

Duchenne muscular dystrophy: Case report and review

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ABSTRACT

Muscular dystrophies are a clinically and heterogeneous group of disorders that all share clinical characteristics of progressive muscular weakness. Duchenne muscular dystrophy (DMD) is the most common X-linked disorder muscular dystrophy in children, presenting in early childhood and characterized by proximal muscle weakness and calf hypertrophy in affected boys. There is usually delay in motor development and eventually wheelchair confinement followed by premature death from cardiac or respiratory complications. Treatment modalities such as corticosteroid therapy and use of intermittent positive pressure ventilation have provided improvements in function, ambulation, quality of life, and life expectancy, although novel therapies still aim to provide a cure for this devastating disorder. Here, we present a case of DMD in a 12-year-old male with remarkable clinical and oral manifestations.

Keywords: Calf hypertrophy, creatine kinase, grower sign, muscle weakness

Introduction

Duchenne muscular dystrophy (DMD) is an 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.^[2,3] According to PubMed literature, approximately 150 cases have been reported till date. Here, we present a rare case of DMD in a 12-year-old child.

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Case Report

A 12-year-old male patient reported to the department with chief complaint of painful decayed tooth in the lower right jaw region. His parents gave medical history of repeated falls, fatigue, muscle weakness, and inability to climb stairs. There was no history of muscular pain and cranial nerve involvement. His intelligence quotient was claimed to be in the normal range. Patient's family history revealed that one of his maternal uncles died of the same illness at a young age.

On general physical examination, the child had an obese appearance and presented with difficulty in standing, walking, getting up from sitting position and climbing stairs, proximal weakness, calf hypertrophy, hamstring muscle contracture, and positive Gower's sign [Figures 1 and 2]. There was no thinning and twitching of muscles, muscle tone, and cranial nerve examination was also found to be normal. Intraoral examination revealed anterior open bite, left posterior cross bite, enlarged tongue, crowding in lower anteriors, decayed 46, and poor oral hygiene status [Figure 3].

The patient was subjected to radiological and laboratory investigations. Panoramic radiography revealed no abnormality

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except for grossly carious 46 indicative of chronic periapical abscess [Figure 4]. Serological analysis showed creatine kinase (CK) level to be elevated to 7342 U/L, lactate dehydrogenase to 595 µg/dl, and alanine transaminase level to 124 U/L. On electromyographic examination, interference pattern analysis revealed myopathic pattern in the right vastus lateralis suggestive of primary muscle disease. Deltoid muscle biopsy revealed positivity for alpha, beta, gamma, delta-sarcoglycan and negativity for DYS1, DY2, and DYS3. Based on the history, clinical examination and investigations, a diagnosis of DMD was established.

The child was advised to consult a pediatrician regarding his general and physical health status. He was counseled to undergo daily physiotherapy, steroid therapy, and regular assessment for progressive muscle and cardiac/respiratory damage. With regard to dental therapy, pulpectomy for 46 and oral prophylaxis was performed. The patient was kept under periodic recall to prevent any further dental complications.

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.^[1,4]

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 consists of an N-terminal actin-binding domain, 24 spectrin-like repeat units interspersed by four hinge regions, followed by a cysteine-rich domain and a C-terminal domain. The cysteine-rich domain binds to laminin-2 through alpha and beta-dystroglycan, and therefore acts as mechanical link between actin in the cytoskeleton and the extracellular matrix. The DMD gene contains 79 exons but accounts for only 0.6% of the gene; the rest made of large introns. The large size of the DMD gene makes it susceptible to mutations, leading to loss of function of dystrophin, resulting in a prematurely truncated, and unstable dystrophin protein. The majority of mutations are intragenic deletions, which account for 65–72% of all DMD patients. The precise mechanism of how dystrophin deficiency leads to degeneration of muscle fibers remains unclear. The absence of dystrophin at the plasma membrane leads to delocalization of dystrophin-associated proteins from the membrane, disruption of the cytoskeleton with resultant membrane instability and increased susceptibility to mechanical stress. In addition, altered membrane permeability and abnormal calcium homeostasis are thought to play a role, with increased



Figure 1: Clinical photograph of the patient



Figure 3: Intraoral photograph showing no abnormality except for carious 46



Figure 2: Proximal muscle weakness of upper and lower limbs and calf hypertrophy



Figure 4: Orthopantomograph showing no abnormality

cytosolic calcium concentration leading to activation of proteases such as calpains.^[3]

Affected boys clinically present with difficulty in running or getting up from the ground, frequent falls, or toe-walking. Patients have a waddling gait, calf enlargement, and lumbar lordosis which disappear on sitting. There is weakness of the proximal muscles of the lower limb as in which a patient uses his hands and arms to “walk” up their own body from a squatting position due to lack of hip and thigh muscle strength suggestive of Gower’s sign.^[5] In this case, the affected child clinically presented with signs of delayed motor development, difficulty in walking and climbing stairs, positive Gower’s sign, and muscle weakness. Oral manifestations include wide dental arches, large tongue, delayed eruption, open bite, and retrognathic facial morphology. The development of malocclusion in these patients is linked to the involvement of the orofacial muscles by the disease which was apparent in the present case.^[4,5]

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.^[2,6] 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 which was provided in our case. However, corticosteroids are associated with significant side effects, including weight gain, decreased bone mineralization, Cushing syndrome, and behavioral disturbances. Alternate regimens have been tried, although the efficacy of these regimens in comparison to daily dosing is incompletely studied.^[7,8] 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.^[7] 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.^[9,10]

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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