Inclusion Body Myositis

Inclusion body myositis is a disease of late adulthood that typically affects patients older than 50 years and is the most common inflammatory myopathy in patients older than age 65 years. Most affected individuals present with slowly progressive muscle weakness that tends to be most severe in the quadriceps and the distal upper extremity muscles. Dysphagia from esophageal and pharyngeal muscle involvement is not uncommon. Laboratory studies usually show modestly elevated creatine kinase levels; most myositis-associated autoantibodies are absent, although an antibody to cN1A has recently been described.

MORPHOLOGY

Inclusion body myositis has a number of features that are similar to those found in polymyositis, including:

- Patchy often endomysial mononuclear inflammatory cell infiltrates rich in CD8+ T-cells
- Increased sarcolemmal expression of MHC class I antigens
- Focal invasion of normal appearing myofibers by inflammatory cells
- Admixed degenerating and regenerating myofibers

Other associated changes, however, are more typical or even specific for inclusion body myositis, as follows:

- Abnormal cytoplasmic inclusions described as "rimmed vacuoles" (Fig. 27-9)
- Tubolofilamentous inclusions in myofibers, seen by electron microscopiy
- Cytoplasmic inclusions containing proteins typically associated with neurodegenerative diseases, like beta-amyloid, TDP-43, and ubiquitin
- Endomysial fibrosis and fatty replacement, reflective of a chronic disease course

Whether inclusion body myositis is indeed an inflammatory condition or a degenerative process with secondary inflammatory changes remains an unresolved question. It has certain features in common with polymyositis, as discussed earlier. On the other hand, it shares some features with neurodegenerative diseases, such as the presence of abnormal protein aggregates. Furthermore, there are several familial inclusion body myopathies that are also associated with chronic myopathic changes and rimmed vacuoles. These typically lack any associated inflammation—hence the designation *inclusion body "myopathy"* rather than *"myositis."*

Treatment of Inflammatory Myopathies

The prognosis for patients with dermatomyositis and polymyositis was poor before the use of corticosteroids, with mortality rates as high as 50% or more. Corticosteroids remain the first-line of treatment for polymyositis and dermatomyositis. Immunosuppressive drugs are used in steroid-resistant disease or as steroid-sparing agents and include azathioprine and methotrexate. Intravenous immunoglobulin (IVIG), cyclophosphamide, cyclosporine, and rituximab (an antibody that targets B cells) are third-line therapies. Inclusion body myositis usually responds poorly to steroids or immunosuppressive therapies, another feature that argues against an inflammatory or immune origin for this disorder.

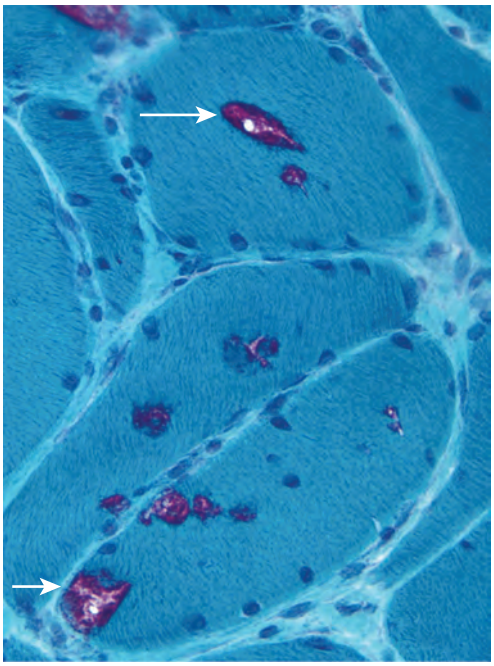

Figure 27-9 Inclusion body myositis, showing myofibers containing rimmed vacuoles—inclusions with reddish granular rimming (*arrows*). Modified Gomori trichrome stain.

Toxic Myopathies

Toxic myopathies can be caused by prescription or recreational drugs, or by certain hormonal imbalances. Among prescription drugs, *statins* are among the leading culprits. Statins are cholesterol-lowering drugs that are widely used to reduce the risks of acute ischemic cardiac events and stroke. *Myopathy is the most common complication of statins* (e.g., atorvastatin, simvastatin, pravastatin). It occurs in approximately 1.5% of users, and is unrelated to dose, cumulative dose, or statin subtype. Genetic variants that influence statin metabolism, on the other hand, may help identify those who are at risk.

Chloroquine and *hydroxychloroquine* were originally used as antimalarial agents and are currently given as long-term therapy to some patients with systemic autoimmune diseases. These drugs interfere with normal lysosomal function and can cause a drug-induced lysosomal storage myopathy that presents with slowly progressive muscle weakness. The muscle tissue shows myopathic changes including vacuolation that predominantly affects type I fibers. Ultrastructural studies identify aggregates of whorled, lamellar membranous structures, including curvilinear bodies that mimic those seen in ceroid lipofuscinoses (Chapter 28).

ICU myopathy or *myosin deficient myopathy* is a neuromuscular disorder seen in patients during the course of treatment for critical illness (usually in an intensive care unit) especially with corticosteroid therapy. There may be relatively selective degradation of sarcomeric myosin thick