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Importance of recognition and improved treatment for antimelanoma differentiation-associated protein 5-associated dermatomyositis

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In this issue of the *BJD*, Koguchi-Yoshioka and colleagues present three patients with antimelanoma differentiation-associated protein 5 anti-(MDA5) dermatomyositis (DM) treated with early intravenous immunoglobulin (IVIg) and combination immunosuppressive therapy. This was associated with a positive outcome in two of the three cases.¹ This case series adds to the literature on anti-MDA5 DM by raising important questions regarding the pathogenesis and appropriate management of this condition.

The pathogenesis of the cutaneous disease and rapidly progressive interstitial lung disease (RP-ILD) in anti-MDA5 DM has yet to be fully determined. However, better understanding of the response of anti-MDA5 DM to IVIg may help elucidate the aetiopathogenesis of the disease. MDA5 is a RIG-I-like receptor helicase enzyme mediating type 1 interferon responses, but the pathogenic mechanism of antibodies to MDA5 is unknown.² Are pathogenic antibodies cleared via the effect of IVIg on the FcRn receptor as has been shown in pemphigus vulgaris?³ Or, rather, is the effect mediated by neutralization of circulating inflammatory cytokines, inhibition of the complement cascade, saturation of FcγR, or inhibition of macrophage activation?

The implications for management are important as well. These patients appeared to benefit from early recognition of the anti-MDA5 DM phenotype followed by aggressive management. While the authors were able to obtain anti-MDA5 antibody enzyme-linked immunosorbent assay (ELISA) in these cases, this ELISA is not yet widely available or reliable. Therefore it is critically important to use the cutaneous features of violaceous macules, papules and ulcers on the palmar creases to increase the pretest probability of anti-MDA5 syndrome and to guide management with the risk of RP-ILD in mind. The lack of an anti-MDA5 antibody should not prevent appropriate monitoring and management of patients

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who otherwise display the appropriate phenotype. The optimal screening modality and intervals for RP-ILD are not known; however, it may be reasonable to obtain a baseline ferritin level, high-resolution computed tomography of the chest and pulmonary function test (PFT) with diffusing capacity of the lung for carbon monoxide (DLCO), and repeat the ferritin and PFTs with DLCO every 3–4 months for early identification and intervention upon disease progression.

Case reports like this are valuable because they are hypothesis generating. The next steps include continued basic science research exploring the pathogenesis of disease, as well as multinational, prospective studies to phenotype the disease across multiple, diverse populations, standardize classification and diagnostic criteria, and research outcomes that allow creation of robust management guidelines. New approaches to therapy for this frequently fatal subset of dermatomyositis are desperately needed.

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