# Duchenne Muscular Dystrophy in a Filipino Boy Reaching Adulthood, and Nine Years into Oral Corticosteroids: A Case Report

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## ABSTRACT

**Rationale** Duchenne muscular dystrophy (DMD) is a disease that primarily manifests in the early stages of life and progressively affects muscle strength resulting in quadriparesis and ultimately resulting in premature death secondary to cardiac or respiratory failure. DMD is the most common x-linked genetic disorder in children that is because of an alteration of a protein called "dystrophin" which is responsible for strengthening muscle fibers and protecting them from injury as muscles contract and relax.

**Objective** To highlight the case of a 19-year-old male who was diagnosed with DMD at 8 years of age and treated with oral corticosteroid and rehabilitation.

**Case** We present the case of a 19-year-old male who developed difficulty climbing stairs and was diagnosed with DMD at 8 years old with the use of clinical exome sequencing. Corticosteroid therapy was initiated and rehabilitation perpetuated which dramatically improved his life expectancy.

**Discussion and Summary** Clinical exome sequencing was employed on our patient to confirm the diagnosis of DMD from other neuromuscular and neurodegenerative diseases. Most cases of DMD succumb to cardiopulmonary arrest before reaching adulthood; however, this case exemplifies DMD from other cases since our patient was able to prolong his life with continuation of oral corticosteroid and rehabilitation and in the absence of extensive life support.

**Key words** Progressive muscle weakness, Dystrophin, Premature death, DMD

## INTRODUCTION

Duchenne muscular dystrophy (DMD) is a genetic disorder that presents with progressive muscle degeneration and weakness. It is caused by alteration of a protein called dystrophin, which keeps muscle cells intact. The alteration may be due to mutations by large insertions or deletions that lead to frameshift errors downstream (60%), though it can also be due to point mutations or small frameshift rearrangements (40%)[1]. Children that are diagnosed with DMD usually manifest with delay in motor development and may eventually be wheelchair-confined followed by premature death from cardiac or respiratory complications.

High-quality multidisciplinary care has proven to slow disease progression and improve function and prolong life expectancy. It is recommended to provide anticipatory and preventive care to

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prolong function as further as possible. Treatment modalities include corticosteroid therapy and the use of intermittent positive pressure ventilation that can provide improvement in function, ambulation, quality of life and life expectancy. With the advent of medical technology, there are new genetically-based therapies that can be offered to patients. Here we present the rare case of a 19-year-old male who was diagnosed with DMD when he was 8 years old, with improved life expectancy from the treatment of steroid and rehabilitation.

## CASE PRESENTATION

### Patient History

We are presented with a 19-year-old male who was diagnosed with DMD when he was 8 years old and came in for consultation due to difficulty climbing stairs. The parents mentioned that he had difficulty arising from a sitting position, difficulty in climbing stairs and frequent falls during the interview on the first consult when the patient was 8 years old. There were no noted neuromuscular and neurodegenerative diseases in the family. The patient was born to a mother who is an only child and is the only boy in a sibling of four, no one in a genogram of three generations had presented with a similar disorder. The parents first noted that there was a delay in his developmental milestone which was evidenced by: rolling over at 3 months of age; being able to sit at 1 year old; being able to stand at 1 year old; cruising at 16-month-old; walking independently at 18-month-old; first word at 3-year-old and feeds using hands at 5-year-old. The disease began when he was 4 years old when he had difficulty climbing stairs but with noted prominent calves and was noted to have progressed every year, by 5 years old he was noted to use his hands and arms to walk up his own body from a squatting position, also known as Gower's sign. When he was 6 years old, he struggled to stand from a chair and bed; the parents noted that he had frequent falls at 7 years old. By 9 years old, he had difficulty maintaining an erect position and was wheel-chair bounded. The patient had normal weight for height appearance, and an ectomorphic build, but with noticeable difficulty in maintaining a standing position during the first consult at 8 years old. Neurological examination revealed no cognitive deficits with repeated tests and no cranial nerve deficits. He had intact sensory with normal cerebellar and tendon reflexes, except at the contracted elbow, wrist and finger joints. However, the patient was proximal-dominant quadriparetic, hence currently wheel-chair bound. This happened at 19 years of age due to contractures over time, with concomitant development of scoliosis (see Figures 1 and 2). Treatment was a combination of corticosteroid with vitamin D3. Methylprednisolone was started at the dosing of 1 mg/kg body weight for 3 months and was tapered 4 mg less per day monthly until 3 months of treatment. The corticosteroid was adjusted to 8 mg every other day for 6 months, then 6 mg every other

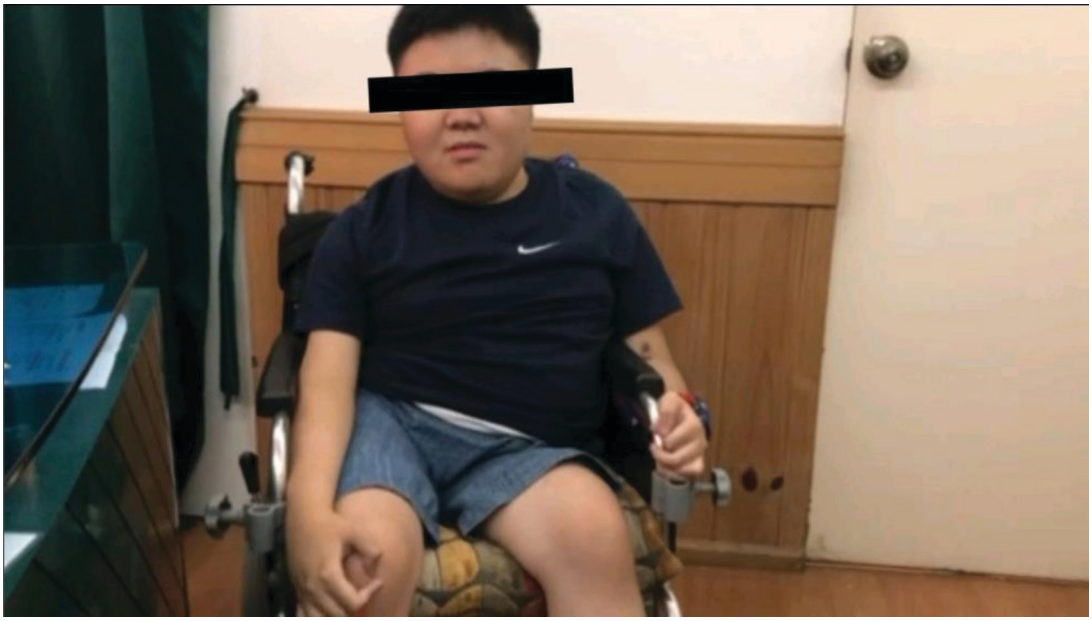

**Figure 1** DMD case on wheelchair at age 19 years old showing scoliosis and contractures of elbow, wrist and finger joints.

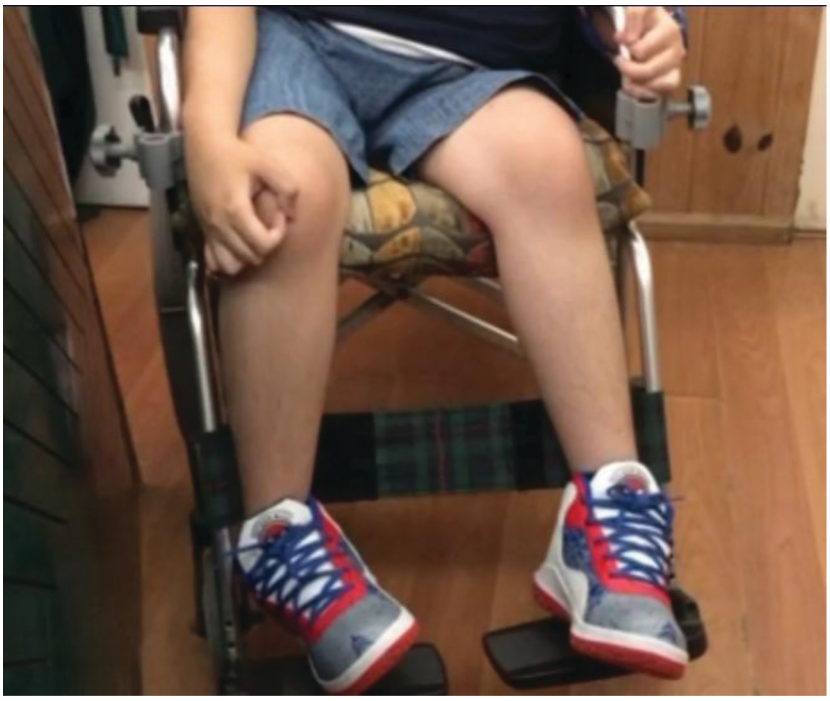

**Figure 2** DMD case at age 19 years old showing contractures of hip, knee and ankle joints.

day for another 6 months, then 4 mg every other day for 4 months, then maintained at 8 mg twice a week.

### Examination Findings

Various laboratory examinations and imaging were requested to aid in the diagnosis of DMD after the initial consult. Serological analysis revealed a high total creatinine kinase level of 14,000 U/L (sensitivity and negative predictive value of 100% and specificity and positive predictive values of 91% and 88.8%, respectively[2]). Brain Imaging via Magnetic Resonance Imaging was normal. A 2D echocardiography and a 12-lead electrocardiography showed no abnormalities. Electrodiagnosis with nerve conduction studies and electromyography yielded a diagnosis of myopathy. Notably, there were fibrillation potentials over sampled muscles together with brief small amplitude polyphasic potentials and early recruitment patterns. Motor and sensory nerve conduction velocities and amplitudes were within normal ranges. Muscle ultrasound was done which revealed scattered areas of marked increase to very strong muscle echogenicity, which is highly indicative of myopathy (Table 1). The diagnosis was confirmed when the patient underwent Clinical Exome Sequencing (CentoDx™) which revealed a positive result of dystrophin frameshift mutation at exon 62 and identified a hemizygous pathogenic variant.

## DISCUSSION

This present patient is an established case of DMD based on clinical features of early-onset proximal muscle weakness (sparing the bulbar muscle), high creatinine kinase, myopathy by electrodiagnosis and dystrophin mutation by genetic study. DMD is one of the four conditions known as dystrophinopathies (with other three diseases namely: Becker Muscular Dystrophy [BMD] – which is milder than DMD; an intermediate clinical presentation between DMD and BMD; and lastly DMD-associated dilated cardiomyopathy). It is the most common x-linked disorder in children, affecting 1 in every 3,600 live male births, and impacting all races and ethnic groups[3]. We are unaware of a DMD case reported in our locale reaching adulthood.

The general clinical features of the disease include progressive proximal-dominant muscle weakness, intellectual impairment, hypertrophy of the calves, and proliferation of connective tissue in muscles. Infants are rarely symptomatic and there is sparing of early motor skills such as rolling over, sitting and standing. There are no sensory nor autonomic impairments; it is only when they get older that signs and symptoms of the disease would become apparent. The first sign

**Table 1** Muscle ultrasound revealing echogenicity of the muscle

| Muscle (Right) | Cross-sectional thickness (cm) | Muscle echogenicity (Heckmatt Score) | Muscle (Left) | Cross-sectional thickness (cm) | Muscle echogenicity (Heckmatt Score) |
|---|---|---|---|---|---|
| **Hamstring Muscles** | | | | | |
| Bicep Femoris | 2.07 | III | Bicep Femoris | 2.17 | III |
| Semitendinosus | 2.17 | III | Semitendinosus | 1.72 | III |
| Gastrocnemius | 1.21 | IV | Gastrocnemius | 0.99 | III |
| **Quadricep Muscles** | | | | | |
| Vastus Lateralis | 0.8 | III | Vastus Lateralis | 0.86 | II |
| Rectus Femoris | 1.11 | IV | Rectus Femoris | 0.79 | III |
| Vastus Medialis | 1.23 | IV | Vastus Medialis | 1.05 | IV |
| Soleus | 1.07 | IV | Soleus | 1.28 | III |
| Sartorius | 0.32 | III | Sartorius | 0.79 | III |
| **Forearm Muscles** | | | | | |
| Extensor Digitorum | 0.35 | I | Extensor Digitorum | 0.41 | II |
| Extensor Carpi Ulnaris | | II | Extensor Carpi Ulnaris | 0.79 | II |
| Extensor Carpi Radialis | 0.64 | I | Extensor Carpi Radialis | | |
| Flexor Digitorum Superficialis | 1.06 | II | Flexor Digitorum Superficialis | 1.02 | I |
| Flexor Carpi Radialis | 0.73 | | Flexor Carpi Radialis | | |
| **Arm Muscles** | | | | | |
| Biceps Brachii | 0.7 | III | Biceps Brachii | 0.74 | IV |
| Triceps | 1.06 | IV | Triceps | 1.44 | I |
| Deltoid | 1.12 | I | Deltoid | 1.73 | II |

*Grading* based on Heckmatt Score: Grade 1 - Normal, Grade 2 – Increased muscle echo intensity with distinct bone echo, Grade 3 – Marked increased muscle echo with reduced bone echo, Grade 4 – Very strong muscle echo and complete loss of bone echo. The patient presented with various areas showing grade 3 and 4 Heckmatt scoring which would signify myopathy.

of weakness usually consists of poor head control. An early Gower's sign is often evident at the age of 3 years old and is fully expressed by the age of 5 or 6 years old, which is evident in the patient at the time of examination at the age of 8 years old. A common presentation during the toddler period includes delayed walking, falling, and trouble using stairs which were all very apparent in the patient. Some patients may even be confined to a wheelchair by the age of 7 years old. A meta-analysis revealed an increase in life expectancy of DMD patients.[4] The median life expectancy in patients diagnosed with DMD who were not on ventilatory support ranged between 14.4 and 27.0 years while those who received ventilatory support was notably higher, ranging between 21.0 and 39.6 years[4]. Notably, during the period of 1960s, the average life expectancy for DMD was 14.4 years, which by 1990 had increased to 19.3 years upon institution of corticosteroid therapy.[5] In Asia and Oceania, a group of experts alluded to the advantages of oral corticosteroid therapy among DMD patients in the region.[6] Although steroid treatment is part of clinical practice for the management of DMD, many clinicians in Asian countries are aware of DMD care recommendation (as high as 91% of clinicians), however, steroid therapy does not appear to be widely utilized among them[6,7].

## CONCLUSION

As far as we are aware, this is the first reported Filipino case of DMD reaching adulthood following an oral steroid regimen for 11 years coupled with rehabilitation.

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