Myositis Testing:

Homing in on Culprit Autoantibodies

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"Given the rarity and heterogeneity presented by myositis, as well as the complexity of defined autoantibody targets, development of diagnostic tests has lagged behind the more common connective tissue diseases," says Tebo. Autoantibody evaluation for myositis is only performed by a small number of laboratories (mainly for research) due to the complexity of performance and interpretation of testing. Here, Tebo discusses myositis testing.

Q: What is myositis?

A: Myositis or idiopathic inflammatory myopathies (IIM) are a rare and heterogeneous group of autoimmune diseases characterized by acute, subacute, or chronic muscle weakness.

Q: What are the different types of myositis disease?

A: IIM may broadly be categorized into dermatomyositis (DM), polymyositis (PM), inclusion body myositis (IBM), necrotizing autoimmune myopathy (NAM), and overlap syndromes. Although patients with IIM share some similarities, a continuum of clinical subsets and serologic phenotypes defined by the presence of certain autoantibodies is now recognized, each with differing demographics, clinical manifestations, laboratory findings, and prognoses.

Q: What causes myositis?

A: This is not completely understood. However, there is evidence that interactions between certain components of the immune system, genes, and the environment play a significant role in immune pathogenesis. For example, antibodies to 3-hydroxy-3-methylglutaryl coenzyme (HMGCR) have been identified in a subset of patients with statin-associated NAM.

Q: How do you test for myositis?

A: The presence of specific autoantibodies is a hallmark in the diagnosis of certain clinical subsets of IIM. Most of these autoantibodies target intracellular proteins, including nuclear and cytoplasmic antigens, and, based on their specificity, can be grouped into myositis-specific (MSA) and myositis-associated autoantibodies (MAA).

Testing for MSA and MAA is a useful aid for the diagnosis, subset classification, and management of IIM. The diversity and complexity of autoantigenic targets, as well as their poor expressions in cells/tissue, have limited the development of more routine diagnostic methods for their evaluation. Thus, testing for MSA is generally performed by immunoprecipitation of radiolabeled proteins or RNA molecules, which is time-consuming and requires interpretation expertise.

Nevertheless, the technique allows for the simultaneous detection of classic and identification of novel autoantibodies. Commercially available fully-validated ELISA or immunoblot assays are likely to become available in the near future.

Q: What markers are used for differential diagnosis?

A: MSA, specific for autoimmune myositis, are mutually exclusive and closely associated with distinct disease subsets differing in clinical involvement and prognosis.

- Antisynthetase syndrome (AS), generally seen in patients with PM, is characterized by myositis, arthralgia, Raynaud phenomenon, mechanic's hands, interstitial lung disease, and the presence of MSA to aminoacyl transfer RNA synthetases (anti-ARS)—mainly histidyl (Jo-1), threonyl (PL-7), alanyl (PL-12), glycyl (EJ), and isoleucyl (OJ).
- MSA associated with dermatomyositis (DM) include autoantibodies targeting chromodomain helicase DNA-binding protein 4 (Mi-2); SAE/small ubiquitin-related modifier (SUMO-1); MJ/ nuclear matrix protein 2 (NXP2); melanoma differentiation-associated gene 5 (MDA5)/clinically amyopathic dermatomyositis p140 (CADM-140); and transcription intermediary factor gamma (TIF- or p155/140). DM-specific antibodies may predict disease course, including muscle, lung involvement, and/or cancer.
- NAM characterized by the absence of primary inflammation on muscle biopsy is associated with two main MSA: SRP and HMGCR.

MAA are not disease-specific, frequently occur in association with MSA, and are mostly found in myositis-overlap syndromes, primarily polymyositis-systemic sclerosis (PM/SSc). MAA can also be found in non-overlap syndromes. The most commonly encountered MAA include SS-A (Ro) 52 kDa, Ku, PM/Scl, and U1RNP.