If Treatment Fails, Think Inclusion Body Myositis

BY DIANA MAHONEY
New England Bureau

BOSTON — Failure to respond to standard immunosuppressant therapy may be the first sign that a patient's apparent polymyositis actually is inclusion body myositis, according to Dr. Chester Oddis of the University of Pittsburgh.

The most common acquired muscle disease in people over 50 years of age, inclusion body myositis (IBM) is a distinct type of inflammatory myopathy characterized by slowly progressing, degenerative muscle changes caused by an antigen-driven inflammatory response, as well as vacuolar degeneration and abnormal protein deposits in distal and proximal muscle cells, Dr. Oddis said at a meeting on rheumatology sponsored by Harvard Medical School.

Because it shares certain clinical and pathologic features with polymyositis, such as varying degrees of muscle weakness, inflammation in the endomysium, muscle fiber necrosis, and elevation of serum muscle enzymes, inclusion body myositis is often mistaken for polymyositis or motor neuron disease by rheumatologists and neurologists, Dr. Oddis noted. "A number of studies have shown that the average time from symptom onset to diagnosis is between 4-6 years. Typically, the first indication that you're dealing with a mimic [of polymyositis] is the failure to respond to immunosuppressant therapy."

The nature of disease onset and presentation also distinguishes IBM from polymyositis. While polymyositis tends to have a subacute onset, typically over a few weeks to months, IBM comes on insidiously over the course of many months and even years, Dr. Oddis explained. Additionally, IBM has a tendency for distal and asymmetric muscle involvement, such as a foot drop, he said. In contrast, polymyositis more commonly encompasses proximal, symmetric muscle weakness.

Pharyngeal muscle weakness is a common characteristic of IBM and polymyositis. In particular, however, proximal dysphagia resulting from cricopharyngeal spasm is more often seen in inclusion body myositis. "Patients often complain of a blocking sensation when they swallow that just doesn't go away," said Dr. Oddis. "This is a little different than pharyngeal myopathy seen in polymyositis because it is persistent; pharyngeal myopathy waxes and wanes with the severity of the involvement of the proximal musculature."

Unlike most connective tissue diseases, inclusion body myositis occurs predominantly in men. "It sneaks up on them in middle age and follows a characteristic pattern of painless muscle atrophy, including the forearm flexors, quadriceps, and the intrinsic muscles of the hands," said Dr. Oddis. "The forearm and quadriceps atrophy is usually obvious on examination. To assess hand muscle strength, I'll often ask patients to form a circle with their fingers. Because of their intrinsic muscle weakness, the circle is often more like a teardrop. This teardrop sign is something you probably won't see in polymyositis."

Magnetic resonance can be especially useful in differentiating IBM from polymyositis, said Dr. Oddis. "The results will be abnormal in both conditions, but MRIs from patients with inclusion body myositis are more likely to show fatty infiltration and atrophy and more widespread abnormalities, while in polymyositis, the predominant abnormality seen on MRI is inflammation distributed along the fascia."

The only definitive test for inclusion body myositis is a muscle biopsy. Because of the possibility of skip lesions, "it sometimes takes two, three, or four biopsies before you get something you can hang your hat on, but when you do, there is no question," said Dr. Oddis. "The distinctive histology that you're looking for includes endomysial inflammation, the presence of rimmed vacuoles, and intracellular amyloid deposits or twisted tubulofilaments [containing hyperphosphorylated tau]."

Management options for inclusion body myositis are often limited to supportive efforts, such as myotomy to relieve dysphagia caused by cricopharyngeal achalasia, said Dr. Oddis. While no definitive treatment has been proven effective in achieving sustained remission and improvement in whole body strength, some reports suggest there may be a subgroup of patients who experience a partial, transient response to anti-inflammatory, immunosuppressant therapy. For this reason, he said, an initial 6-8 week trial of prednisolone and an immunosuppressive drug such as methotrexate or azathioprine is a reasonable option for newly diagnosed patients. ■