MAYO CLINIC

# Diagnosis and Management of Immune-Mediated Myopathies

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## CME Activity

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**Learning Objectives:** On completion of this article, you should be able to (1) diagnose the most common immune-mediated myopathies, (2) associate antibodies with specific immune-mediated myopathies, and (3) differentiate muscle pathologic features of common immune-mediated myopathies.

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## Abstract

Immune-mediated myopathies (IMMs) are a heterogeneous group of acquired muscle disorders characterized by muscle weakness, elevated creatine kinase levels, and myopathic electromyographic findings. Most IMMs feature the presence of inflammatory infiltrates in muscle. However, the inflammatory exudate may be absent. Indeed, necrotizing autoimmune myopathy (NAM), also called immune-mediated necrotizing myopathy, is characterized by a necrotizing pathologic process with no or minimal inflammation in muscle. The recent discovery of antibodies associated with specific subtypes of autoimmune myopathies has played a major role in characterizing these diseases. Although diagnostic criteria and classification of IMMs currently are under revision, on the basis of the clinical and muscle histopathologic findings, IMMs can be differentiated as NAM, inclusion body myositis (IBM), dermatomyositis, polymyositis, and nonspecific myositis. Because of recent developments in the field of NAM and IBM and the controversies around polymyositis, this review will focus on NAM, IBM, and dermatomyositis.

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Immune-mediated myopathies (IMMs) are a heterogeneous group of acquired muscle disorders characterized by muscle weakness, elevated creatine kinase (CK) levels, and myopathic electromyographic findings. Because of the frequent presence of inflammatory infiltrates on muscle biopsy, IMMs are often referred to as idiopathic

inflammatory myopathies (IIMs). However, the inflammatory exudate may be absent in the muscle in some IMMs. Indeed, muscle biopsy of necrotizing autoimmune myopathy (NAM), also called immune-mediated necrotizing myopathy, often reveals prominent muscle fiber necrosis and regeneration with minimal or no inflammation.[1,2] Since the 1975 classification of polymyositis (PM) and dermatomyositis (DM) by Bohan and Peter,[3] there has been a constant effort to define diagnostic criteria and reclassify the IMMs, but to date, no diagnostic criteria or classification has found unanimous consensus.

On the basis of the clinical and muscle histopathologic findings, IMMs can be distinguished as DM, PM, inclusion body myositis (IBM), NAM, and nonspecific myositis.[2] The entity PM is controversial, and although still recognized as a specific IIM, it seems to be overdiagnosed.[4,5] Many patients with PM have been later diagnosed as having IBM or overlapping myositis.[6,7] The distinction of DM, PM, IBM, NAM, and nonspecific myositis does not entirely reflect the true spectrum of IMMs. Indeed, a subset of IIM can have extramuscular involvement consisting of lung, skin, or joint involvement (overlap myositis). In addition, the recently discovered myositis-associated antibodies link to specific clinical and pathologic phenotypes and may even guide treatment.[8] These antibodies complement the clinical and myopathologic findings and contribute to the characterization of the IMMs. Therefore, these antibodies could be of tremendous value in the reclassification of IMMs.

This article will discuss NAM, IBM, and DM as defined by clinical and myopathologic features.

## NEEDS IN THE FIELD

In light of the knowledge on noninflammatory IMMs, the rarity of PM, and the discovery of myositis-associated antibodies, it has become evident that the old Bohan and Peter classification,[3] as well as the more recently proposed classifications of IMMs, are in need of verification and revision.[2,9,10] Diagnostic criteria for each subtype require definition and consensus.

## NECROTIZING AUTOIMMUNE MYOPATHY

### Clinical Features

Necrotizing autoimmune myopathy manifests with subacute proximal limb muscle weakness and persistently elevated CK levels. In contrast to immune-mediated inflammatory myopathies, NAM muscle biopsies often reveal no or minimal inflammation but prominent muscle fiber necrosis and regeneration (Figure 1, Table 1).[1,11] Necrotizing autoimmune myopathy most frequently affects adults but can also occur in children.[12,13] The weakness is predominantly proximal and more prominent in the lower limbs. In a recent Mayo Clinic study, coexisting distal weakness involving foot dorsiflexors and finger extensors was documented in more than 40% of patients.[11] Neck muscle weakness and dysphagia are common. Occasionally, head drop and camptocormia are the predominant clinical features.[11,14] Myalgia may or may not be present. Respiratory muscle weakness is common as suggested by dyspnea, a restrictive pattern on pulmonary function tests, and abnormal findings on overnight oximetry. The respiratory muscle weakness can result in hypercapnic respiratory failure and the need for mechanical ventilation,[11,15] not only in the setting of generalized weakness but also at disease onset.[16] Cardiac involvement is infrequent and occurs in the form of left ventricular wall motion abnormalities or takotsubo cardiomyopathy.[11,17] Necrotizing autoimmune myopathy can be associated with cancer; therefore, cancer screening is needed.[11,18,19] Although NAM is commonly a subacute myopathy, it can also manifest with slowly progressive weakness mimicking muscular dystrophies, clinically and pathologically.[20]

### Diagnosis

The diagnosis of NAM relies on the combination of clinical and pathologic features and the exclusion of other etiologies that can result in a similar muscle histopathologic pattern. The histologic features of NAM (necrotizing myopathy with minimal or no inflammation) are nonspecific and also compatible with early muscular dystrophy or toxic myopathies.[21] The subacute onset of the weakness makes hereditary myopathy unlikely. The presence of serologic markers (see "Necrotizing