

A 2-year-old boy is brought to the physician because he has difficulty keeping up with other children at day care. Over the past couple of months, he has been more fatigued than usual and seems weak. The boy has had some difficulty climbing stairs, which he has never experienced before. He also has difficulty rising from the floor and often has to use his hands to help him stand up. His mother thinks that she had a relative with a disorder that caused weakness but is unsure of the diagnosis. His temperature is 37 C (98.6 F), pulse is 94/min, blood pressure is 90/50 mm Hg, and respirations are 18/min. Examination shows an alert and cooperative child. Auscultation shows normal first and second heart sounds with no murmurs. The patient's lungs are clear to auscultation and his abdominal examination is within normal limits. Neurologic examination demonstrates 1+ patellar and Achilles reflexes bilaterally. Both calves appear enlarged. Diagnostic workup would most likely show which of the following findings?

- ☐ A. Decreased serum aldolase
- ☐ B. Decreased serum creatine kinase
- ☐ C. Elevated antinuclear antibodies
- ☐ D. Muscle biopsy with absent dystrophin
- ☐ E. Muscle biopsy with reduced dystrophin
- ☐ F. Myotonic discharges on electromyography

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- ☐ A. Decreased serum aldolase [0%]
- ☐ B. Decreased serum creatine kinase [0%]
- ☐ C. Elevated antinuclear antibodies [0%]
- ☒ D. Muscle biopsy with absent dystrophin [76%]
- ☐ E. Muscle biopsy with reduced dystrophin [23%]
- ☐ F. Myotonic discharges on electromyography [1%]

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Explanation:

User Id: [REDACTED]

Muscular dystrophies			
Diagnosis	Duchenne	Becker	Myotonic
Genetics	X-linked recessive deletion of dystrophin gene on chromosome Xp21		Autosomal dominant expansion of a CTG trinucleotide repeat in DMPK gene on chromosome 19q 13.3

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Clinical presentation	<ul style="list-style-type: none"> Onset: age 2-3 Progressive weakness, Gower maneuver, calf pseudohypertrophy 	<ul style="list-style-type: none"> Onset: age 5-15 Milder weakness compared to Duchenne muscular dystrophy 	<ul style="list-style-type: none"> Onset: age 12-30 Facial weakness, hand grip myotonia, dysphagia
Comorbidities	<ul style="list-style-type: none"> Scoliosis Cardiomyopathy 	<ul style="list-style-type: none"> Cardiomyopathy 	<ul style="list-style-type: none"> Arrhythmias Cataracts Balding Testicular atrophy/infertility
Prognosis	<ul style="list-style-type: none"> Wheelchair-dependent by adolescence Death by age 20-30 from respiratory or heart failure 	Death by age 40-50 from heart failure	Death from respiratory or heart failure depending on age of onset

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This patient's age, sex, presentation, and family history are consistent with Duchenne muscular dystrophy (DMD). DMD is caused by **dystrophin gene deletion**, which disrupts the amino acid coding sequence for dystrophin, a protein found on the plasma membrane of muscle fibers. The result is severe **proximal lower-extremity weakness**

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(Choices A and B) Muscle degeneration in the muscular dystrophies releases muscle enzymes into the blood, resulting in markedly elevated serum creatine phosphokinase and aldolase.

(Choice C) Increased antinuclear antibodies and myositis-specific antibodies can be seen in autoimmune myositis (dermatomyositis, polymyositis). Although autoimmune myositis symmetrically weakens proximal muscles, interstitial pulmonary disease, dysphagia, and polyarthritis are usually seen. In addition, bilateral calf enlargement is unique to DMD and Becker muscular dystrophy (BMD).

(Choice E) BMD is a similar but milder version of DMD. In BMD, the dystrophin gene deletion preserves the reading frame for dystrophin, resulting in decreased (but not absent) dystrophin and muscle weakness later in childhood.

(Choice F) Myotonic dystrophy is an autosomal dominant disease that generally presents in the teenage years with muscle weakness, myotonia, cataracts, and cardiac conduction abnormalities. The muscular groups that are most affected include the facial muscles, intrinsic hand muscles, and ankle dorsiflexors. Myotonia, or delayed muscle relaxation, is a prominent feature of the disease and manifests as a myotonic pattern on electromyography. In contrast, a myopathic pattern would be seen in DMD and BMD.

Educational objective:

Duchenne muscular dystrophy should be suspected in a boy age <5 with proximal muscle weakness, Gower sign, and bilateral calf pseudohypertrophy. Serum creatine phosphokinase and aldolase levels are elevated even before the manifestation of weakness. An absent dystrophin gene on genetic testing and undetectable dystrophin protein on muscle biopsy confirm the diagnosis.

References:

1. [Entries in the Leiden Duchenne muscular dystrophy mutation database: an overview of mutation types and paradoxical cases that confirm the](#)

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