High-Yield Muscular Dystrophy Pathology

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Case-Based Questions (please see page 3 for answers)

1.	What histopathologic finding is <u>most helpful</u> to strongly consider a diagnosis of a muscular dystrophy?	
	a.	Complement C5b-9 deposition along myofibers
	b.	Diffuse MHC Class I expression
	c.	Endomysial chronic inflammation
	d.	Grouped angular atrophic fibers
	e.	Grouped regenerating fibers

2.	A 15-year-old boy is having trouble keeping up with his peers in gym class and his pediatrician discovered a highly elevated CK level. A muscle biopsy was performed that showed myonecrosis and regeneration. Immunostaining for DYS1, DYS2, and DYS3 was intact. Loss of protein expression for which of the following antibodies is most concerning for a dystrophinopathy?	
	a.	Collagen VI
	b.	Dysferlin
	c.	MHC Class I
	d.	nNOS
	e.	Utrophin

3.	A 34-year-old woman with proximal muscle weakness had a muscle biopsy that showed rare regenerating and necrotic fibers. Amyloid deposition was noted with a congo red stain along some myofibers and vessels. Dysferlin immunostaining was normal. What other form of muscular dystrophy can show similar histopathologic findings?	
	a.	Anoctaminopathy
	b.	Dystroglycanopathy
	c.	Merosin deficiency/LAMA2-related muscular dystrophy
	d.	Sarcoglycanopathy

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Question 1: Correct answer and rationale: The correct answer is grouped regenerating fibers (choice e). Grouped regeneration should prompt investigation for a muscular dystrophy, although it is not entirely specific. Endomysial inflammation, complement deposition, and diffuse MHC Class I expression are *more* characteristic of an inflammatory or immune-mediated necrotizing myopathy. Grouped angular atrophy is characteristic of denervation and neurogenic change.

Question 2: Correct answer and rationale: The correct answer is nNOS (choice d). The case is describing a young boy with likely Becker muscular dystrophy. Often DYS1, DYS2, and DYS3 immunostaining misses in-frame deletions in the rod domain hot spots. In these dystrophinopathy cases, loss of nNOS immunopositivity can be helpful because many of the BMD deletions occur within or near the nNOS binding position on the dystrophin protein. Utrophin is often upregulated in cases of DMD or BMD, not lost. Loss of collagen VI or dysferlin are not typically seen in dystrophinopathies, although secondary loss of proteins within the dystrophin-glycoprotein complex can occur. MHC Class I is not normally expressed in myofibers.

Question 3: Correct answer and rationale: The correct answer is antoctaminopathy (choice a). Amyloid deposition has been described in both dysferlinopathies and anoctaminopathies. It has not been described as a characteristic feature of other muscular dystrophies.