Do Myositis-Specific Antibodies have Specific Histopathological Marks?

In 1975, Bohan and Peter defined inflammatory myopathies based on clinical, creatine kinase, electromyographic and pathologic findings.[1] They distinguished dermatomyositis from polymyositis, the only two known inflammatory myopathies at that time, based on the presence or absence of skin lesions. Since, there have been several substantial changes in our understanding of the classification, etiology, pathophysiology, and treatment of inflammatory myopathies. First, the description and characterization of inclusion body myositis (IBM), first by Yunis and Samaha[2] and now recognized as the most common new onset myopathy in patients above the age of 50 years, has been revolutionary in the field and placed continuous controversy over the incidence or even existence of polymyositis. Second, the description and characterization of autoimmune necrotizing myopathy (NAM – also referred to as IMNM – immune-mediated necrotizing myopathy), the emergence of statin myopathies, and the identification of myositis-specific antibodies added to the complexity of immune-mediated inflammatory myopathies.

Myositis-specific antibodies have significantly improved the diagnosis, clinical phenotyping, and prognostication of immune-mediated inflammatory myopathies. Their detection confirms a humoral component to the inflammatory process. NAM, which lacks inflammatory infiltration in muscle tissue, has a strong association with signal recognition particle (SRP) and 3-hydroxy-3-methylglutaryl coenzyme A reductase (HMGCR) antibodies. Anti-Jo-1 is often associated with anti-synthetase syndrome and interstitial lung disease, and anti-Mi-2 is intricately linked to classic dermatomyositis.

In this issue of the Annals of Indian Academy of Neurology®, Mathukumalli, *et al*., set out, in a pilot study, to correlate between muscle tissue findings and myositis-specific antibodies in patients with immune-mediated inflammatory myopathies.[3] They retrospectively reviewed muscle tissue in patients who are seropositive to one of the myositis-specific antibodies. More specifically, they assessed for perifascicular atrophy and necrosis, scattered necrotic fibers, microinfarcts, type of inflammatory infiltrate (lymphocytes or macrophages), and location of inflammation (endomysial or perivascular). They identified 64 cases, with more than half of them seropositive for Mi-2, Jo-1, or SRP antibodies. They compared them to 35 seronegative cases. Eleven patients with borderline positive or showing more than two antibodies were excluded. Cytosolic 5′-nucleotidase 1A and HMGCR antibodies, autoantibodies associated with IBM and NAM respectively, were not included since they were not available. Age, clinical phenotype, and associated conditions were comparable between seropositive and seronegative groups. The authors concluded that perifascicular atrophy and perivascular inflammation are quite common in patients with Mi2 antibody; both findings are highly specific for dermatomyositis.[4] In contrast, they found that perifascicular atrophy never accompanies SRP positivity, and is rare with Jo-1 antibody. NXP2 antibody, which also shows perifascicular atrophy, was associated with microinfarcts. The number of patients with other myositis-specific antibodies were too small for any meaningful conclusions.

Myositis-specific autoantibodies are extremely useful and have been a welcome addition to our armamentarium used in the diagnosis and prognosis of immune-mediated inflammatory myopathies.[5] However, they have not yet reached the level of specificity that acetylcholine binding antibody has achieved in the diagnosis of myasthenia gravis. Only in a few current clinical situations, seropositivity could spare patients another testing, including muscle biopsy.

Bashar Katirji

Neuromuscular Center, Neurological Insitute, University Hospitals Cleveland Medical Center and Case Western Reserve University School of Medicine, Clevland, Ohio, USA

Address for correspondence: Prof. Bashar Katirji, Neuromuscular Center, Neurological Insitute, University Hospitals Cleveland Medical Center and Case Western Reserve University School of Medicine, Clevland, Ohio, USA.
E-mail: bashar.katirji@uhhospitals.org

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