Necrotizing autoimmune myopathy with tubular aggregates

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The formation of tubular aggregates (TA) within muscle fibers has been associated with toxic, metabolic, and hereditary myopathies, congenital myasthenic syndromes (CMS),¹ and recently with pembrolizumab-associated myopathy.² On electron microscopy, TA have the appearance of parallel tubules in crystalline arrangements, and are continuous extensions of the sarcotubular membrane system.¹ TA have not been reported in necrotizing autoimmune myopathy associated with 3-hydroxy-3-methyl-glutaryl-CoA reductase (HMGCR) antibodies. A 60-year-old man experienced muscle pain and cramping within 18 months of initiating statin treatment, followed by bilateral proximal lower limb and hand grip weakness that progressed over 8 months. Creatine kinase (CK) was 18,674 U/L (normal < 250), and anti-HMGCR antibodies were >200 units (normal < 20). The quadriceps muscle biopsy is shown in the figure. Repetitive nerve stimulation showed no decrement. Next-generation sequencing of 166 myopathy/CMS genes, including those associated with TA, demonstrated no pathogenic variants. IV immunoglobulin therapy led to clinical improvement and normalization of CK.

Figure Quadriceps muscle biopsy with tubular aggregates and necrotizing myopathy

(A–D) Quadriceps muscle biopsy showed subsarcolemmal tubular aggregates (arrows) and scattered necrotic fibers (asterisk). Aggregates are (A) basophilic on hematoxylin & eosin; (B) fuchsinophilic on trichrome-stained sections; (C) confined to type 2 fibers, and overreacting to NADH dehydrogenase; (D) but not to succinate dehydrogenase, indicating their sarcoplasmic reticulum rather than mitochondrial origin.

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Nicolas N. Madigan, MBBCh, PhD	Mayo Clinic, Rochester, MN	Author	Study concept and design; acquisition, analysis, and interpretation of data; drafting manuscript; critical revision of final manuscript for intellectual content
Teerin Liewluck, MD	Mayo Clinic, Rochester, MN	Author	Acquisition, analysis, and interpretation of data; critical revision of final manuscript for intellectual content

Appendix (continued)

Name	Location	Role	Contribution
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