Crafting a Meaningful Muscle Pathology Report- Dermatomyositis and its Mimickers.

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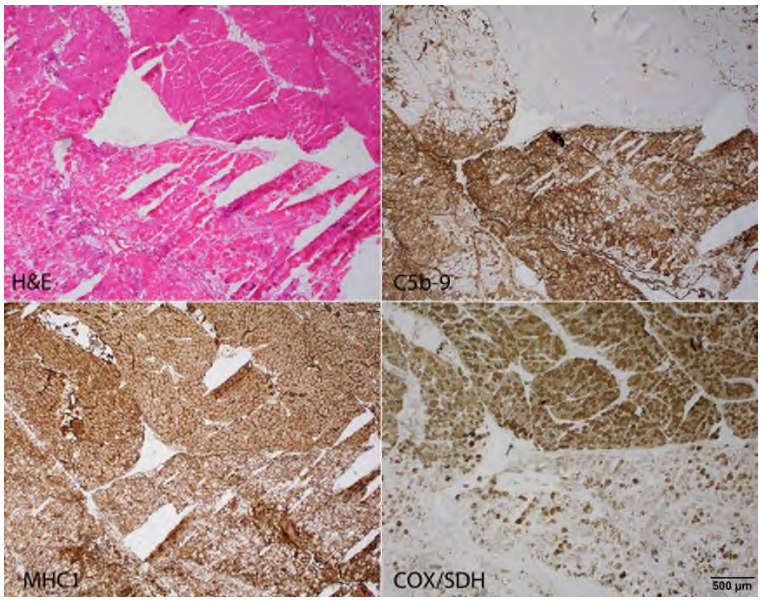
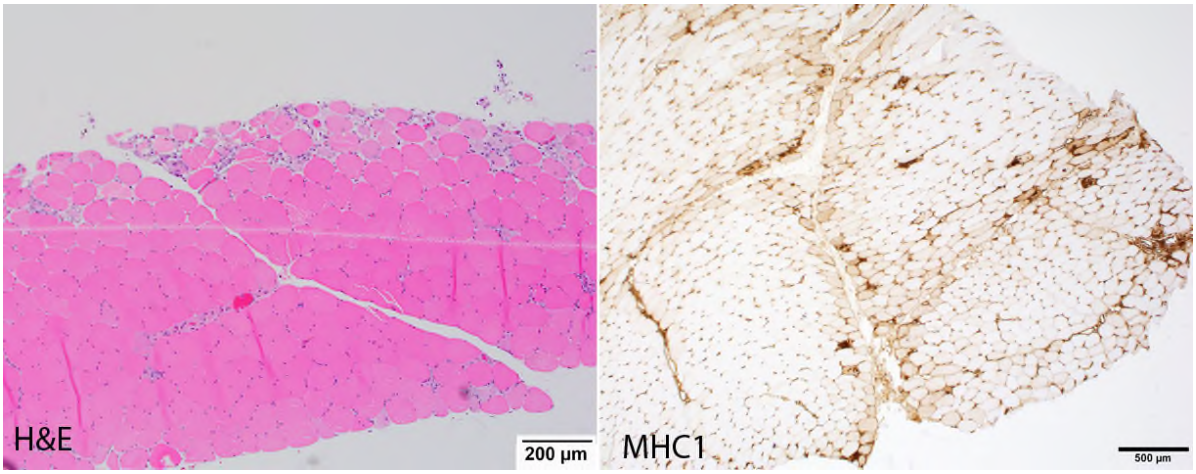
Case-Based Questions (please see page 5 for answers)

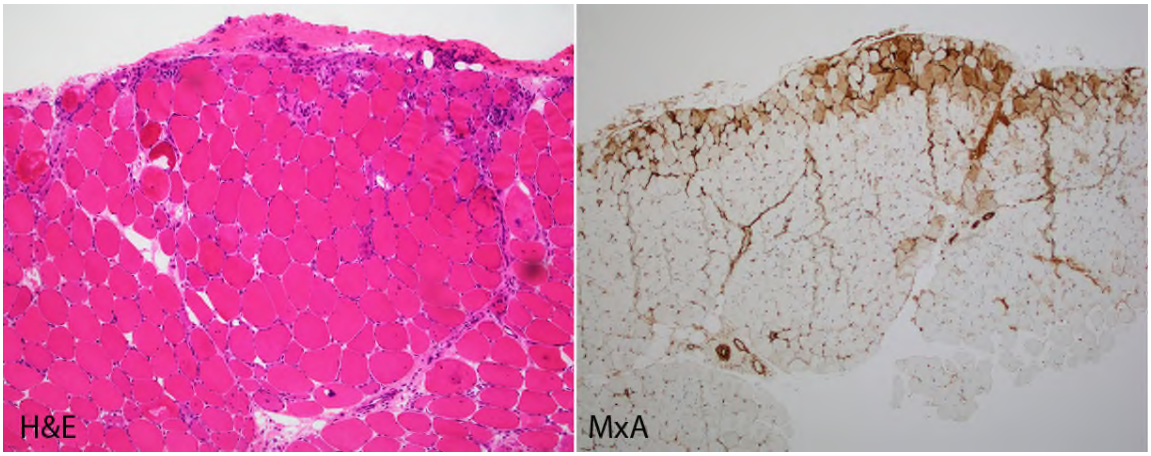


1.	Patient is a 67-year-old women with history of hypertension, diabetes, squamous carcinoma of the vulvar status post radical vulvectomy 6 months ago, who presented with 2 weeks of bilateral arm and back pain and weakness. The patient is recently inoculated with the COVID vaccine. Her CK is elevated in the range of 3000. MRI shows multifocal myositis of the right chest wall and arm with areas of myonecrosis. Muscle biopsy from the deltoid muscle shows pathology illustrated in the figure. Which of the following autoantibody is the patient most likely to have?	
	a.	Mi-2
	b.	MDA5
	c.	NXP2 or TIF1y
	d.	HMGCR
	e.	Jo-1



2.	The patient is a 17 year old female who presented with three months of fatigue, weight loss, and progressive proximal muscle weakness. Her CK is elevated to over 18,000. She has evidence of myositis on MRI pelvis and lab work, however she does not have typical dermatomyositis type rash. In addition, she has CT findings of ground glass opacities with pulmonary nodules. Myositis autoantibody panel is pending. A right thigh muscle biopsy demonstrated pathology findings in figure. Which of the following is the most likely diagnosis?	
	a.	Dermatomyositis, NXP2 variant
	b.	Dermatomyositis, MDA5 variant
	c.	Dermatomyositis, Mi-2 variant
	d.	Antisynthetase syndrome associated myositis
	e.	Lupus myositis

3.	Which of the following ancillary studies will be most helpful to differentiate DM from antisynthetase syndrome associated myositis in such a muscle biopsy?	
	a.	MHC1, MHC2, C5b-9
	b.	MHC1, MHC2, MxA
	c.	MHC2, MxA, C5b-9
	d.	MHC2, MxA, EM
	e.	MHC1, MxA, EM



4.	The patient is a 44 year old female with history of hypertension, migraines who presented with complaints of sharpness of breath, bilateral lower extremities swelling and right upper quadrant pain for 3 weeks. She also has diffused joint pain diffuse myalgias in upper and lower extremities. Pertinent labs CK 4856, positive ANA, SM, RNP, RF antibodies and low C3/C4. Subsequent work up also found anemia, thrombocytopenia, myocarditis, and nephritis. Muscle biopsy demonstrated a perifascicular necrotizing myopathy with strong MxA myofiber expression as illustrated in figure. The most likely muscle biopsy diagnosis is which of the following?	
	a.	Dermatomyositis, NXP2 variant
	b.	Dermatomyositis, MDA5 variant
	c.	Dermatomyositis, Mi-2 variant
	d.	Antisynthetase syndrome associated myositis
	e.	Lupus myositis

Scroll to Page 5 for answers

Correct Answers and Rationales

Question 1 Correct Answer and Rationale: **C. NXP2 or TIF1y**

Rationale: The figure illustrates a case of paraneoplastic necrotizing myopathy with NXP2 auto-antibody. There is a large area of infarct composed of confluent necrotic fibers in vascular border zone, with very little inflammation. Serial sections from this area show that the necrotic fibers are positive for C5b-9, and show loss of both COX and SDH reactivity. MHC1 is diffusely overexpressed in myofibers, including the necrotic fibers.

This paraneoplastic regional infarct is a variant of dermatomyositis and demonstrate the typical type 1 interferon pathway activation markers MxA expression and presence of endothelial tubuloreticular inclusion on EM. The vast majority of those patients have either NXP2 or TIF1y autoantibody.

Among the other choices, immune mediated necrotizing myopathy with HMGCR antibody has scattered rather than confluent necrotic fibers. Mi-2 and Jo-1 related myositis have a perifascicular necrosis pattern. MDA5 typically associated with minimal myofiber necrosis.

Question 2 Correct Answer and Rationale: **D. Antisynthetase syndrome associated myositis**

Rationale: The clinical presentation is characterized by acute onset proximal weakness, very high CK, and radiographic evidence of interstitial lung disease. Pathologically the muscle demonstrated perifasicular necrotizing myopathy and selected MHC1 upregulation in perifascicular myofibers. The clinical phenotype and pathology findings are most consistent with antisynthetase syndrome associated myositis. The patient is subsequently found to have positive EJ autoantibody, which confirms the diagnosis.

Among the other choices, the lack of DM type rash argues against DM, although it does not completely rule DM out. DM-NXP2 is usually characterized by perifascicular atrophy without significant perifascicular necrosis. DM-MDA5 patient may have ILD, but muscle findings are typically mild to near normal. DM-Mi2 and lupus myositis patients can both demonstrate a perifascicular necrotizing myopathy pattern on muscle biopsy and have very high CK, but typically have no lung involvement.

Question 3 Correct Answer and Rationale: **D. MHC2, MxA, EM**

Rationale: Dermatomyositis are usually negative for MHC2, positive for MxA, and EM usually demonstrates frequent well-formed endothelial tubuloreticular inclusions. Antisynthetatse syndrome associate myositis usually demonstrate positive MHC2 expression in perifascicular myofibers, negative for MxA. EM may find intranuclear filamentous inclusions and negative or sparse endothelial tubuloreticular inclusions.

Among other choices, MHC1 are usually upregulated in perifascicular fibers in both DM and antisynthetase syndrome. C5b-9 highlights necrotic fibers. These two IHCs usually show similar findings in the DM-Mi2 variant and antisynthetase syndrome associated myositis.

Question 4 Correct Answer and Rationale: **E. Lupus myositis**

Rationale: Both dermatomyositis and lupus myositis can show a perifascicular necrotizing myopathy with strong MxA expression in myofibers. The diagnosis is sometime impossible to be made on muscle pathology alone. However, clinically lupus patients are relatively easy to differentiate from dermatomyositis. Majority of lupus patients have other systemic manifestations such as malar rash, arthritis, leucopenia and/or anemia, serositis or myocarditis, nephritis or vasculitis. Serologically lupus patients are characterized by positive ANA, SM, dsDNA, RNP antibodies and low C3/C4.