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DUCHENNE MUSCULAR DYSTROPHY: CASE REPORT AND REVIEW

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ABSTRACT

Duchenne muscular dystrophy (DMD) is a recessive X-linked mediated, musculoskeletal disorder that affects only males. It is the most common and severe form of muscular dystrophy where there is failure to manufacture dystrophin. Clinically, it is characterized by progressive muscle wasting eventually leading to premature death. DMD is described as progressive myopathy leading to muscle weakness and eventually its degradation. Muscle weakness progresses from hip girdle muscles and neck flexors, the shoulder girdle and distal limb and trunk muscles. Usually boys are affected at the age of 3 to 5 years, present due to difficulty in climbing stairs or rising from sitting position, most patients using Gowers maneuvers, and enlarged calf muscles are present classically, due to replacement of muscles by fats by the age of 12 years. Here, we present a case of DMD in a 11-year-old male with remarkable clinical manifestations.

Keywords: Disorder, Hereditary, Recessive, Calf hypertrophy, Creatine Kinase, Grower sign, Muscle weakness

INTRODUCTION:

Duchenne muscular dystrophy (DMD) is atypical inherited musculoskeletal disorder which shows clinical characteristics of progressive muscular weakness at an early stage and pathologic features of fibrosis and fatty replacement, particularly late in the disease course. It is a recessive X-linked disorder occurring 1 in every 3500 live male births and named after a French neurologist Guillaume Benjamin Amand Duchenne in 1860.[1]

It is the most common and severe form of muscular dystrophy, beginning at 3–5 years of age and characterized by proximal muscle weakness and calf hypertrophy in affected boys.[1,2] DMD has a very high mutation rate with distinctive and relentless clinical presentation. Patients usually become wheelchair-bound by the age of 12 and die in their late teens to early twenties.

CASE REPORT:

A 11yr old male child resident of Karaikal presented with complaint of difficulty in walking and running and difficulty in standing from sitting position. Patient was apparently normal 6 months back than his mother notice that his child is not walking properly and difficulty while walking which is gradual in onset. Immunisation is complete as per the age. On examination, he had difficulty jumping onto the examination table, a Gower sign (a sequence of maneuvers for rising from the floor, proximal weakness of pectoral and pelvic girdle muscles, a waddling gait tight hell cords, and apparently enlarged calf muscles. No gross milestone delay. Serological analysis showed creatine kinase (CK) level to be elevated to 3467 U/L, lactate dehydrogenase to 540 µg/dl, and alanine transaminase level to 112 U/L. To confirm the diagnosis muscle biopsy was planned and done sample taken from calf muscle, muscle biopsy confirmed muscular dystrophy (Fig 1,2).

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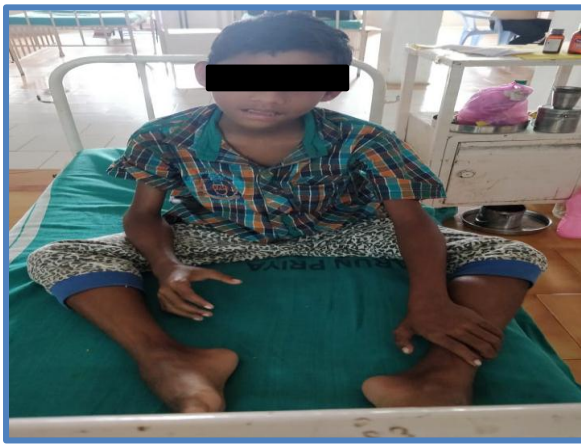

Fig 1: 11 years male boy with DMD

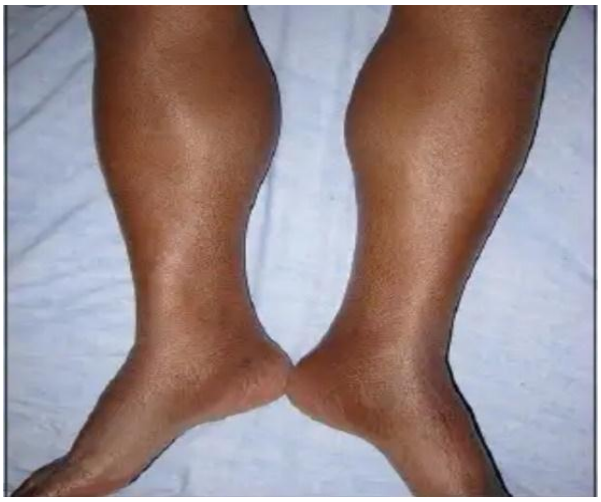

Fig 2: Calf muscle hypertrophy in DMD

DISCUSSION:

DMD is the most common muscle dystrophy in India as well as the world, caused by mutations in dystrophin gene as a result of which the body is unable to synthesize the protein dystrophin required for muscle contraction. Every time the muscle contracts, muscle damage occurs which is repaired but with deficient protein resulting in repaired muscle which is also a damaged one. This continuous succession of damage and repair and eventually replacement of muscle with fibrofatty tissue is responsible for the clinical signs of progressive muscle wasting and degeneration that is usually evident by 3–4 years.[4]

DMD is caused by mutations in the DMD gene encoding a protein called dystrophin, which localizes to the cytoplasmic face of the sarcolemma of the skeletal muscle, forming one component of a large glycoprotein complex (dystrophin-associated glycoprotein complex).

Dystrophin is a structural protein in skeletal muscle, cardiac muscle and brain. It interacts with multimeric protein complex associated with sarcolemma proteins which plays an important role to maintain integrity of muscle membrane [5]. Molecular genetic studies indicate that dystrophin is a huge gene located on the short (p) arm of the X chromosome at position 21.2.and about two thirds of mutations in this gene lead to DMD but no clear correlation found between the extent of deletion and severity of disorder.

The protein, called dystrophin, is about 400 kD in size and represents about 0.002% of total striated muscle protein [6]. The finding of dystrophin mRNA in brain may explain mental retardation in DMD patients [7]. Dystrophin in brain is transcribed from a different promoter from that used in muscle. The brain-type promoter of the dystrophin gene is highly specific to neurons.

By contrast, the muscle-type promoter is active in a wider range of cell types, including not only striated and smooth muscle, but also glial cells to a lesser extent, and probably neurons [8]. The replacement of the missing protein, dystrophin, using myoblast transfer in humans or viral/liposomal delivery in the mouse DMD model is insufficient and short-lived. An alternative approach to treatment would be to upregulate the closely related protein, utrophin, which might be able to compensate for the dystrophin deficiency in all relevant muscles [9].

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Diagnosis is confirmed by high serum marker levels of CK, muscle biopsy, electromyography, and genetic analysis. The increased permeability of the sarcolemma damaged due to repeated contractions in DMD patients leads to leakage of proteins, such as CK into the plasma resulting in elevated levels of CK in the serum, characteristic in DMD patients. Other enzymes such as alanine transaminase, aspartate transaminase, aldolase, and lactate dehydrogenase are also raised.[2,10] In this case, serum markers such as CK, lactate dehydrogenase, and alanine transaminase levels were markedly increased. Muscle biopsy and electromyography also revealed positive results.

Current management of DMD involves physiotherapy and corticosteroid therapy which delays loss of ambulation 1–3 years but does not cure the disease. However, corticosteroids are associated with significant side effects, including weight gain, decreased bone mineralization, Cushing syndrome, and behavioural disturbances. Alternate regimens have been tried, although the efficacy of these regimens in comparison to daily dosing is incompletely studied.[11,12] A growing number of reports suggest that treatment before the age of 5 years is especially beneficial, though the data to support early use are limited.[11] Recent treatment modalities include gene therapy and stem cell therapy which appear very promising and suggest that an upregulation of dystrophin-like protein has beneficial effects. Prenatal counseling and genetic tests like multiplex ligation-dependent probe amplification are being used to offer hope in this progressive and eventually fatal muscle dystrophy to prolong and improve the quality of patient's life.[13,14]

CONCLUSION:

Duchenne muscular dystrophy is the most common hereditary neuromuscular disorder and is inherited in an X linked recessive manner. Raised CPK level and muscle biopsy are cheap and easily available test for the confirmation diagnosis of Duchenne muscular dystrophy.

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