Dermatomyositis
Muscle Pathology According to Antibody Subtypes

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Study Question
What are the characteristic pathologic features of myxovirus resistant protein A (MxA)–positive muscle biopsy in different dermatomyositis-specific antibody (DMSA) subtypes?

What Is Known and What This Paper Adds
Discoveries of DMSAs in dermatomyositis raised awareness of various myopathologic features among subtypes. Sarcomplasmic MxA expression of any pattern was highly specific with DMSAs. However, only perifascicular atrophy and perifascicular MxA expression were officially included as the definitive pathologic criteria for dermatomyositis. Using MxA expression of any pattern as inclusion criteria, this study shows distinct myopathologic features in different DMSA subtypes.

Methods
The authors performed a retrospective study on muscle biopsies diagnosed as dermatomyositis in a tertiary laboratory for muscle diseases. The authors included all muscle biopsies with sarcomplasmic MxA expression and DMSA seropositivity. MxA-negative but DMSA-seronegative muscle biopsies were included as seronegative dermatomyositis. The authors evaluated histologic features stratified according to 4 pathology domains (muscle fiber, inflammatory, vascular, and connective tissue) and histologic features of interest by histochemistry, enzyme histochemistry, and immunohistochemical study commonly used in the diagnosis of inflammatory myopathy. The authors performed ultrastructural studies of 54 available specimens.

Results and Study Limitations
This study included 249 DMSA-seropositive patients (87 anti–transcription intermediary factor 1-γ [TIF1-γ], 40 anti–complex nucleosome remodeling histone deacetylase [Mi-2], 29 anti–melanoma differentiation gene 5 [MDA5], 83 anti–nuclear matrix protein 2 [NXP-2], and 10 anti–small ubiquitin-like modifier-activating enzyme [SAE] dermatomyositis) and 7 DMSA-seronegative patients (n = 256). Tubuloreticular inclusions were present in all 54 specimens. Characteristic myopathologic features in each DMSA subtype were as follows: anti-TIF1-γ with vacuolated/punched-out fibers (64.7%; p < 0.001) and perifascicular enhancement in HLA-ABC stain (75.9%; p < 0.001); anti-Mi-2 with prominent muscle fiber damage (score 4.9 ± 2.1, p < 0.001), inflammatory cell infiltration (score 8.0 ± 3.0, p = 0.002), perifascicular atrophy (67.5%; p = 0.02), perifascicular necrosis (52.5%; p < 0.001), increased perimysial alkaline phosphatase activity (70.0%; p < 0.001), central necrotic peripheral regenerating fibers (45.0%; p = 0.002), and sarcolemmal membrane attack complex deposition (67.5%; p < 0.001); anti-MDA5 with scattered/diffuse staining pattern of MxA (65.5%; p < 0.001) with less muscle pathology and inflammatory features; anti-NXP2 with microinfarction (26.5%; p < 0.001); and anti-SAE and seronegative DM with HLA-DR expression (50.0%; p = 0.02 and 57.1%; p = 0.02, respectively). Due to the retrospective nature of this study, the clinical information was limited. The small number of anti-SAE-DM was likely because of the lower prevalence in Japanese populations.

Study Funding and Competing Interests
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