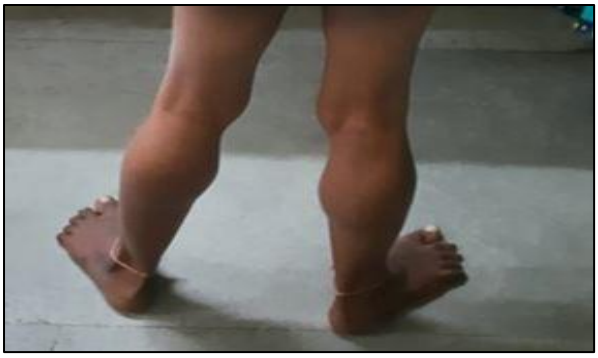

Figure 1: Pseudohypertrophy of calf muscle in both legs.

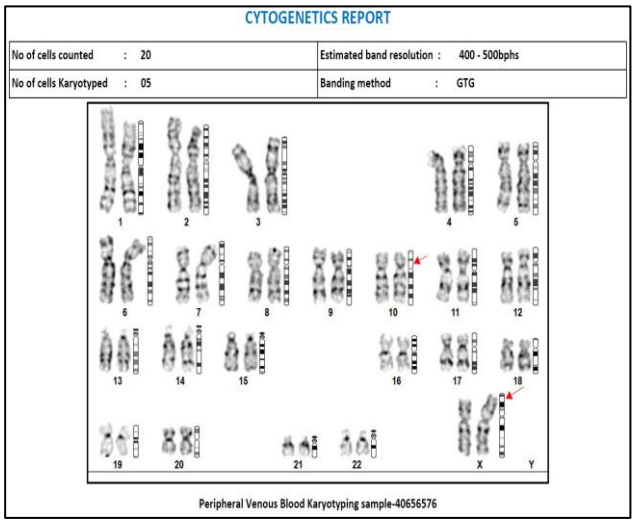

Figure 2: Karyotyping report from peripheral venous sample by GTG banding method showing Xp22 and autosome 10 translocation.

Investigations done revealed elevated serum creatinine kinase of 1214 U/l. Rest other investigations including electrolytes were within normal limits. Electromyography done showed muscular dystrophy pattern. Muscle biopsy done from gastrocnemius muscle stated degenerating and regenerating fibres and fibrofatty tissue. Ultrasound abdomen and pelvis show poorly visible ovaries bilaterally and prepubertal uterus. 2D Echo was found normal suggesting no cardiac involvement. CPK levels of her mother were also high (457IU/l) suggestive of carrier state. CPK levels of all siblings could not be done due to nonavailability of them and home being far away.

As muscular dystrophy is transmitted X linked recessive pattern, it was unusual to find these features in female child, so karyotyping was done by GTG banding method with band resolution of 400 to 500 bphs on peripheral venous blood sample by peripheral blood lymphocyte culture method to look for chromosomal abnormality. Karyotyping (Figure 2) revealed 46 XX pattern and translocation between autosome 10 and X chromosome at p22 and p 11.2 location.

DISCUSSION

The disease is inherited as an X-linked recessive trait, thus females don't manifest the disease and act as carriers only as second x chromosome prevents the manifestation of disease. This could be explained by Lyon hypothesis in which the normal X chromosome becomes inactivated and one with the gene deletion is activated1. Incidence of disease in females is rarest 1:50,000,000 live births This disorder caused by a mutation in the dystrophin gene, located on the X chromosome (Xp21). The dystrophin gene codes for dystrophin protein which is 427 kDa protein and localised at the sarcoplasmic membrane of normal skeletal muscle.[1,2] Dystrophin also normally expressed in cardiac muscles, visceral and smooth muscles and brain. Lack of dystrophin causes breakdown of muscle fibres and loss of muscle power. Dystrophin can easily be detected in a small muscle biopsy specimen using anti dystrophin antibodies.[3]

20 females with Duchenne or becker muscular dystrophy who have X chromosome within band Xp21 have been documented so far. Several of these translocations have been mapped with genomic probes to regions throughout the large (approximately 2000 kb) DMD gene.[4] Our patient is female manifesting as full DMD phenotype as a result of structural alteration in X chromosome.

Several disease-causing mechanisms have been implicated in DMD manifesting carriers. These include X-autosomal translocations disrupting the DMD gene, mutations on both DMD alleles and co-occurrence of DMD mutations together with other genetic abnormalities such as X-chromosome monosomy, X-chromosome uniparental disomy as well as male pseudohermaphroditism caused by a mutation in the androgen receptor gene. However, the most frequently reported mechanism to provoke symptoms in DMD carriers is skewed X-inactivation, favoring the expression of the X chromosome with the DMD mutated allele. Turner syndrome with an XO pattern is another rare situation which may co-exist with DMD in a girl, since the abnormal X is not suppressed by the missing normal chromosome.[5]

Till date 7 cases of X chromosome and autosome translocation have been reported. In 6 out of 7 cases X p 21 part of X chromosome was involved, one had p11.06 part involved. Autosome documented till date are 9,11,21,1,3,5,6 in various studies done by various authors, our study is different as it involves translocation between X p 22 and autosome no 10.[6]

There are several possible mechanisms to explain this exceptional case. The first is that her mother is heterozygote and the maternal Duchenne carrying X chromosome is the one involved in translocation. The second is translocation event itself causes the duchenne mutation by interrupting or altering a structural gene, or by causing a position effect on structural gene high level of CPK in mother indicate carrier status of mother. Out of 7

previous documented case only two mother had carrier status

The observation that seven different autosomes are involved in these DMD translocations strongly suggests that translocation itself causes the mutation by alteration or interruption of the structural gene, rather than a position effect of pre-existing mutation.

CONCLUSION

Karyotyping should be done in all cases of unusual presentation of a genetic disorder to look for any aberrations in chromosomal structure.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. Diana X., Goebel B. Muscular Dystrophies Chapter 627, page3281 in Nelson Text Book of Pediatrics 21st Edition, Elsevier Publishers. 2019.
2. Nozoe KT, Akamine RT, Mazzotti DR. Phenotypic contrasts of Duchenne Muscular Dystrophy in women: Two case reports. Sleep Sci. 2016;9(3):129-133.
3. Hoffman EP, Kunkel IM. Dystrophin abnormalities in Duchenne and Becker muscular dystrophy. Neuron. 1989;2:1019-29.
4. Bodrug SE, Burghes AH, Ray PM, Worton RG. Mapping of four translocation breakpoints within the Duchenne muscular dystrophy gene. Genomics.1989;4(1):101-4.
5. Nahrel R, Kosam A. Duchenne Muscular Dystrophy in a Female Child with Turner syndrome: A Case report. Int J Med Res Rev. 2014;2(3):262-266.
6. Emanuel BS, Zackai E, Tucker SH. Further evidence for Xp21 location of Duchenne muscular dystrophy (DMD) locus: X;9 translocation in a female with DMD. J Med Genet. 1983;20.6:461-63.

Cite this article as: Sanadhya A, Jyani R, Goyal S, Asora N, Gurjar MK. Duchenne muscular dystrophy in a female with x-autosome translocation. Int J Contemp Pediatr 2021;8:770-2.