Epilepsy and abnormal MRI brain findings in a patient with Duchenne’s muscular dystrophy – A rare association

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Abstract

Epilepsy in Duchene’s muscular dystrophy, though more prevalent than in general population, is seen in only 6-10% cases of DMD. Earlier studies have reported nonspecific MRI findings in DMD patients with epilepsy. We report a patient of DMD, diagnosed on muscle biopsy who had definite MRI brain imaging abnormalities. Our case highlights the rare association of MRI brain signal changes in this patient with DMD.

INTRODUCTION

Duchene muscular dystrophy (DMD) is an X-linked disease affecting 1 in 3600–6000 live male births. Affected individuals mostly present with delayed motor milestones and progressive muscle weakness, most often noticed by parents when their physical ability lags markedly from that of their peers. The disease slowly progresses and by the end of the second decade, complications emerge with cardiorespiratory pathologies being the commonest cause of death in these individuals. DMD occurs as a result of mutations (mainly deletions) in the dystrophin gene (DMD; locus Xp21.2). Pathologic studies have demonstrated that muscle weakness is due to an irreversible, ongoing loss of skeletal muscle which is due to a mutation in dystrophin gene. Similarly, loss or absence of dystrophin from the central nervous system (CNS) in these patients impact brain function, and likely underlie the cognitive deficits seen in children with DMD. Structural brain abnormalities are not common in DMD and the commonest MRI brain finding is that of diffuse cerebral atrophy or non-specific periventricular changes. Apart from mental retardation, about 6-12% of DMD patients have epilepsy. We report a case of a child who had progressive muscle weakness with history of seizures and MRI brain abnormalities and was diagnosed as DMD on muscle biopsy.

CASE REPORT

A 10 year old boy, 2nd born of a non-consanguineous parentage came with motor developmental delay and progressive muscle weakness. The parents noted that he was always slow in running and would sustain frequent falls trying to catch up with peers of his age. Subsequently, he started requiring support to get up from squatting position, and over the last 3-4 years had similar weakness in the upper limbs as well. Since the last two years, the child has been having frequent seizures, the semiology was suggestive of generalized tonic clonic seizures with no preceding aura, automatism or any post ictal abnormalities. In addition, he gave history of occasional episodic loss of awareness to surroundings, lasting a few seconds with no motor accompaniments. He was diagnosed as complex partial seizure with secondary generalization and started on sodium valproate following which there have been no further episodes till the last follow up.

On examination, he had a lordotic posture with pseudo hypertrophy of the calves. He was thin built with generalized hypotonia without contractures. He had bifacial weakness, proximal more than distal limb weakness with selective involvement of neck flexors, wrist extensors, brachioradialis, biceps, triceps, tibialis anterior and quadriceps. He would walk with a waddle and Gower’s sign was positive. There was generalized areflexia.

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Routine blood investigations were normal. His creatine phosphokinase (CPK) was markedly raised at 16,330 U/L and electromyography suggested a myopathic pattern. ECHO cardiogram did not reveal any cardiac pathology.

An open biopsy of the left biceps muscle was performed under local anaesthesia. The biopsy revealed marked replacement by fibrous tissue with variation in size of muscle fibers with degenerating and regenerating fibers. The fibers showed frequent internal nuclei, occasional splits and myophagocytosis thereby suggesting a myopathic pattern. There was complete absence of staining with all three Dystrophin antibodies in contrast to normal staining controls (Figure 1). Thus, a diagnosis of DMD was confirmed.

![Figure 1](image1.png)

Figure 1. Top panel shows muscle largely replaced by fibrous tissue (left) with variation in fiber size and internal nuclei (right) (Hematoxylin & Eosin). Lower three panels show complete absence of Dystrophin immunostaining for N, C and rod domain in this patient’s muscle biopsy (left) as compared to normal sarcolemmal staining in control tissue (right) (Diaminobenzidine, x200)
MRI brain showed ill-defined T2 hyper intensities in bilateral central semi ovale, corona radiata and right frontal lobe (Figure 2). EEG showed diffuse theta to delta slowing with no focal abnormalities.

DISCUSSION

Our patient with muscular dystrophy was diagnosed as DMD based on muscle biopsy. Mental retardation is seen in about 30% cases of DMD. There is a greater frequency of psychiatric comorbidities, such as attention deficit disorder and hyperactivity in DMD. The prevalence of epilepsy in DMD is much more than that in general population. Etemadifar et al. observed that 7 out of 54 patients with DMD suffered from epilepsy (12%). Similarly, Paine et al. found this association to be 6%. The brain imaging findings were not described in the former study while in the latter study that included 14 out of 222 patients with epilepsy, only 2 patients had nonspecific periventricular changes on MRI brain. The authors postulated that dystrophin has a role in anchoring and stabilization of GABA-A receptors. Thus, a reduction in GABAergic inhibition predisposes DMD patients to seizure activity. Our patient with DMD had definitive evidence of hyper intensities in bilateral centrum semiovale and periventricular and frontal subcortical white matter on MRI brain. This appears to be a rare association in patients of DMD who have concomitant epilepsy. A genetic analysis for gene deletions and duplications could not be performed in our patient.

In conclusion, the current case highlights the infrequent occurrence of epilepsy in patients of DMD and its rare association with brain abnormalities. This may be due to altered GABAergic signaling resulting in epilepsy in this patient. A genetic analysis to study the correlation between exon mutations and epilepsy in DMD patients is worthwhile to further elucidate this rare association.

DISCLOSURE

Conflict of interest: None

REFERENCES