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Delayed onset of Duchenne muscular dystrophy in a case of 22-year male with normal developmental milestone

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ABSTRACT

Duchenne muscular dystrophy (DMD) presents more commonly in males which is inherited as an X linked recessive trait. It is very uncommon to see DMD in females. It occurs when there is mutation in a dystrophin gene present on X chromosome. The common time of appearance of clinical feature of this disease is in early childhood. These patients are normal at the time of birth but by the time patient is one year of age they present with delay in attaining developmental milestones. They clinically present with frequent history of falls, difficulty to raise themself from ground this is because of weakness in proximal group of muscle. On examination calf hypertrophy, deltoid hypertrophy is a very common finding. This patient dies before the age of 30. The cause of premature death in these cases is commonly due to cardiomyopathy. This case report of male aged 22-years, who clinically started developing the symptoms of DMD when he reached 14 years of age, is a very uncommon finding. The main highlight of this case is normal development at the time of childhood. Patient had presented with weakness in bilateral lower limb which progressed to weakness in bilateral upper limbs also. Currently he is wheelchair bound. Patient currently has fewer episodes of breathlessness. On examination levoscoliosis and foot deformity that is equinovarus was seen. At this point the main aim is to enhance the wellbeing of the patient, henceforth management is symptomatic treatment and by providing physiotherapy for the purpose of muscle strengthening to improve the muscle power and tone.

Keywords: Duchenne muscular dystrophy, levoscoliosis, Developmental delay, Weakness in limbs, equinovarus, muscle biopsy.

1. INTRODUCTION

Duchenne muscular dystrophy (DMD) is a widespread disease of neuromuscular system; affecting one in 3600 male births worldwide (Chung et al., 2016). It presents more commonly in males because of its inheritance as an X linked recessive trait. Females act as a carrier for this disease. Only 10% of female carriers develop cognitive and/or cardiac dysfunction. This produces

very mild symptoms in female as compared to males of the same age groups (Bushby et al., 1993). Mutation of dystrophin gene which is present on X chromosome is responsible for this condition (Hoffman et al., 1987). Symptoms and signs of DMD are rarely present at birth. Most commonly, symptoms occur at four years of age and hence, this is the time when usually the diagnosis of DMD is made (Pane et al., 2013). The main highlights of this case are that, usually, the cases of DMD presents with developmental delay. But more unusual finding that was seen in this case was no developmental delay. As a child he attained all developmental milestones at corresponding age and time. Moreover, late onset of first signs and symptoms of DMD are seen in very rare cases. Here the first symptom that is weakness of both upper and lower limbs appeared when the patient had already reached his teen age group which is a very uncommon finding. These cases are at greater risk of developing cardiomyopathy which starts showing clinical features by ten years of age and develops into full-fledged severe cardiomyopathy at 20 years of age. They die often because of cardiomyopathy (Van-Westering et al., 2015). According to one study the usual time till which patient survives is hardly up till 30 years of age (Findlay et al., 2015). On examination he has levoscoliosis, limb length discrepancy and equinovarus of the foot. DMD clinically presents with elevated levels of serum biomarkers like creatinine phosphate (CK), alanine transaminase (ALT) and aspartate transaminase (AST). As the chances of survival of cases of DMD are very minimal also, despite of the fact that patient is having deformity of spine and foot, the management is focused on providing symptomatic relief to the patient. Home exercises and physiotherapy can also be given. The only thing that one cannot control is to reverse the damage that has already occurred but, one can try to improve the quality of life that is remaining with this patient. This case report of male aged 22-years, born from a non-consanguineous marriage, started developing the symptoms of DMD after 16 years of age. He is the first case of DMD in his family.

2. PATIENT AND OBSERVATION

Patient information

The patient is a 22-year-old male, reported at the hospital with complains of weakness in bilateral lower limbs since last 10 years, weakness in upper limb since last 8 years.

Clinical Findings

Weakness in lower limbs is insidious in onset, gradually progressive. It first developed in proximal group of muscle and then progressed to distal group of muscle. He used to walk on his toes since the time he started walking thus, developed bilateral foot deformity. Presently when sitting he is unable to get up on his own, cannot stand without support, cannot roll over bed, cannot get out of bed. Presently he is wheelchair bound and lies most of the time in bed. After 2 years the weakness then progressed to the upper extremities first in proximal group of muscle then in distal group of muscle. Currently he has difficulty in performing overhead activities. His parents gave history of repeated falls on every attempt to walk. He has had few episodes of difficulty in breathing since the last 2 months. Later, he developed dysphagia to solids and liquids both. There was no pain in muscle or involvement of any cranial nerve. His mental caliber had been found as normal. No developmental delay when considering gross motor, fine motor, language and social milestones. On physical examination patient was examined in sitting and supine position. Attitude of limb when examined in supine position was back, hip and knee were in extended position and foot externally rotated. On inspection spinal curvature seen, limb length discrepancy was seen. There is hypertrophy of calf muscle present. Gower's sign was found positive initially when the patient was ambulatory but since he is now wheelchair bound it was difficult to elicit Gower's sign. Hamstring muscle contracture was also seen in this patient. Foot deformity that is equinovarus was seen in this patient. On palpation of Lumbosacral spine, paraspinal spasm was present (Table 1, 2).

Table 1 Showing tone in muscles of upper and lower limb

Muscle tone	Right side	Left side
Upper limb	Hypotonia	Hypotonia
Lower limb	Hypotonia	Hypotonia

Table 2 Showing power in different groups of muscle

Power in group of muscles involved	Grade of right side	Grade of left side
Shoulder	1	1
Elbow	1	1
Wrist	2	2

Hip	1	1
Knee	1	1
Ankle	1	1

Timeline of current episode

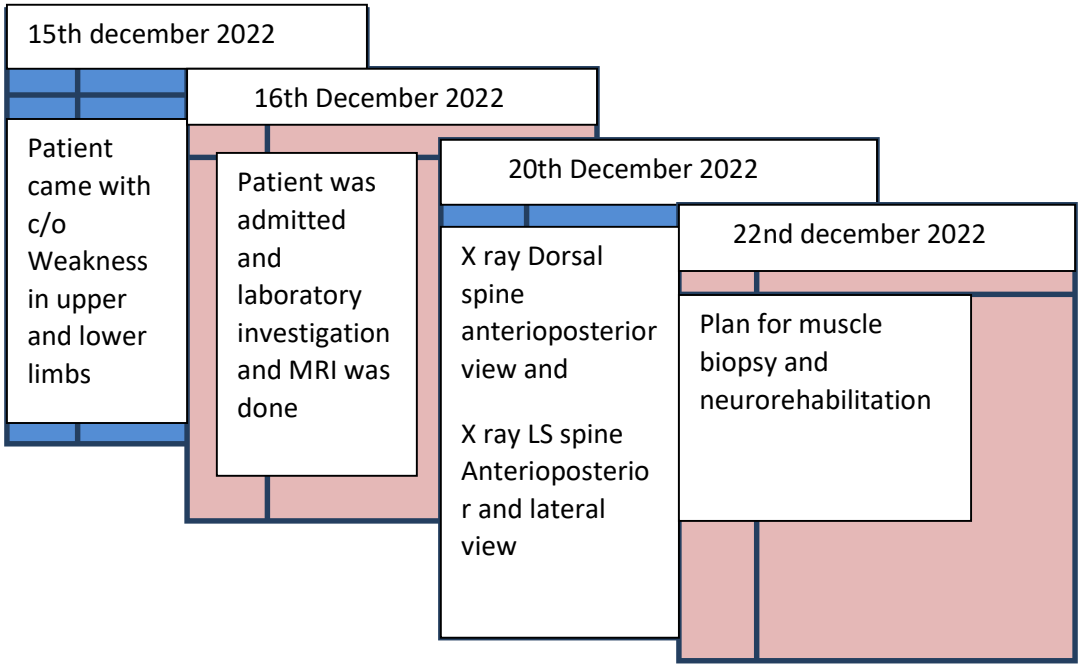

Figure 1 Showing timeline of current episodes

Diagnostic assessment

Laboratory investigations revealed some derangement (Table 3).

Table 3 Showing Different Laboratory parameters

Parameter	Result	Unit	Normal Value
Haemoglobin	14	Gm/dl	13-16
Total WBC count	5400	WBC/microliter	4,000-11,000
Total platelet count	1.23	Platelets/microliter	1.5-4.5 lacs
Alkaline phosphatase	150	IU/L	44-147
Alanine transaminase	49	U/L	7-55
Aspartate transaminase	83	U/L	8-48
Total protein	6.6	Gm/L	6-8.3
Total bilirubin	1.0	mg/dl	1.2
Activated partial thromboplastin clotting time	31.4	Seconds	25-35
Prothrombin time	12.8	Seconds	11-13.5

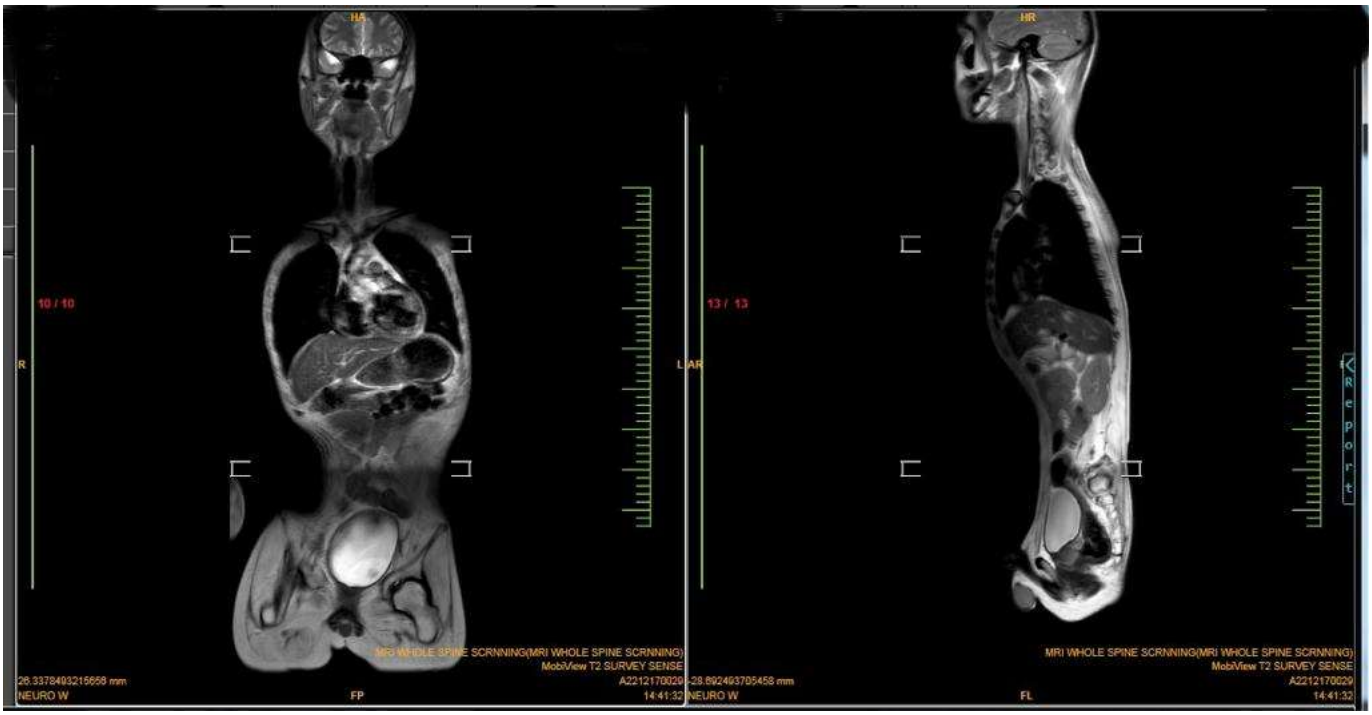

Figure 2 Showing MRI whole spine screening. There was evidence of levoscoliosis noted (Cobb's angle measuring approximately 30 degree). Sign of left side moderate scoliosis.

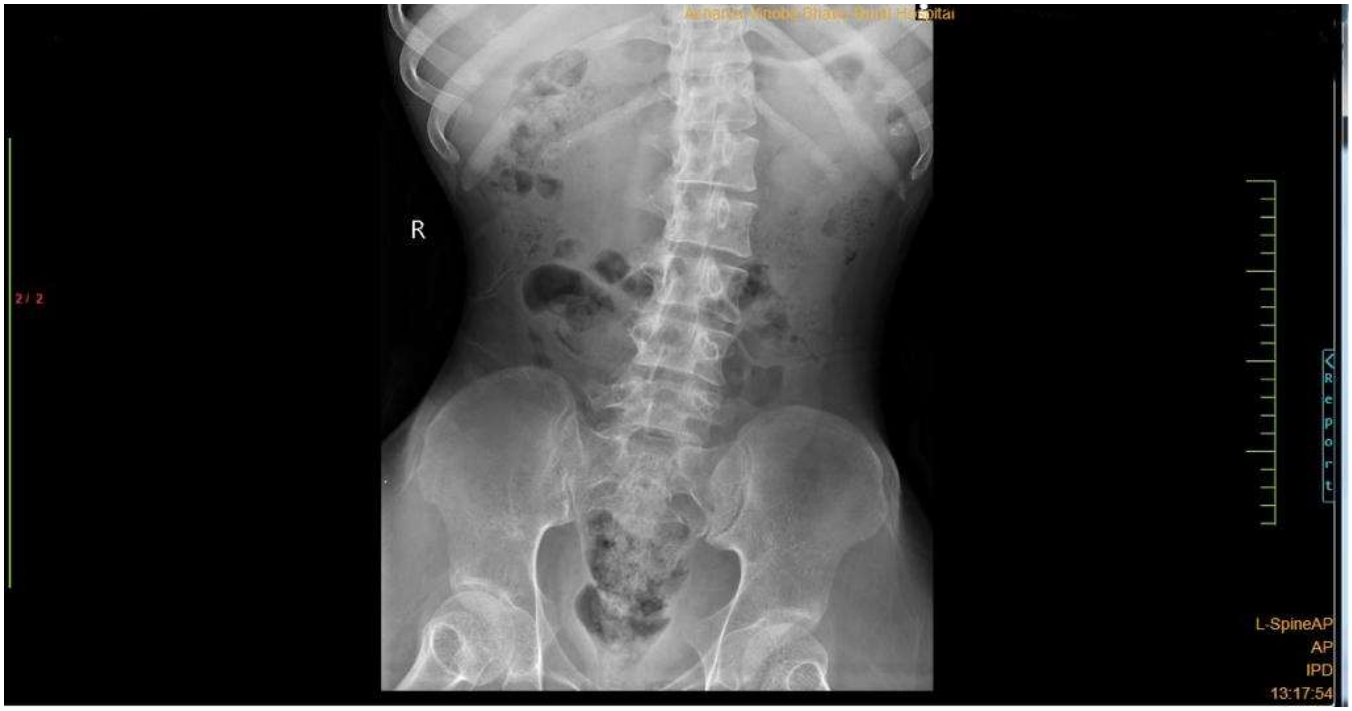

Figure 3 Radiographs showing Dorso lumbar spine Anteroposterior view showing left lateral tilting of spine on X ray

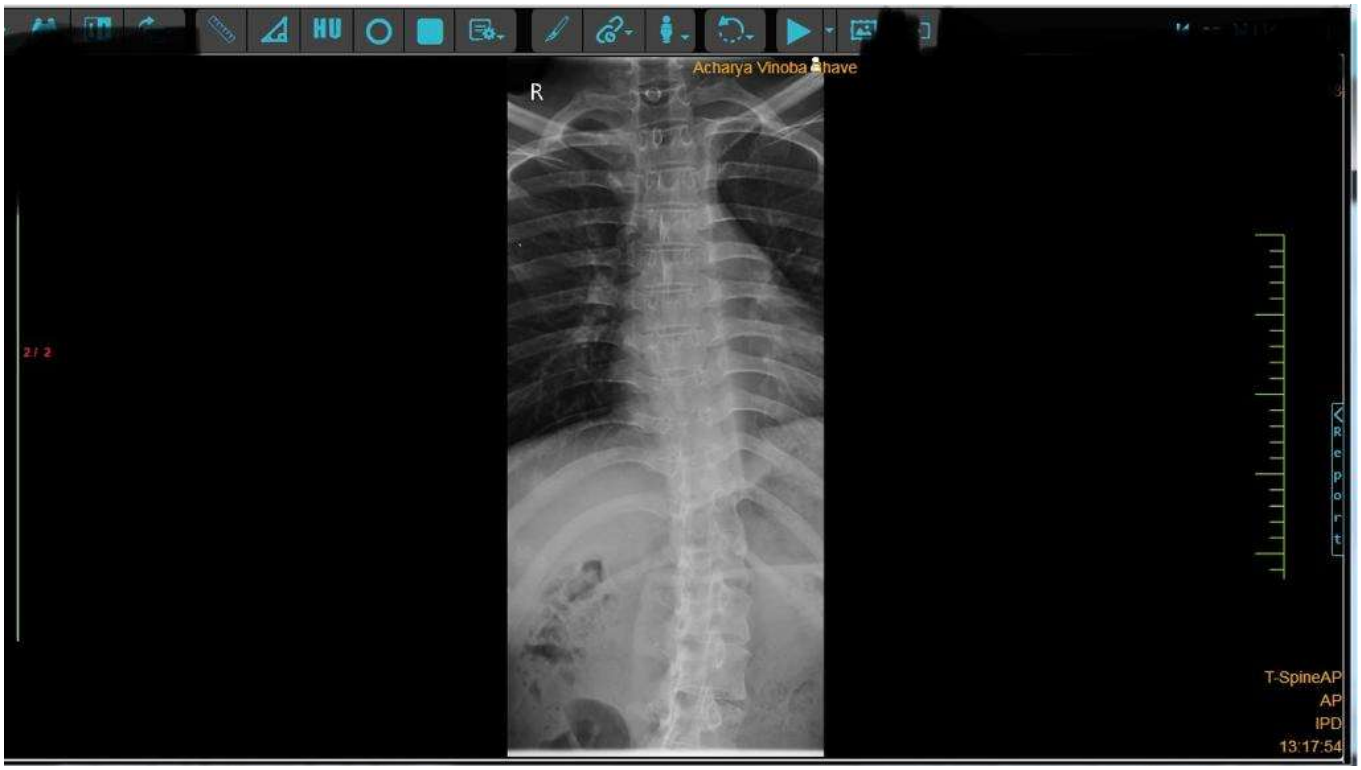

Figure 4 Radiographs showing an anteroposterior view of chest of a DMD patient with scoliosis demonstrating the curve pattern

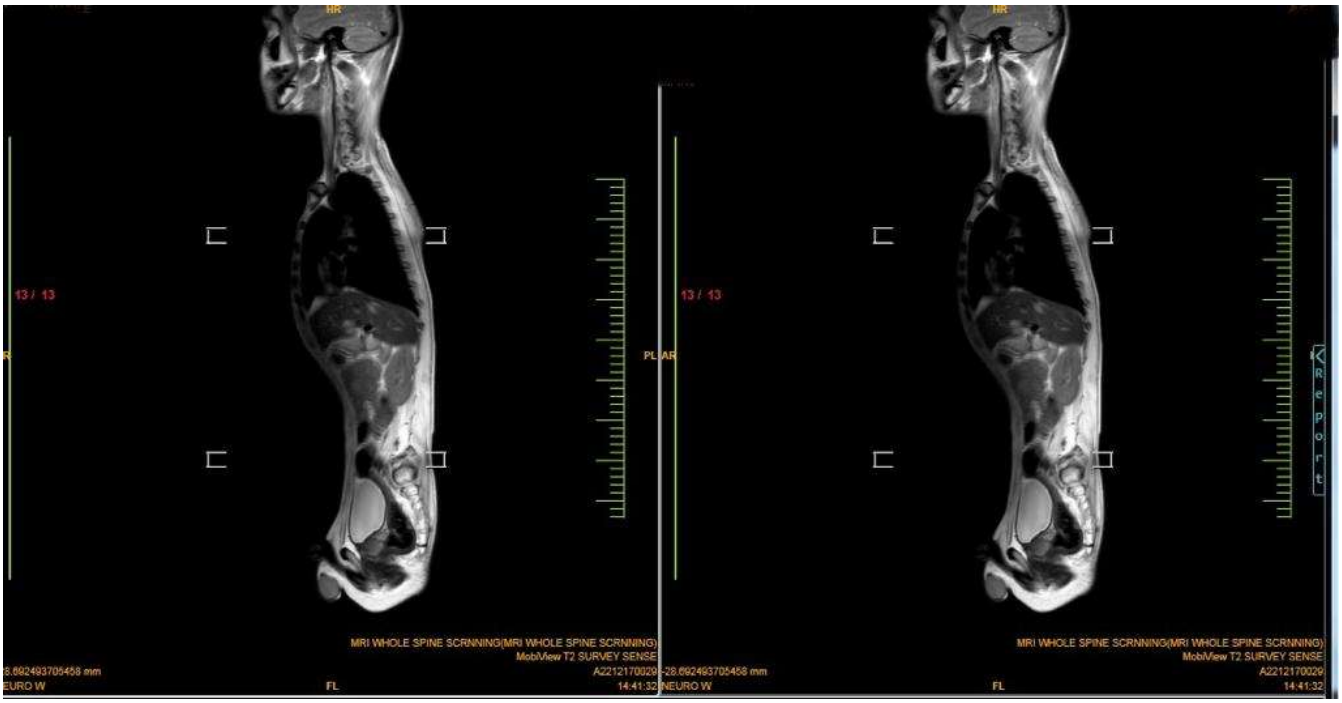

Figure 5 Showing MRI whole spine screening radiograph. Straightening of cervical spine. Altered curvature of Dorso lumbar spine. Posterior disc bulge indenting over anterior thecal sac noted at D12- L1 to L4- L5 disc level.

Muscle Biopsy

Showed focus of necrosis of muscle fibre, infiltration of mononuclear cells around necrotic focus, reduplication and intermediation of sarcolemma nuclei suggested the possibility of Duchenne muscular dystrophy.

Figure 6 Showing left sided scoliosis

Figure 7 Showing calf muscle hypertrophy, equinovarus deformity

Diagnosis

Clinical diagnosis of Duchenne muscular dystrophy was made based on the diagnostic assessment, laboratory investigations and muscle biopsy report.

Medical management

DMD is a progressive disease, the amount of damage that has been already caused can't be reversed neither can be halted. Symptomatic medical management along with muscle strengthening exercises can aid improving further outcome of the disease. Moreover, adult patients present with more severe symptoms and have more considerable muscular worsening and therefore present with more severe symptoms. Thus, symptomatic and social support must be provided. Despite of the supportive care provided to the patient the chances of survival in the patient are very minimal. In our case patient was advised to take Tab. Limcee, Tab B complex, Tab. Neurobion Forte, Tab. Flovite. Besides medical management he was given physiotherapy for a period of 15 days in our hospital. Patient was given stretching exercises for strengthening of muscle and to reduced already formed contractures.

3. DISCUSSION

Muscular dystrophy affects mainly skeletal muscle and there is no involvement of central or peripheral nervous system. DMD results from dystrophin gene mutation (Muntoni et al., 2003). Dystrophin gene (DG) is mainly located on sarcolemma through the entire length of the myofibrils of a healthy skeletal or cardiac muscle (Ljubicic et al., 2014). DG along with dystroglycan, sarcoglycan and nitric oxide synthase which is present in neuron form dystrophin glycoprotein complex (Ogura et al., 2014; Cirak et al., 2011). Associated gene mutations in DMD such as deletions in majority of cases, duplications, small mutations or other smaller rearrangements in some cases that interferes in frame reading of RNA. Consequently, expression of dystrophin protein in the skeletal and cardiac muscle is reduced leading to muscle wasting, respiratory paralysis, cardiac failure and death (Findlay et al., 2015). It presents clinically with episodes of frequent falls, difficulty to get up while sitting or walking on toes. They also present with waddling gait, calf muscle hypertrophy. They can develop lumbar lordosis and Trendelenburg gait. It is very difficult to raise themselves up, child first gets into knee-elbow position, then extends elbows and knees, brings hands and feet close together, places hands on knees first then on thighs and then tries to stand in erect posture which is termed as the Gower's maneuver (Jansen et al., 2010). This case shows features of levoscoliosis on examination of spine. Various conditions are responsible for paralysis of extensor group of muscle which is the main cause of spinal deformity (Gibson and Wilkins, 1975). Rideau et al., (1984), Siegel, (1978), Dubousset, (1996) and Dubousset and Queneau, (1983) proposed that major cause of deformity of spine is inclination of pelvis. Kurz et al., (1983) observed that in a patient of DMD when vital capacity (VC) decreases by 4% there is progression of the curve by 10°. According to Galasko et al., (1992) and Galasko et al., (1995), in patient with scoliosis secondary to DMD, VC decreases by 8% per year.

Diagnosis is made when there are elevated levels of biomarkers like creatinine kinase (CK), muscle biopsy, electromyography and genetic analysis. Due to repeated contractions of muscles, CK levels usually increases in plasma. Other enzymes such as AST, ALT, aldolase and lactate dehydrogenase are also raised (Yiu and Kornberg, 2008; Hathout et al., 2015).

Currently this condition is predominantly managed by use of corticosteroids and by physiotherapy. Presently, despite of the fact that corticosteroids are associated with variety of adverse effects like gain of weight, cushingoid appearance, disturbances in central nervous system, gastrointestinal system, metabolic disturbances, increased risk of vertebral fractures, corticosteroids are the only drugs which have shown documented evidence of benefit in improving this condition (Scully et al., 2013; Bonfanti et al., 2015). Prednisolone and deflazacort are commonly used corticosteroid. In gene therapy and stem cell therapy where there is up regulation of dystrophin-like protein provides with more promising results and beneficial effects. Dystrophin replaced by stem cell therapy is a possible DMD cure. Also, they help the muscles to regenerate by self-renewal and differentiate into various cell types (Noviello et al., 2014). Another treatment option for DMD is delivering of a therapeutic gene to skeletal and cardiac muscle, thus restoring the dystrophin protein. DG is very large to be delivered into human muscle cells hence this is a more refined technique to deliver a reduced-size dystrophin version. Prenatal counseling and genetic testing are being used that adds a little hope in prolonging and enhancing the wellbeing of the patients with DMD (Dey et al., 2015; Sakthivel-Murugan et al., 2013).

4. CONCLUSION

In this case of DMD, patient has already progressed to the severe version of this disease where the patient is wheelchair bound. He has weakness in both upper and lower limb, power of muscle is reduced to a grade of 1 and tone of muscle is hypotonia. Despite of the fact that DMD develops in 4^{th} to 5^{th} year of life with preceding developmental delay, but in our case the patient had achieved

normal development milestones and the disease started its onset when he reached his teens that are in when he was 14 years of age. Management of this case is symptomatic and conservative treatment and even though patient already has developed foot deformity, limb length discrepancy and scoliosis of spine. Also, the disease is being progressing very rapidly. Patient has already started facing respiratory complications. Hence corrective surgeries of scoliosis are withheld at this point of time. Thus, symptomatic medical management and providing physiotherapy can add up in adding some extra years for survival in this case.

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Author Contributions

All authors had equal contribution in making of this case report.

Informed consent

Informed consent was taken from the patient

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Conflict of interest

The authors declare that there is no conflict of interests.

Data and materials availability

All data sets collected during this study are available upon reasonable request from the corresponding author.

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