August 2019 | Healthcare Providers

Spotlight on Health

Quest Diagnostics™

Autoimmune Muscle Inflammation

Inflammation of the skeletal muscles (myositis) has many causes. For example, a very strenuous workout or viral infection can cause myositis. However, the most severe and chronic forms of myositis are caused by autoimmune diseases. Collectively they are called idiopathic inflammatory myopathies (IIMs). Nonspecific symptoms can delay diagnosis, and these diseases can lead to severe disability if early and appropriate treatment is not provided. Appropriate laboratory testing can aid diagnosis and facilitate early treatment that may lessen disease severity by bringing these diseases into remission.

This newsletter will discuss autoimmune myositis and how the laboratory can assist in diagnosis.

Idiopathic Inflammatory Myopathies (IIMs)

The major IIMs include polymyositis (PM), dermatomyositis (DM), immune-mediated necrotizing myopathy (NM), and inclusion body myositis (IBM).[1,2] IIMs can also occur in combination with another autoimmune disease such as systemic lupus erythematosus as overlap myositis (OM).[1,2] Although all IIMs are autoimmune in nature, the primary cause of myositis is not always clear.

Patients with IIMs often report nonspecific symptoms (such as feeling tired after a short period of walking), but typically have common complaints (see Sidebar). In addition, the different IIMs have characteristic symptoms, extra-muscular manifestations, and clinical courses. PM, DM, and NM typically present with subacute onset of arm and leg weakness.[1,2] In contrast, IBM symptoms are slowly progressive.[1,2] Characteristic rashes distinguish DM from the other IIMs, and one form of DM (amyopathic DM) lacks muscular symptoms. Some patients with DM and PM can develop a phenotype called antisynthetase syndrome. It is characterized by interstitial lung disease, myositis, Raynaud's phenomenon, and arthritis.[3]

IIMs typically occur in middle-aged adults (45 to 60 years old).[4] Although children can develop both DM and PM, juvenile PM is rare.[5] IBM is twice as common in men as women; all other types are twice as common in women.[4] All IIMs are considered rare diseases, with an estimated prevalence in the United States ranging from 1.4 cases per 100,000 persons for IBM to 1 to 6 cases per 100,000 persons for DM.[1] OM, NM, and DM are estimated to make up 90% of IIM cases.[1]

Statin-induced Immune-mediated Necrotizing Myopathy (NM)

Statin-induced NM is associated with the development of antibodies against the enzyme 3-hydroxy-3-methylglutaryl-CoA reductase (HMGCR; the enzyme inhibited by statins).[6] It is a serious condition that does not typically resolve with stopping statins.[6] Patients experience progressive proximal muscle weakness involving both limb girdles, and creatine kinase levels 10 to 100 times the upper limit of normal.[6] Muscle biopsy specimens show necrosis. The condition is sometimes seen in "statin-naïve patients" who may have been exposed to natural statins in foods (eg, oyster mushrooms).[6]

Typical Presentations of IIMs

Many symptoms of IIMs are nonspecific. However, typical symptoms in patients with myositis are[1,4]

- Difficulty rising from a seated position
- Difficulty walking up stairs
- Difficulty lifting up the arms
- Problems swallowing or breathing
- Unexplained muscle soreness or pain

Diagnosis

The diagnosis of IIMs is based on clinical symptoms, physical examination findings, and the results of laboratory testing. Relevant physical findings include the pattern of muscle weakness and the presence of a rash, while relevant laboratory markers include creatine kinase and other enzymes, as well as myositis-specific and myositis-associated antibodies.[1,2] A skeletal muscle biopsy may also be useful for diagnosis.[1,2]

Numerous myositis-specific antibodies can be informative in the diagnosis and differentiation of IIMs.[7,8] Classic myositis-specific antibodies include Jo-1, EJ, OJ, PL-7, and PL-12 aminoacyl-transfer RNA synthetase antibodies, and Mi-2 and SRP antibodies.[8,9] One or more of these antibodies are found in about 50% of patients with PM/DM.[8,9] The antisynthetase syndrome phenotype is associated with antibodies to the synthetases.[3] TIF1-γ (p155) and NXP-2 (p140) antibodies are seen in adults with cancer-associated DM and children with juvenile DM.[9] MDA-5 antibody is associated with amyopathic DM and interstitial lung disease.[9] HMGCR antibodies are diagnostic of statin-induced NM.[6] In patients with a suspected IIM, it is important to screen for many antibodies at once because most patients only have a single autoantibody.[7,8]

Prognosis

Most patients with IIMs, except those with IBM, respond to immunosuppressive therapies.[1,2] Statin-induced NM also typically requires treatment with immunosuppression, in addition to discontinuation of statins.[6] A delay in beginning treatment can result in irreversible muscle damage.[1] On the other hand, no currently available treatments are effective for IBM.[1]

How the Laboratory Can Help

Quest Diagnostics offers general testing for muscle enzyme levels and myositis-specific antibody tests. These include a panel for antisynthetase syndrome-associated antibodies (test code 38075, Jo-1, EJ, OJ, PL-7, and PL-12), a broader panel that additionally includes other myositis-specific antibodies (test code 94777, Jo-1, EJ, OJ, PL-7, PL-12, SRP, Mi-2α, Mi-2β, MDA-5, NXP-2, and TIF1-γ), and single-analyte assays for most of the myositis-specific antibodies in the panels, as well as HMGCR antibodies.

References

1. Schmidt J. Current classification and management of inflammatory myopathies. *J Neuromuscul Dis.* 2018;5:109-129.
2. Lundberg IE, Miller FW, Tjärnlund A, et al. Diagnosis and classification of idiopathic inflammatory myopathies. *J Intern Med.* 2016;280:39-51.
3. Witt LJ, Curran JJ, Strek ME. The diagnosis and treatment of antisynthetase syndrome. *Clin Pulm Med.* 2016;23:218-226.
4. Oldroyd A, Lilleker J, Chinoy H. Idiopathic inflammatory myopathies - a guide to subtypes, diagnostic approach and treatment. *Clin Med (Lond).* 2017;17:322-328.
5. Tansley S, Wedderburn LR. Comparing and contrasting clinical and serological features of juvenile and adult-onset myositis: implications for pathogenesis and outcomes. *Curr Opin Rheumatol.* 2015;27:601-607.
6. Selva-O'Callaghan A, Alvarado-Cardenas M, Pinal-Fernández I, et al. Statin-induced myalgia and myositis: an update on pathogenesis and clinical recommendations. *Expert Rev Clin Immunol.* 2018;14:215-224.
7. Lundberg IE, Tjärnlund A, Bottai M, et al. 2017 European League Against Rheumatism/American College of Rheumatology classification criteria for adult and juvenile idiopathic inflammatory myopathies and their major subgroups. *Ann Rheum Dis.* 2017;76:1955-1964.
8. Lega JC, Fabien N, Reynaud Q, et al. The clinical phenotype associated with myositis-specific and associated autoantibodies: a meta-analysis revisiting the so-called antisynthetase syndrome. *Autoimmun Rev.* 2014;13:883-891.
9. Damoiseaux J, Vulsteke JB, Tseng CW, et al. Autoantibodies in idiopathic inflammatory myopathies: clinical associations and laboratory evaluation by mono- and multispecific immunoassays. *Autoimmun Rev.* 2019;18:293-305.

Model used for illustrative purposes

QuestDiagnostics.com