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Anti-SRP Immune Mediated Necrotizing Myositis Masquerading as Immune Checkpoint Inhibitor-Myositis: Two Case Reports and Scoping Review of the Literature.

Immune checkpoint inhibitor (ICI)-myositis is an immune-related adverse event that usually occurs shortly after ICI initiation. Anti-SRP immune-mediated necrotizing myositis (IMNM) is an idiopathic myopathy that presents with severe myositis. While the histopathology of anti-SRP IMNM is well described, consisting of scattered necrosis with minimal inflammation, MHC-I upregulation and complement deposition, the distinctive features of ICI-myositis remain less certain.

We describe two cases of patients with cancer who developed myositis after exposure to ICI but were subsequently diagnosed with anti-SRP IMNM. We performed a scoping review of the literature to identify distinct features of ICI-myositis on muscle biopsy.

Case 1: A 53-year-old man with metastatic melanoma developed severe myositis and myocarditis after a single course of ipilimumab and nivolumab. Despite high-dose steroids, IVIG, plasmapheresis, tofacitinib, abatacept, ATG, cyclosporine and tacrolimus, he failed to improve. Skeletal muscle biopsy was performed after initiation of immunosuppression. Pathology revealed scattered necrosis, no appreciable inflammatory cells, and minimal MHC-I upregulation and complement deposition. He was found to be ANA positive 1:160 (AC-4,5 nuclear speckled and AC-15-23 cytoplasmic), anti-SRP antibody 3+ and anti-Ro52 1+. He improved with Rituximab and IVIG.

Case 2: A 63-year-old man presented with proximal muscle weakness and head drop. For the past five years, he had been treated at another institution with pembrolizumab for metastatic non-small cell lung cancer. Shortly after initiating ICI, he was found to have asymptomatic hyper-CKemia. Weakness and myalgias appeared insidiously thereafter. On presentation, ICI was stopped and high-dose prednisone was started. A muscle biopsy showed rare necrosis, no inflammation and no significant MHC-I upregulation or complement deposition. He was found to be ANA positive 1:1280 (AC-19 cytoplasmic), as well as anti-SRP antibody 1+ and anti-Ro52 2+. He improved with IVIG and tofacitinib.

A scoping review of the literature on the histopathology of ICI-myositis returned 886 papers, of which 96 were selected for full-text review. The predominant findings include inflammatory lympho-histiocytic infiltrates characterized by the presence of CD8+ T cells and CD68+ macrophages, MHC-I upregulation, complement deposition on non-necrotic fibers and at times on capillaries, and PD-1/PD-L1 positivity.

ICI-myositis is characterized by inflammatory features. The absence of inflammatory infiltrates should prompt consideration of alternative diagnoses. We are currently exploring more specific biomarkers across various myositis subsets to improve diagnostic accuracy. In the meantime, integration of clinico-sero-pathological findings are key to making the right diagnosis.