

## Case report

# **A Rare Presentation of Duchenne Muscular Dystrophy: Cardiac and Neurological Involvement**

### **Abstract**

Duchenne muscular dystrophy (DMD) is one of the most severe types of inherited muscular dystrophies. It is the most prevalent genetic neuromuscular disorder and does not show any racial or ethnic bias. Small variations or significant deletions/duplications in the DMD gene inhibit the generation of functional dystrophin protein, which is the cause of DMD that leads to muscle fiber degeneration and weakening. The risk factors associated with DMD include family history, gender, muscle weakness, low BMI, poor lung function and genetic variation. Based on ambulation, the DMD Care Consideration Working Group created a classification system for DMD patients. In most cases, there is a delay in motor development, resulting in wheelchair confinement and, ultimately, an early death from respiratory or cardiac issues. In addition to taking a patient's history, testing for genes, and detecting elevated creatine kinase and other transaminases in the lab, progressive motor weakness is still the most significant finding of the illness. Although new treatments continue to strive for a cure for this life-threatening condition, treatment approaches include corticosteroid therapy and intermittent positive pressure breathing have improved function, ambulation, quality of life, and life expectancy. Here, we report a 27-year-old male patient, who has DMD and exhibits notable cardiac, neurological and clinical symptoms.

**Key words:** Duchenne muscular dystrophy, dystrophin, ambulation, motor development, transaminases.

### **INTRODUCTION**

Duchenne muscular dystrophy (DMD) is an early-onset, severe, rapidly progressive neuromuscular disease belonging to a pathological group of diseases known as dystrophinopathies

with muscle weakness as the primary clinical manifestation. [1] It is a lethal progressive genetic disorder characterized by muscle deterioration and muscle wasting. [2] Muscular dystrophies are a heterogeneous group of inherited myopathies that share similar clinical features and dystrophic changes on muscle biopsies which was first described by French neurologist Guillaume Benjamin Amand Duchenne in 1860's. [3] It is caused by mutation of the dystrophin gene present in X chromosome leading to absence or structural damage to the gene. The prevalence of DMD is found to be 2.8 out of 100,000 of the general population. [4] It manifests as toe walking, climbing stairs, difficulty in running, frequently falling, waddling gait, calf enlargement, lumbar lordosis, and Gower's sign. Weakness is more pronounced in proximal than distal muscles. [5] [6] Higher levels of cardiac damage biomarkers, a lower body mass index (BMI), and worse lung function were all linked to an increased risk of mortality, according to the study. Furthermore, the onset and natural evolution of muscular dystrophies may be influenced by biological, socioeconomic, environmental, psychological, and concomitant genetic variables. Muscle contraction initiates and advances the pathophysiology of DMD. In the early stages of DMD, the amount of creatine kinase (CK) leakage into the extracellular space can be used to gauge the extent of muscle cell destruction. Numerous mechanisms have been identified as cell-damaging in DMD, including calpain activity, activation of nuclear factor kappa beta (NFκB), and buildup of reactive oxygen species. On the other hand, excessive calcium ion (Ca<sup>2+</sup>) inflow into skeletal muscle cells, coupled with heightened vulnerability to plasma membrane disruption, is thought to be the primary cause of muscle damage in DMD. [7] DMD eventually can also lead to cardiovascular, pulmonary and orthopedic complications. [5] Here is a case presentation of DMD.

## **CASE REPORT**

A 27 years old male patient was referred to hospital already diagnosed with dilated cardiomyopathy presented with mild grade fever, loss of appetite and nausea, shortness of breath grade 1 to 3 with orthopnea in the last one week. Upon detailed investigation the patient had complaints of low-grade intermittent fever not associated with arthralgia, myalgia and rash in the past 6 months and high-grade intermittent fever since 10 days which was relieved with medication (acetaminophen 650mg). Dysphagia to solids followed by vomiting (pseudo bulbar palsy) in the last 1 month, Dysphagia (solids >> liquids) in the past 3 months which increased in the last 10 days. Loss of weight, Loss of appetite for 1 year.

The past medical and medication history revealed that the patient had psychiatric symptoms for 5 years (not on medications), hearing loss 7 years ago (cause not identified) and multiple episodes of vomiting (4-5 hospital admissions). No significant family history was presented.

The provisional diagnosis of dilated cardiomyopathy with cardiogenic shock, post infectious metabolic encephalopathy was made and further laboratory investigations revealed.

Upon further referral to neurologist and ENT specialist the parent reports a history of delayed milestones, aggressiveness within appropriate laughter, talking to self, weakness of LL since 3 years, weakness of UL since one year, weakness of LL Proximal > Distal increased since last 6 months. Inability to lift heavy objects, hoarseness of voice since 3 years, difficulty in getting up from sitting position and climbing stairs since 2 years, difficulty in wearing slippers since 6 months and dysarthria since 1 yr. The patient was subjected to radiological and laboratory investigations. Serological analysis showed elevated levels of Creatine kinase (7342 U/L), lactate dehydrogenase (565 µg/dl) and aspartate aminotransferase (543 U/L). The echocardiography revealed all 4 chambers dilated, severe LV systolic dysfunction, no DDF, severe MR, TR, PAH, no veg/clot/PE. On electromyography examination revealed motor sensory axial neuropathy B/L LL > UL. MRI Brain revealed no abnormality and urine culture sensitivity revealed presence of candida species. Based on history and laboratory investigations, the diagnosis of Duchenne Muscular Dystrophy was established.

The patient was treated with aldosterone receptor antagonists (Spironolactone- 50 mg/day/BD), ACE inhibitors (Lisinopril 40 mg/ day) , beta blockers (Metoprolol 50 mg/ OD) and counseled to undergo regular physiotherapy and regular assessment for further complications.



Figure 1: Muscle wasting; patient with DMD showing muscle wasting in the upper.

## DISCUSSION

DMD is the most prevalent form of muscle dystrophy in both India and the rest of the globe. [8] DMD is caused by mutations in DMD (encoding dystrophin) that prevent the production of the muscle isoform of dystrophin (Dp427m). Mutations in DMD can also cause Becker muscular dystrophy (BMD), which is a milder disease with a later onset and a slower progression than DMD. According to the sarcolemma hypothesis, DMD is caused by structural and functional defects of a sarcolemma protein owing to mutations in the encoding gene. [9] It is characterized by progressive muscle weakness that affects limb, axial, and facial muscles to a variable degree. In specific forms, other muscles, including respiratory muscles, cardiac smooth muscles, and swallowing muscles, can also be affected. In rare variants, the disorder is associated with involvement of other organs or tissues, such as the brain, inner ear, eyes, or skin. [10] Analyzing serological testing can lead to early detection, the diagnosis is rarely made before the patient is 2 to 6 years old. The appearance of the disease is insidious and usually overlooked in its early stages. The disease becomes apparent with the onset of a clumsy, waddling gait, frequent falling, and delayed motor milestones (sitting, walking, running). (11) Here the patient is presented with delayed milestones like muscle

weakness, dysphagia, dysarthria, and cardiomyopathy is consistent with DMD. The diagnosis was confirmed by elevated creatine kinase (CK) levels, electromyography (EMG) findings, and characteristic clinical features of DMD. Due to the mutations in the dystrophin gene, leading to absent or deficient dystrophin protein. This protein plays a crucial role in maintaining muscle cell membrane integrity. Without dystrophin, muscle cells undergo necrosis, leading to progressive weakness and degeneration. Patients also suffer from Cardiomyopathy which is a common complication of DMD, occurring in approximately 90% of patients, whereas echocardiography findings revealed that dilated cardiomyopathy, severe left ventricular systolic dysfunction, mitral regurgitation (MR), tricuspid regurgitation (TR), and pulmonary arterial hypertension (PAH) are consistent with DMD-related cardiomyopathy. The patient has beneficial effect in reducing the symptoms of the disease by the usage of Corticosteroids (Prednisolone 40 mg), ACE inhibitors (Lisinopril 40 mg), Aldosterone antagonists (Spironolactone 50 mg), beta blockers (Metoprolol 50 mg) and regular sessions physiotherapy.

**Table -1: Laboratory Findings**

<b>Lab Parameters</b>	<b>Results</b>
Serum creatinine	7342 U/L
Lactate dehydrogenase	565 ug/dl
Aspartate Aminotransferase ( AST )	543U/L

Elevated CK levels (7342 U/L) and abnormal EMG findings confirm muscle damage. Serum lactate dehydrogenase (LDH) and aspartate aminotransferase (AST) elevations indicate muscle and cardiac damage. Treating Duchene muscular dystrophy (DMD) primarily aims to control symptoms and enhance quality of life because there is presently no cure for the condition. The patient is administered with the following supportive therapy like corticosteroids (prednisolone 40 mg) which help to improve lung function, prevent the loss of muscle strength, reduce the onset of cardiomyopathy (heart weakness), and increase survival. Aldosterone receptor antagonists(Lisinopril), ACE inhibitors (Spironolactone)and beta blockers (metoprolol)are given to manage cardiomyopathy and regular sessions of physiotherapy helps to maintain muscle

strength and mobility on another hand ensuring adequate nutrition to prevent malnutrition the patient has beneficial effect in reducing the symptoms of the disease.

## CONCLUSION

Duchenne muscular dystrophy is a progressive inherited myopathy with an early onset in childhood. It progresses to the bed-bound state in the second decade of life and patients usually prone to respiratory or heart complications. Conservative management, active physiotherapy, genetic counseling and other supportive therapies hold the key to successful management of the case. A lack of disease awareness and subsequent failure to recognize DMD signs and symptoms, especially atypical presentations of disease, leads to delayed diagnosis of DMD worldwide. This case highlights the necessity for ongoing investigations into novel therapies, improved management strategies, and enhanced supportive care to improve the quality of life for patients with DMD. By sharing this case, we hope to increase awareness and promote better understanding of DMD, which will ultimately lead to improved patient outcomes and advancements in the field.

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