A 14-year-old boy was referred for evaluation of muscle weakness. The patient had complained of slowly progressive muscle weakness for 2 years prior to admission, worsening with the onset of the child’s growth spurt. He complained of mild weakness during his early childhood. He denied shortness of breath suggestive of cardiac or respiratory involvement during this period. However, the child was floppy at the age of 3 months and his motor milestones though reached were delayed. Development in other parameters was normal. His parents were consanguineous. There was no family history of myopathy. He had generalized hypotonia and muscle weakness (proximal and distal) with a positive Gower’s sign at presentation to hospital. He was a thin boy with an elongated face and a high arch palate [Figure 1].

Creatine phosphokinase (CPK) was normal. Electromyogram (EMG) demonstrated myopathic changes. Muscle histology with H and E, was normal. Nemaline bodies were visible with Gomori trichrome in subsarcolemmal and sarcoplasmic regions [Figure 2]. Echocardiography was normal. Spirometry showed mild restrictive pattern.

**Commentary**

Nemaline myopathy (NM) is a rare muscle disorder defined by the presence of inclusions known as nemaline bodies in muscle fibers. It was first described by Shy et al, and Conen et al. This rare form of congenital myopathy is characterized by hypotonia and muscle weakness and has an estimated incidence which varies from 1 in 50,000 to 500,000. This patient presented with clinical and EMG evidence of myopathy. The onset of the disease and normal CPK suggested a form of congenital myopathy. There are several forms of congenital myopathies, which are characterized by their respective histological features. NM, Central Core disease and Myotubular myopathy are common congenital myopathies. This patient’s morphological features and the histology of muscle biopsy were characteristic of NM.

NM is genetically as well as phenotypically, a heterogeneous group of disorder. NM is classified as: Severe congenital, intermediate congenital, typical congenital, childhood and adult forms based on the age of onset and severity of motor and respiratory involvement.

The severe congenital form presents at birth with muscle weakness and severe hypotonia, difficulties with sucking, swallowing, and respiratory insufficiency. Most die in utero. Intermediate congenital form is characterized by independent respiration at birth, but fails to achieve motor milestones, develops joint contractures and requires respiratory support or is wheelchair-bound by 11 years of age.

The Mild congenital or typical NM form occurs either in the neonatal period or 1st year of life. Weakness is mainly proximal and may extend distally in the latter periods. Mile stones are delayed, but reached and should be classified as typical congenital NM, if they crawl before 12 months and walk before 18 months of age. Respiratory muscles are affected, although, it may be sub-clinical. Cardiac involvement is rare and clinical course is usually static or slowly progressive. Some may deteriorate during the pre-pubertal period of rapid development. This patient had the typical congenital form where progression of weakness in the pre-pubertal period was seen. In the congenital forms of NM the face is often elongated and expressionless with a high arch palate [Figure 1].

The Childhood form of NM occurs in the first or early in the second decade with normal early motor development. Weakness progresses until they are wheelchair bound by 40 years. The Adult form of NM is heterogeneous with regard to clinical presentation and disease progression. Weakness starts in the third to the sixth decade without a family history.
Weakness progresses usually without cardiac and respiratory involvement.[9]

NM is caused by mutations in at least 6 genes coding for skeletal muscle proteins. Many of these proteins interact within the sarcomere to facilitate muscle contraction. These mutations cause disorganization of proteins found in the sarcomeres of skeletal muscles, which cannot interact normally and disrupt muscle contraction. The changes in muscle cells can be detected histologically and the abnormal muscle cells contain rod-like structures called nemaline bodies as seen here [Figure 2]. Inheritance in NM is usually autosomal recessive. Less commonly it is autosomal dominant. Most cases occur sporadically due to new mutations.[9]

NM may not be rare, as was evident in a study in India where out of 750 muscle biopsies during a period of 1.5 years, 15 were congenital myopathies and 4 were NM (0.53% of all muscle diseases and 22.6% of all congenital myopathies).[8] NM may be going undiagnosed as clinical suspicion and special staining are necessary for diagnosis.

This case highlights the importance of histochemistry and clinico-pathological correlation for the diagnosis of this rare form of congenital myopathy in the absence of facilities for genetic assays.

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