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Case report

DUCHENNE MUSCULAR DYSTROPHY DIAGNOSED BY DYSTROPHIN GENE DELETION TEST: A CASE REPORT

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ABSTRACT

Duchenne muscular dystrophy (DMD) is an X-linked recessive disease affecting 1 in 3600—6000 live male births. A muscle biopsy is not necessary if a genetic diagnosis is secured first, particularly as some families might view the procedure as traumatic. DMD occurs as a result of mutations (mainly deletions) in the dystrophin gene (*DMD*; locus Xp21.2). Mutations lead to an absence of or defect in the protein dystrophin, which results in progressive muscle degeneration leading to loss of independent ambulation. Ninety percent of out frame mutations result in DMD, while 90% of in-frame mutations result in BMD. Electron microscopy is not required to confirm DMD. Genetic testing is mandatory irrespective of biopsy results. But the muscle biopsy is not required if the diagnosis is secured first by genetic testing.

Keywords: Duchenne Muscular Dystrophy, dystrophin gene deletion test.

INTRODUCTION

DMD is an X-linked disease that affects 1 in 3600-6000 live male births.[1] Affected individuals are unable to run and jump properly due to proximal muscle weakness, which also results in the use of the classic Gowers' manoeuvre when arising from the floor. Most patients are diagnosed at approximately 5 years of age, when their physical ability differs markedly from their peers. Respiratory and cardiac complications emerge, and without intervention, the mean age at death is around 19 years. Non-progressive cognitive dysfunction might also be present.[2] DMD occurs as a result of mutations (mainly deletions) in the dystrophin gene. Mutations lead to an absence of or defect in the protein dystrophin, which results in progressive muscle degeneration and loss of ambulation by the age of 13 years.[3]

CASE REPORT

A 7 years old male child, second by order of birth, born of non consanguineous marriage, brought with complaints of frequent falls while walking since 2 years. And difficulty in standing from sitting position since 1 year. Birth history was uneventful. Milestones were achieved as per age till 5 years of age.

On admission general condition was good, speech normal, no mental retardation; calf hypertrophy was present, Gower's sign positive, and tone normal. Power grades in various muscle groups of the lower limbs were as shown in Table 1.

Truncal weakness was present. Neck flexors were weak as compared to extensors.

Investigation: Hb 11.4 gm%, total leukocyte count - 6600/cmm platelets- 3.55 lac/cmm.CPK-12600 IU/Lit.

Table 1: Grading of power in various muscle groups of lower limb.

Region	Muscle group	Right side	Left side
Hip	Flexors	4	4
	Extensors	3	3
	Abductors	3	3
Knee	Extensors	4	4
	Flexors	4	4
Ankle	Dorsi-flexion	4	4
	Plantar flexion	5	5
Reflexes	Knee reflex	Absent	Absent
	Ankle reflex	+	+

Muscle biopsy was not done because relatives were not ready. Molecular test for deletion of dystrophin gene showed Deletion has seen of exons 45, 46, 47, 48, 49and 50. These deletions indicating out frame mutations. This is along with the age of the patient is consistent with DMD. (90% of out frame mutations result in DMD, while 90% of in-frame mutations result in BMD).

Clinical manifestations: Infants rarely symptomatic, though some manifest by mild hypotonia. Early gross motor milestones are usually achieved at the proper ages or may be mildly delayed. Poor head, holding in infancy may be the earliest sign of weakness. In toddlers lordotic posture is to compensate for gluteal weakness. A Gowers' sign and Trendelenburg gait is often evident by age 5 or 6 yr.

Some are confined to a wheelchair by 7 yr of age; most patients normal till 10 yr of age. With orthotic prostheses, physiotherapy, and sometimes minor surgery (Achilles tendon lengthening), most are able to walk until age 12 yr. Apart from postponing the psychological depression ambulation even for as little as 1 hour per day prevents scoliosis.

The weakness progresses continuously into the 2nd decade. The distal muscles are relatively well preserved. Respiratory involvement like weak and ineffective cough, frequent respiratory infections, and decreasing respiratory reserve, with pharyngeal weakness leading to aspiration, nasal regurgitation of liquids, and nasal voice quality.

Contractures involving the ankles, knees, hips, and elbows are common. Pseudohypertrophy of the calves and wasting of thigh muscles are classic features of DMD. It is due to hypertrophy of some muscle fibers, infiltration of muscle by fat, and proliferation of collagen. After the calves, the next most common site of muscular hypertrophy is the tongue, followed by muscles of the forearm. The voluntary sphincter muscles rarely become involved.

Unless ankle contractures are severe deep tendon reflexes remain well preserved. The knee deep tendon reflexes may be present until about 6 yr of age, but are less brisk than the ankle jerks and are eventually lost. In the upper extremities, the brachioradialis reflex is usually stronger than the biceps or triceps brachii reflexes.

Cardiomyopathy is seen in 50–80% of patients and its severity of cardiac involvement does not necessarily correlate with the degree of skeletal muscle weakness. Some patients die early of severe cardiomyopathy while still ambulatory; others in terminal stages of the disease have well-compensated cardiac function. Smooth muscle dysfunction, particularly of the gastrointestinal tract, is a minor, but often overlooked, feature.

Mental retardation is common, although only 20–30% have an IQ <70. The majority has learning disabilities that still allow them to function in a regular classroom, particularly with remedial help. A few patients are profoundly mentally retarded, but there is no correlation with the severity of the myopathy. Epilepsy is slightly more common than in the general pediatric population. Dystrophin is expressed in brain and retina, as well as in striated and cardiac muscle, though the level is lower in brain than in muscle. This distribution may explain some of the CNS manifestations. Abnormalities in cortical architecture and of dendritic arborization may be detected neuropathologically; cerebral atrophy is demonstrated by MRI late in the clinical course. The degenerative changes and fibrosis of muscle constitute a painless process. Myalgias and muscle spasms do not occur. Calcinosis of muscle is rare. Death occurs usually at about 18–20 yr of age. The common causes of death are respiratory failure in sleep, intractable heart failure, pneumonia, or occasionally aspiration and airway obstruction.[4]

DIAGNOSIS

An open muscle biopsy is necessary if the differential diagnosis includes DMD among other types of muscular dystrophy, so that adequate tissue will be available for further analysis. A needle biopsy may be appropriate if testing is only for DMD. The key tests done on biopsy are immunocytochemistry and

immunoblotting for dystrophin.[3] Electron microscopy is not required to confirm DMD. Genetic testing is mandatory after a positive biopsy. However, if genetic testing is negative for mutation, but creatine kinase concentrations are increased and signs or symptoms consistent with DMD are present, then the next necessary diagnostic step is to do a muscle biopsy. This is also the case if there is a family history of DMD and a suspicion of the diagnosis, but no family mutation is known.[5]

Treatment: Gluco-corticoids slow the decline in muscle strength and function in DMD. The goal is to preserve ambulation and decrease in later respiratory, cardiac, and orthopaedic complications. Other dietary supplements, such as coenzyme Q10, carnitine, aminoacids (glutamine, arginine), anti-oxidants (fish oil, vitamin E, green-tea extract), and others, are being used. Expert doesn't recommend the use of these supplements due to lack of supportive data.[6]

CONCLUSION

A muscle biopsy is not necessary if a genetic diagnosis is secured first, particularly as some families might view the procedure as traumatic. Electron microscopy is not required to confirm DMD. However, if genetic testing has been done and no mutation identified, but creatine kinase concentrations are increased and signs or symptoms consistent with DMD are present, then the next necessary diagnostic step is to do a muscle biopsy.

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