A case of congenital myopathy masquerading as paroxysmal dyskinesia

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Abstract

Gastroesophageal reflux (GER) disease is a significant comorbidity of neuromuscular disorders. It may present as paroxysmal dyskinesia, an entity known as Sandifer syndrome. A 6-week-old neonate presented with very frequent paroxysms of generalized stiffening and opisthotonic posture since day 22 of life. These were initially diagnosed as seizures and he was started on multiple antiepileptics which did not show any response. After a normal video electroencephalogram (VEEG) was documented, possibility of dyskinesia was kept. However, when he did not respond to symptomatic therapy, Sandifer syndrome was thought of and GER scan was done, which revealed severe GER. After his symptoms got reduced to some extent, a detailed clinical examination revealed abnormal facies with flaccid quadriparesis. Muscle biopsy confirmed the diagnosis of a specific congenital myopathy. On antireflux measures, those episodic paroxysms reduced to some extent. Partial response to therapy in GER should prompt search for an underlying secondary etiology.

Key Words

Congenital myopathy, gastroesophageal reflux, paroxysmal dyskinesia, Sandifer syndrome

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Introduction

Paroxysmal dyskinesia is a rare, heterogeneous, genetic condition manifesting as brief episodes of dystonia, chorea, and ballismus or a combination of these movement disorders. The age of onset varies from early childhood to 5th decade of life. Infantile onset is known with convulsions and paroxysmal choreoathetosis, an entity that manifests beyond 3 months of age.[1] Secondary causes include central nervous system pathologies which can be demyelinating, vascular, traumatic, metabolic, infectious, toxic, autoimmune, or endocrine in nature.[2]

Sandifer syndrome is an entity which manifests as paroxysmal dyskinesia secondary to gastroesophageal reflux (GER).[3] Esophagitis, between esophagitis and GER, or gastroesophageal dysmotility are not so uncommon in central and peripheral neurological conditions. Significant proportion of neuromuscular disorders have GER.[4,5] Herein, a case of congenital myopathy is being described presenting primarily as paroxysmal dyskinesia.

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Case Report

A 6-week-old boy presented with paroxysmal events starting from day 22 of life. The events started with a cry, followed by ophistotonic posturing and stiffening of all four limbs, which lasted from 15-20 min to 2-3 h. The events occurred very frequently multiple times a day. They were not associated with uprolling of eyeballs, vacant stare, loss of consciousness, tongue bite, perioral cyanosis, or passage of stool or urine. He also had associated swallowing difficulty and occasional choking episodes. His antenatal, neonatal, and family history were insignificant. Prior to presenting to the current center, these episodes were treated as seizures and he was on multiple antiepileptics (valproate, clonazepam, levetirecetam, and zonisamide). When he presented to the outpatient department of the current center at 6 weeks of life, he was continuously having those episodes. A video electroencephalogram (VEEG) was done, which was normal. He was diagnosed as status dystonicus and put on trihexiphenydyl and intravenous lorazepam. Rest of the antiepileptics were discontinued. His magnetic resonance imaging (MRI) brain, arterial and cerebrospinal fluid lactate,

blood pH, sugar, and ammonia were normal. Even after 24 h of intravenous lorazepam, there was no significant response. A possibility of GER causing Sandifer syndrome was kept. Technetium-99 scan revealed severe GER. Subsequently, he was started on antireflux measures (proton pump inhibitors, prokinetic agents, thickened feeds and appropriate posture). Within a week there was decrease in frequency of those episodes. During that time a detailed clinical examination was possible. General physical examination revealed facial dysmorphism in the form of elongated face, tented upper lip, and retromicrognathia. His central nervous system examination had shown subtle facial and bulbar weakness and flaccid areflexic quadriparesis with occasional antigravity movements without any contracture. However, there was no ocular weakness, impaired vision or hearing. A possibility of neuromuscular disorder was kept. His serum creatine phosphokinase and nerve conduction study were normal and electromyography was inconclusive. His echocardiography and genetic study for myotonic dystrophy were normal. His mother's human immunodeficiency virus (HIV) serology was negative.

A muscle biopsy was done, which showed features suggestive of nemaline rod myopathy [Figure 1a-d].

Two months on antireflux measures, he has shown marked improvement in his symptoms.

Discussion

Nemaline myopathy is a genetically heterogeneous group of disorder linked by common histological features on muscle biopsy. Clinically, six phenotypes have been described, viz. severe congenital (neonatal), Amish, intermediate congenital, mild congenital, childhood, and adult onset forms. The first four phenotypes usually have neonatal or early infantile onset. However, respiratory insufficiency at birth and occasional cardiomyopathy differentiates the first two subtypes from the other two. Early contractures are seen in the intermediate form along with the former two.[6] The current case appears to be a mild congenital variant in view of preserved spontaneous respiration, absence of cardiac or ocular involvement or contractures.

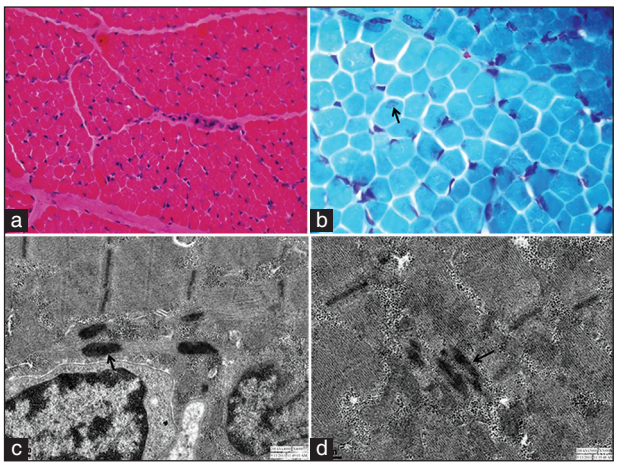

Figure 1: (a) Hematoxylin and eosin staining showing normal fascicular architecture with minimal fiber size variation (×200). (b) Modified Gomori trichrome stain demonstrating greenish granular material in the myofibers (×400). (c and d) Electron micrographs showing perinuclear and central nemaline rods (C and D, ×4000 and ×5000 respectively, original magnification)

Nemaline rods have also been described in mitochondrial myopathies, myotonic dystrophy, dermatomyositis and HIV myopathy. However, primary nemaline myopathy is diagnosed when the muscle histological findings are seen in a relevant clinical scenario, as in the current case.[6]

Up to one-fourth patients with congenital nemaline myopathy have GER.[4] Lower esophageal sphincter dysfunction and esophageal dysmotility secondary to defects in hormonal and neural activity and defective functional integrity of smooth and skeletal muscles including diaphragm underlie this defect.[7,8] In the current case, the features most probably got accentuated secondary to the bulbar dysfunction.

Sandifer syndrome is a rare clinical entity characterized by GER, irritability, and abnormal movements of the body. Classically, the movements described are head or eye version, torticollis, extensor spasm and dystonic posture. These movements are a mechanism to protect the air passages from reflux or to relieve the abdominal pain caused by acid reflux. Documentation of GER by scintigraphy along with normal VEEG and disappearance of symptoms after treatment is sufficient for diagnosis.[9] In the current case although the diagnosis was based on these investigations, there was partial response to medical treatment. This may be due to the underlying myopathy causing lower resting esophageal sphincter tone.[7]

Sandifer syndrome is known to masquerade various epileptiform and movement disorders.[10] Diagnosing it early is crucial as in primary cases response to treatment is dramatic and poor or partial response hints towards an underlying secondary cause.

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