Common Neuromuscular Disorders in Pediatrics

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KEYWORDS

• Pediatric neuromuscular disease • Duchenne muscular dystrophy
• Spinal muscular atrophy • Myotonic dystrophy

KEY POINTS

- Duchenne muscular dystrophy (DMD) is an X-linked disorder that affects 1 in 3600 to 6000 live male births. It is due to mutations in the dystrophin-encoding *DMD* gene and is the most common muscular dystrophy.
- Spinal muscular atrophy (SMA) is an autosomal recessive disorder characterized by degeneration of anterior horn cells in the spinal cord and motor neurons in the brainstem. It is due to mutations in the survival motor neuron (*SMN*) gene. Four forms of the disease are recognized in pediatrics.
- Myotonic dystrophy type 1 (DM1) is an autosomal dominant, multisystem disease arising from mutations in the dystrophia myotonica protein kinase (*DMPK*) gene. There are 5 phenotypes of DM1, including congenital myotonic dystrophy (CDM) and childhood-onset myotonic dystrophy.

Video content accompanies this article at http://www.physicianassistant.theclinics.com.

INTRODUCTION

Neuromuscular disease is a term used to describe rare acquired or inherited conditions that affect a part of the neuromuscular system comprised of anterior horn cells, peripheral motor and sensory nerves, the neuromuscular junction and muscles. The Muscular Dystrophy Association estimates that neuromuscular diseases affect more than 1 million people in the Unites States; approximately 40% of patients are under the age of 18.

All neuromuscular diseases result in varying degrees of muscle weakness and/or muscle fatigue and may present at birth or in childhood or may manifest in adulthood. Life expectancy varies by disease and severity. Neuromuscular diseases are

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commonly associated with an increased risk of cardiac, respiratory, gastrointestinal, and orthopedic comorbidities, directly related to the effects of muscle deterioration.

Pediatric patients identified as having a neuromuscular disease often present with a history of nonspecific concerns, including hypotonia, developmental delay, and/or muscle weakness. Differential diagnosis can become somewhat of an odyssey for the pediatric provider. Early identification has become essential, given advances in treatment and research opportunities. This article discusses the pathophysiology, diagnosis, and management of 3 common pediatric neuromuscular disorders: DMD, SMA, and myotonic dystrophy.

DUCHENNE MUSCULAR DYSTROPHY

Overview

DMD is an X-linked disorder that affects 1 in 3600 to 6000 live male births.[1] DMD is the most common muscular dystrophy[2] and occurs as a result of mutations in the dystrophin-encoding *DMD* gene. The *DMD* gene is the largest known human gene, containing 79 exons spanning 2.2. Mb. The mutation rate is high, with approximately one-third of cases caused by de novo mutations.[3] Mutations in this gene ultimately lead to an absence of or defect in the dystrophin protein; resulting in either Duchenne or Becker Muscular Dystrophy. This discussion will focus on DMD. Abnormal dystrophin causes progressive muscle degeneration and subsequent muscle weakness. Dystrophin is expressed in skeletal, cardiac, and smooth muscle tissues. Additionally, dystrophin isoforms are expressed in the human central nervous system (CNS).[4] Phenotypic expression can be variable and is directly related to the type of mutation and its effect on the production of dystrophin. Approximately 10% of female carriers show some disease manifestations that may include abnormal cognitive and/or cardiac function.[5]

Clinical Presentation

Patients often present between the ages of 3 and 5 years with a history of mild to moderate delay of motor milestones and progressive muscle degeneration. Parents may cite specific concerns, including frequent falls, difficulty arising from the floor, difficulty climbing stairs, or the inability to run. A history of muscle pain or muscle cramping is commonly associated with the disease as well. A referral to a neurologist or neuromuscular specialist is indicated with these concerns.

On other occasions, patients present to the gastroenterology clinic after identification of persistently elevated aspartate aminotransferase (AST) and alanine aminotransferase (ALT). Although transaminases are typically markers of hepatocellular injury, they are also highly concentrated in muscle cells. The finding of an elevated AST/ALT in the absence of other laboratory abnormalities or clinical concerns associated with hepatic disease warrants further investigation of muscle disease.

Lastly, patients may present secondary to neurobehavioral concerns. Recent literature suggests that 27% of patients have a full-scale IQ of less than 70; 44% have a learning disability; 19% suffer from intellectual disability; 32% struggle with attention-deficit/hyperactivity disorder; 15% carry a secondary diagnosis of autism spectrum disorder; and 27% of patients suffer from anxiety.[4] These concerns, combined with a history of motor delay and/or muscle weakness, deserve further evaluation.

Physical Examination

On examination, patients are found to be mildly to moderately hypotonic with an increase in muscle bulk most commonly in the calves (**Fig. 1**) or in the form of