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# Inflammatory myopathies: Narrowing the differential diagnosis

## ■ ABSTRACT

Muscle weakness is a feature of numerous conditions, but the muscle weakness of inflammatory myopathies, especially polymyositis and dermatomyositis, is easy to differentiate by specific clinical, laboratory, electromyographic, and histological features.

## ■ KEY POINTS

Diagnostic criteria currently include proximal muscle weakness, increased creatine kinase, abnormal (myopathic) electromyogram, typical histologic appearance on muscle biopsy, and cutaneous abnormalities typical of dermatomyositis.

A muscle biopsy specimen demonstrating typical histologic features in the absence of metabolic myopathy, infection, or drug effect establishes the diagnosis of polymyositis.

Numerous prescription and over-the-counter drugs, notably the statins, are associated with myopathy. Prudent practice is to check the creatine kinase levels of patients taking statins.

Although there is an association between inflammatory myopathy and malignancy, there is no consensus for screening for cancer in patients with myositis.

**W**HEN A PATIENT PRESENTS with weakness, the first step is to distinguish true muscular weakness from the perception of “weakness” due to other problems, such as arthritis, anemia, congestive heart failure, neuropathy, or deconditioning. Once muscular weakness is confirmed via manual resistive testing, the next step is to consider inflammatory myopathy—polymyositis, dermatomyositis, and inclusion body myositis—and drug-induced and metabolic myopathy.

This article addresses how to differentiate inflammatory myopathy from other causes of muscle weakness by observation of clinical, laboratory, and histologic features. The focus is mainly on polymyositis and dermatomyositis, the most common types of inflammatory myopathy.

## ■ CLASSIFICATION

The original classification of inflammatory myopathies by Bohan and colleagues<sup>1</sup> included five types of myositis:

- Adult polymyositis
- Adult dermatomyositis
- Juvenile polymyositis and dermatomyositis
- Myositis associated with cancer
- Myositis associated with another connective tissue disease, also called “overlap syndrome.”

This classification has since been modified to include:

- Amyopathic dermatomyositis, an uncommon condition affecting only the skin
- Inclusion body myositis, an inflammatory myopathy with different clinical and pathologic features and course.



## ■ Polymyositis and dermatomyositis vs inclusion body myositis

Polymyositis and dermatomyositis are frequently considered together because they have similar clinical, laboratory, and pathologic features and because they progress at the same tempo. While inclusion body myositis shares some features with polymyositis and dermatomyositis, it generally follows a more indolent course and is more refractory to therapy. Other distinguishing features are discussed below.

### ■ PREVALENCE

Polymyositis and dermatomyositis are uncommon, with an annual incidence ranging from 2 to 10 new cases per million persons.<sup>2</sup> By comparison, scleroderma is twice as common, and systemic lupus erythematosus is about four times as common. The mean age of onset of polymyositis is 45 years, whereas a bimodal age distribution is observed with dermatomyositis, with peaks at around 10 and 40 years of age. Among adults, women are affected twice as often as men, while among children both sexes are affected equally. In the case of overlap syndrome, the peak age of onset and male-female ratios reflect the underlying connective tissue disease.<sup>2</sup>

Inclusion body myositis is considerably more common in men than in women and is more prevalent in patients over 50 years old.<sup>3</sup>

### ■ KEY DIAGNOSTIC CRITERIA

The criteria used by Bohan et al<sup>1</sup> to establish the diagnosis of polymyositis and dermatomyositis include:

- Symmetrical proximal muscle weakness
- Increased serum enzyme levels, especially creatine kinase
- Electromyographic signs of myopathy
- Muscle biopsy abnormalities
- Typical cutaneous abnormalities (of dermatomyositis).

### ■ CLINICAL FEATURES

#### Symmetrical proximal muscle weakness

The chief clinical feature of polymyositis and dermatomyositis is gradual, progressive, pain-

less symmetrical proximal muscle weakness, with symptoms dating back to 3 to 6 months by the time of the first physician visit.

Upper-extremity muscle weakness manifests as difficulty in performing activities that require holding the arms up, such as hair washing, shaving, or reaching into overhead cupboards. Neck muscle weakness may lead to difficulty raising the head from a pillow or even holding it up while standing. Involvement of pharyngeal muscles may result in hoarseness, dysphonia, dysphagia, and nasal regurgitation after swallowing.

Lower-extremity proximal muscle weakness manifests as difficulty climbing stairs and rising from a seated or squatting position. Patients seek chairs with armrests to push off from or grab the sink or towel bar to rise from the toilet.

#### Other clinical features

Weakness is the major complaint, but proximal myalgias and constitutional symptoms such as fever, fatigue, and weight loss may occur.

#### Cutaneous features of dermatomyositis

In dermatomyositis, patients may have an erythematous, often pruritic rash over the face, including the cheeks, nasolabial folds, chin, and forehead. Heliotrope (purplish) discoloration over the upper eyelids with periorbital edema is characteristic, as is the “shawl sign,” an erythematous rash in a V-distribution on the chest and across the shoulders posteriorly.

**Gottron papules**—flat-topped raised non-pruritic lesions found over the dorsum of the metacarpophalangeal, proximal interphalangeal, and distal interphalangeal joints—are virtually pathognomonic for dermatomyositis (FIGURE 1).<sup>4,5</sup> Often pinkish to violaceous, sometimes with a slight scale, they are distinguished from cutaneous lupus in that lupus has a predilection for the dorsum of the fingers between the joints.

**Calcinosis cutis.** Children with dermatomyositis are also particularly prone to calcinosis cutis, the development of dystrophic calcification in the soft tissues and muscles, which may lead to skin ulceration, secondary infection, and joint contracture. Calcinosis

Muscle weakness is gradual, progressive, painless



**FIGURE 1.** Gottron papules—the flat-topped raised nonpruritic lesions found over the dorsum of the metacarpophalangeal, proximal interphalangeal, and distal interphalangeal joints—are pathognomonic for dermatomyositis. In contrast, cutaneous lupus erythematosus has a predilection for the dorsum of the fingers between the joints.

Serum creatine kinase elevation is often dramatic

cutis occurs in up to 40% of children with dermatomyositis and less commonly in adults; there is no proven therapy to prevent this complication.<sup>4</sup> Anecdotal use of calcium-channel blockers,<sup>6</sup> probenecid,<sup>7</sup> aluminum hydroxide,<sup>8</sup> and warfarin<sup>9</sup> has been described in established calcinosis cutis.

#### Features specific to inclusion body myositis

Inclusion body myositis tends to present with a more gradual onset of weakness, which may date back several years by the time of diagnosis. While the muscle weakness is proximal, distal muscle groups may also be affected, and asymmetry of involvement is characteristic. Atrophy of the deltoids and quadriceps is often present, and weakness of forearm muscles (especially finger flexors) and ankle dorsiflexors is typical. Peripheral neuropathy with loss of deep tendon reflexes may be present in some patients.<sup>10</sup>

#### ■ INCREASED SERUM ENZYME LEVELS

##### Creatine kinase serum levels

The laboratory hallmark of polymyositis and dermatomyositis, although not specific to either of these, is a dramatic elevation of the

serum creatine kinase, often in the range of 1,000 to 10,000 mg/dL, though early in the disease process milder elevations may be seen. In inclusion body myositis, creatine kinase elevations tend to be less striking, often rising only to the 600 to 800 mg/dL range; 20% to 30% of patients with inclusion body myositis may have a normal creatine kinase at presentation.

With initiation of effective treatment, creatine kinase levels fall rapidly, and periodic measurements are used to follow disease activity over the course of long-term follow-up.

**Caution is advised** when interpreting creatine kinase elevations, as levels may remain mildly elevated chronically in the face of clinically quiescent disease. In addition, the degree of elevation does not correlate well with the degree of muscle weakness. Significant elevations accompany a disease flare in most instances, exceptions being patients with severe muscle atrophy.<sup>2</sup>

#### Usefulness of creatine kinase MB levels and other studies

Skeletal muscle regeneration and myocardial involvement may cause an elevation of the serum creatine kinase myocardial band (MB) enzyme (normal range 0-4 ng/mL). Elevated serum levels of aldolase, lactate dehydrogenase (LDH), aspartate aminotransferase (AST), and alanine aminotransferase (ALT) are less sensitive and specific for active myositis.<sup>2</sup> Measurements of acute-phase reactants (eg, via the sedimentation rate) may show moderate elevations.

#### ■ AUTOANTIBODIES IN POLYMYOSITIS AND DERMATOMYOSITIS

Autoantibodies may be present in polymyositis and dermatomyositis, but they are generally absent in inclusion body myositis.

Autoantibodies present in polymyositis and dermatomyositis include the myositis-specific autoantibodies anti-Jo-1, seen in 20% of patients, and the less commonly encountered anti-PL-7, anti-PL-12, anti-OJ, and anti-EJ. These antibodies recognize cytoplasmic transfer RNA synthetases (for instance, anti-Jo-1 recognizes histidyl trans-



fer RNA synthetase), and they are markers of the subset of polymyositis and dermatomyositis patients described as having anti-synthetase syndrome, which is characterized by fever, inflammatory arthritis, Raynaud phenomenon, and interstitial lung disease and is associated with a reduction in survival compared with uncomplicated polymyositis and dermatomyositis.<sup>11</sup>

### Anti-signal recognition particle

Anti-signal recognition particle is a myositis-specific autoantibody that identifies a subgroup of polymyositis patients with particularly aggressive and refractory disease (5-year survival 30%). It is associated with a tendency for myocardial involvement.<sup>11</sup>

### Other autoantibodies

Other autoantibodies that may be present “nonspecifically” in patients with polymyositis and dermatomyositis include anti-nuclear antibody (ANA), Sjögren syndrome-A (SSA) antibodies, and antibodies to ribonucleoprotein (RNP). Such autoantibodies may be seen in 80% of patients with myositis, but their lack of specificity make them of little clinical utility to the general internist.

## ■ ELECTROMYOGRAPHIC FEATURES

A key criterion in the diagnosis of polymyositis is an abnormal (myopathic) electromyogram. The evaluation of the patient with suspected myositis should include electromyography and nerve conduction studies.

In addition to helping to exclude many neuropathic etiologies, electromyography also helps to identify the most inflamed muscle groups.

Typical electromyographic findings in inflammatory myopathy include:

- Spontaneous fibrillations at rest or with needle insertion
- Short-duration, small-amplitude polyphasic motor unit potentials with muscle contraction
- Spontaneous bizarre high-frequency discharges.<sup>1</sup>

Usually, one arm and one leg are studied,

leaving the contralateral side (typically the deltoid or quadriceps) for muscle biopsy should the physical exam and typical electromyographic abnormalities indicate active involvement.

## ■ MUSCLE BIOPSY ABNORMALITIES

A muscle biopsy specimen demonstrating typical histologic features (described below) in the absence of markers of metabolic myopathy, infection, or drug effect establishes the diagnosis of polymyositis. Muscle biopsy may not be necessary in a patient presenting with proximal muscle weakness, creatine kinase elevation, and the classic cutaneous manifestations of dermatomyositis.

When biopsy is performed, however, care must be taken not to select a muscle that is so weak or atrophic that the biopsy reveals end-stage disease.

### Magnetic resonance imaging as a guide to biopsy site selection

In recent years magnetic resonance imaging (MRI) has been explored as a means to assess the presence and activity of myositis noninvasively. Enhancement of muscle tissue on T<sub>2</sub>-weighted images (but not T<sub>1</sub>-weighted images) indicates edema consistent with active inflammation. In contrast, enhancement of both T<sub>1</sub>-weighted and T<sub>2</sub>-weighted images indicates fat infiltration (lipomatosis), which may be seen later in the course of the illness. MRI with short tau inversion recovery (STIR) images can identify edema distinct from fatty infiltration, which makes it a useful tool in detecting recurrent disease activity in patients with long-standing inflammatory myositis, secondary muscle atrophy, and lipomatosis.<sup>12</sup>

To date, MRI does not replace the need for biopsy for initial evaluation and diagnosis. However, it is useful in identifying the biopsy site with the most actively inflamed muscle, or in helping to distinguish steroid myopathy from flaring myositis in the patient developing recurrent weakness during treatment with corticosteroids.

### Pathophysiologic features

The common pathophysiologic features of polymyositis, dermatomyositis, and inclusion

**A myopathic abnormality on the electromyogram is a key to the diagnosis**



body myositis are chronic inflammation, an attempt at healing by fibrosis, and a net loss of myofibrils.

The inflammatory infiltrate is composed mainly of lymphocytes. In polymyositis and inclusion body myositis, the lymphocytes are found predominantly within the fascicles; in dermatomyositis they are found predominantly in the perivascular and perifascicular regions.<sup>13</sup> Perifascicular atrophy is diagnostic of dermatomyositis regardless of the presence of inflammatory cells.<sup>13</sup> Myophagocytosis by macrophages occurs with myocyte necrosis and degradation. Centralization of the myofibril nuclei is also seen. Inflammation may be patchy and skip areas may occur. An adequate biopsy sample improves diagnostic yield.<sup>14</sup>

#### Histochemical analysis

Histochemical analysis of biopsy tissue is used to identify a metabolic cause of myopathy, such as the glycogen storage diseases, and neuropathic injuries.

**The pattern of myocyte atrophy**, as determined by histochemical staining, hints at the underlying mechanism of injury: denervation (ie, muscle injury from damage to the nerve supplying it) results in fiber type grouping, in which the atrophic fibers are of the same type (type I or slow-twitch oxidative vs type II or fast-twitch glycolytic), whereas in polymyositis and dermatomyositis, both groups are affected. Steroid-induced myopathy is associated with selective type II fiber atrophy.<sup>14</sup>

**Immunophenotypical differences** have been noted between polymyositis and dermatomyositis. Polymyositis is characterized by the predominance of CD8+ T cells and by the presence of major histocompatibility complex (MHC) class I markers on myofibrils. Analysis of the T-cell receptor genes has shown that the invading T cells are clonally restricted, consistent with an antigen-driven response. It is notable that healthy resting myocytes do not express class I HLA antigens on their surface; the stimulus that triggers expression of the class I HLA and the antigen or antigens being presented to the cytotoxic T cells are not known.<sup>13,15</sup> Both viral peptide antigens and endogenous mus-

cle peptides have been proposed as the triggering stimulus, but thus far data demonstrating viral peptides on polymerase chain reaction analyses are lacking.

**Inclusion body myositis is immunohistologically similar to polymyositis** in that in both conditions cytotoxic CD8+ T cells invade muscle tissue exhibiting class I HLA antigens. Data suggesting clonality of the T cells are less compelling thus far, with some but not all studies demonstrating clonality of the TCR gene.<sup>15</sup> On routine histochemical analysis, myocytes exhibit a variety of abnormal inclusions, including eosinophilic cytoplasmic inclusions, vacuoles rimmed with basophilic granules, and foci that stain positively with Congo red, consistent with amyloid deposits. On electron microscopy, inclusion body myositis is characterized by the presence of cytoplasmic helical filaments (tubofilaments) which contain beta-amyloid protein.<sup>16</sup>

Immunohistochemical studies suggest that dermatomyositis is quite different pathophysiologically from polymyositis and inclusion body myositis. The predominant infiltrating lymphocytes are B cells and CD4+ T cells, suggesting a humorally mediated process. Furthermore, molecules of the terminal complement membrane attack complex can be demonstrated early in the disease process within the walls of muscle capillaries. Capillary injury results in marked capillary depletion and possibly ischemic injury to myocytes.<sup>13</sup>

#### ■ DIFFERENTIAL DIAGNOSIS

The differential diagnosis of inflammatory myopathy is broad and includes conditions that present with myalgia, weakness, or serum creatine kinase elevation or any combination of these features, and may or may not be associated with an infiltrate of inflammatory cells on muscle biopsy.

For example, though many drugs and toxins can induce a metabolic myopathy with weakness, serum creatine kinase elevation, and myalgia, only penicillamine and zidovudine are associated with inflammatory infiltrates. Infection, endocrinopathy, neurological illness, metabolic myopathy, fibromyalgia,

Consider any condition that causes myalgia, weakness, or high serum creatine kinase



polymyalgia rheumatica, sarcoid, and paraneoplastic phenomena require consideration (TABLE 1).<sup>14</sup>

If the characteristic rashes of dermatomyositis are absent, no single marker of inflammatory myopathy is diagnostic, and the clinical and laboratory findings must be considered carefully to exclude other diagnoses.

In the case of drug or toxin ingestion, discontinuation of the offending drug usually results in rapid resolution of the myositis.

#### Viral causes

Viral myositis can cause dramatic elevations in serum creatine kinase levels with corresponding weakness. A rapid progression of disease in the setting of an antecedent viral syndrome hints at the diagnosis. Often, such as in adenovirus or influenza infection, the clinical picture spontaneously improves in the time it takes to obtain an electromyogram and other diagnostic tests.

Human immunodeficiency virus (HIV) and the antiretroviral agent zidovudine may cause myositis with inflammatory infiltrates. Ragged red fibers, indicative of abnormal mitochondria, are seen in myositis secondary to zidovudine, but not HIV-induced myositis.<sup>13</sup>

#### Parasitic causes

Parasitic infections such as trichinosis and toxoplasmosis can cause myositis with inflammatory infiltrates. The diagnosis requires a heightened index of suspicion and directed questioning about potential exposure: ingestion of undercooked pork for trichinosis, and handling or ingesting cat feces or undercooked pork, lamb, or beef for toxoplasmosis.

#### Polymyalgia rheumatica

Distinguishing between polymyalgia rheumatica and polymyositis is usually not difficult if one keeps in mind that polymyalgia rheumatica causes aching pain and stiffness in the proximal muscle groups, but not true weakness on manual resistive testing. While the sedimentation rate is typically elevated in polymyalgia rheumatica, the serum creatine kinase level is normal. Furthermore, the patient with polymyalgia rheumatica describes

TABLE 1

### Differential diagnosis of inflammatory myopathy

Drug or toxin (see also TABLE 2)

#### Infection

Bacterial (staphylococcal, streptococcal, pneumococcal, *Salmonella*)

Treponemal (syphilis)

Mycobacterial (*Mycobacterium tuberculosis*, *M leprae*)

Viral (cytomegalovirus, Epstein-Barr virus, HIV, herpes simplex virus, adenoviruses, others)

Fungal (cryptococcosis, mucormycosis)

Parasitic (trichinosis, toxoplasmosis)

#### Metabolic myopathy

Glycogen storage diseases

Carnitine deficiency

Carnitine palmityltransferase deficiency

#### Endocrinopathy

Hypothyroidism

Hyperthyroidism\*

Hyperparathyroidism\*

Cushing syndrome

Vitamin D deficiency

Polymyalgia rheumatica\*

Fibromyalgia\*

Sarcoidosis

#### Neuromuscular disorders

Amyotrophic lateral sclerosis

Muscular dystrophy

Myasthenia gravis\*

\*Because presentations vary, generalizations about the presence and magnitude of serum creatine kinase elevation in these disorders are difficult; however, entities marked with an asterisk are associated with normal creatine kinase levels, and elevation of creatine kinase in a patient with these disorders should prompt further evaluation.

ADAPTED FROM BUNCH TW. POLYMYOSITIS: A CASE HISTORY APPROACH TO THE DIFFERENTIAL DIAGNOSIS AND TREATMENT. MAYO CLIN PROC 1990; 65:1480-1497.

improvement in symptoms as the day progresses, while the patient with polymyositis has the same degree of weakness throughout the day.

#### Drug interactions: Lipid-lowering drugs

Numerous prescription and over-the-counter medicines are associated with myopathy that can mimic polymyositis. A partial list of

TABLE 2

**Drugs associated with myopathy\***

Amiodarone  
 Chloroquine  
 Cimetidine  
 Clofibrate  
 Cocaine  
 Colchicine  
 Corticosteroids  
 Danazol  
 Emetine  
 Ethanol  
 Gemfibrozil  
 Heroin  
 HMG-CoA reductase inhibitors (statins)  
 Hydralazine  
 Ipecac  
 Ketoconazole  
 Levodopa  
 Nicotinic acid  
 Penicillamine  
 Phenytoin  
 Procainamide  
 Rifampin  
 Sulfonamides  
 Vincristine  
 Zidovudine

\*Only myopathy caused by penicillamine and zidovudine is associated with inflammatory infiltrates.<sup>13</sup>

Check CK levels periodically in patients taking statin drugs

potentially offending drugs is found in TABLE 2.

Several lipid-lowering agents have been associated with myalgia, myopathy, or rhabdomyolysis. Originally described in patients being treated with the combination of gemfibrozil and lovastatin,<sup>17</sup> myositis has also been reported to occur in patients treated with gemfibrozil and the other statins (simvastatin, pravastatin, fluvastatin, atorvastatin).<sup>17</sup>

**Combination lipid-lowering therapy is attractive** in a large subset of patients with hyperlipidemia—ie, those with both hypercholesterolemia and hypertriglyceridemia. In one series of 252 patients treated with combination therapy, 6 patients (3%) stopped the treatment regimen because of myalgias in the setting of normal serum creatine kinase levels, and 1 (0.4%) stopped the treatment because of presumed myositis (myalgias with 12-fold elevation of creatine kinase).<sup>17</sup> This result was

concordant with another study of 265 patients on a combination of gemfibrozil and pravastatin or simvastatin, in which no patient developed myopathy.<sup>17</sup>

**Cytochrome P450 3A4 inhibition increases the risk.** Use of drugs that significantly inhibit cytochrome P450 3A4 (cyclosporine A, nefazodone, itraconazole, ketoconazole, erythromycin, clarithromycin, and protease inhibitors) is associated with an increased risk of myopathy in patients taking simvastatin, which is metabolized by cytochrome P450 3A4. Lovastatin and atorvastatin are also metabolized by cytochrome P450 3A4. Pravastatin is not significantly metabolized through this pathway, yet patients who take both pravastatin and cyclosporine concomitantly tend to have higher plasma levels of pravastatin and a greater risk of myopathy than do patients taking pravastatin alone. This suggests that cyclosporine may alter statin metabolism by mechanisms other than cytochrome inhibition.<sup>18</sup>

**When to stop the statin.** Sinzinger et al<sup>19</sup> described the occurrence of exertional myalgias with normal creatine kinase levels in patients taking an HMG-CoA reductase inhibitor (statin), which resolved upon discontinuation of the offending drug. Notably, all patients were able to switch to a different HMG-CoA reductase inhibitor for long-term use without development of myalgias, though the myalgias returned if the original agent was reintroduced. This suggests that this side effect was not a class effect, but dependent on individual drug characteristics.

Prudent practice is to check creatine kinase levels periodically in patients taking a statin drug, and to discontinue the drug if the creatine kinase level rises above the upper limit of normal. New onset of myalgias or exertional cramping or weakness should also prompt alteration of therapy. Elevated creatine kinase levels generally return to normal within a few weeks after the drug is stopped.

If a patient is doing well on statin therapy but requires a limited course of therapy with another agent known to be a strong inhibitor of cytochrome P450 3A4, statin therapy should be stopped for the short time that treatment with the other drug is in effect.<sup>18</sup>



## ■ TREATMENT OF INFLAMMATORY MYOPATHY

### Polymyositis and dermatomyositis

The mainstay of therapy for polymyositis and dermatomyositis is oral prednisone given initially at a dose of 1 mg/kg in the morning. Tapering the dose may be attempted after 4 to 6 weeks, with very gradual tapering afterwards<sup>2</sup>: as a guide, the tapered dose of prednisone should be roughly half the starting dose after 6 months of treatment.<sup>4</sup>

If the diagnosis and treatment occur soon after disease onset, the response to treatment is generally rapid, both in terms of laboratory abnormalities and strength. However, symptomatic improvement is slower when the diagnosis is delayed.<sup>20</sup>

The dose of prednisone should not be tapered quickly even if a prompt normalization of creatine kinase occurs. Patients should expect to be on prednisone for at least 1 year.

Adverse effects of high-dose steroid therapy are common, and active prophylaxis for steroid-induced osteoporosis should be considered in patients of both sexes. Steroid-induced myopathy is a common problem that may occur within the first several months of therapy, leading to confusion about whether new weakness represents a flare of the underlying disease or an adverse effect of therapy. There is no specific test to distinguish between these possibilities; even muscle biopsy does not reliably settle the issue. Type II fiber atrophy, while associated with steroid use, may also be seen in postinflammatory states and in disuse atrophy.

MRI with STIR images may offer another tool for distinguishing patients with muscle edema consistent with inflammation from those with lipomatosis.<sup>12</sup>

In patients whose disease responds only partially to corticosteroids, or who require an unacceptably high dose to maintain disease control, other agents such as methotrexate or azathioprine are alternatives. Use of either agent requires an understanding of its toxicity profile and careful monitoring for adverse effects; this is most appropriately handled by the consulting rheumatologist. Other options for the treatment of polymyositis and dermatomyositis include combining methotrex-

ate and azathioprine, or using agents such as cyclosporine or chlorambucil. Intravenous immunoglobulin infusion on a monthly basis may be helpful in some patients with refractory dermatomyositis.<sup>21,22</sup>

### Inclusion body myositis

Inclusion body myositis was once believed to be refractory to any medical therapy, but a few small series have been published reporting stabilization and even improvement in some patients treated with prednisone alone or in combination with azathioprine<sup>3,10,23</sup> or methotrexate.<sup>10</sup>

## ■ POTENTIAL COMPLICATIONS OF UNTREATED INFLAMMATORY MYOPATHY

### Pulmonary complications

Involvement of the respiratory system may occur as a result of several different processes:

- Weakness of the diaphragm and intercostal muscles may lead to dyspnea, ventilatory insufficiency, and atelectasis
- Pharyngeal muscle weakness increases the risk of aspiration
- Interstitial pneumonitis occurs in approximately 10% of patients with polymyositis, usually developing gradually over the course of the illness, leading to interstitial lung disease and restrictive physiology, or occasionally remaining asymptomatic.<sup>13,14,24</sup>

### Myocardial complications

Myocardial involvement in polymyositis and dermatomyositis is well described. Autopsy studies have shown the presence of active myositis, contraction band necrosis, and myocardial fibrosis.<sup>25,26</sup>

The reported frequency of congestive heart failure (with or without cardiomegaly) ranges from fewer than 5% of patients<sup>27</sup> to 45%.<sup>26</sup>

Electrocardiographic abnormalities are more common, with left anterior fascicular block and right bundle branch block representing the most frequent conduction defects.<sup>27</sup>

Elevations in creatine kinase MB do not correlate with the presence or the extent of myocardial disease, as regenerating skeletal muscle fibers release this isoform of the enzyme.<sup>2,27</sup>

**If untreated, patients risk pulmonary, myocardial complications**



### Associated malignancy

An association between inflammatory myopathy and malignancy was first reported in the late 1800s, and despite much attention to this topic in the literature the actual incidence and types of malignancies in patients with polymyositis and dermatomyositis are still the subject of controversy.

While some experts have said that the relative risk of malignancy is higher in patients with dermatomyositis compared with the normal population, and that the relative risk in patients with polymyositis is not substantially increased,<sup>4,28</sup> we have data to refute this belief. A recent report reviewing 618 cases of dermatomyositis and 914 cases of polymyositis<sup>29</sup> addressed the standardized incidence ratio (SIR) of specific malignancies and the time they were discovered relative to the diagnosis of the myositis.<sup>29</sup> (The SIR is the number of cancer cases that arose among dermatomyositis or polymyositis patients divided by the expected number of cancer cases according to national age-specific, sex-specific, and period-specific cancer rates.) Of note, both polymyositis and dermatomyositis were associated with an increased risk of malignancy, with a threefold risk demonstrated in patients with dermatomyositis and a 1.4-fold risk for patients with polymyositis. The types of malignancy generally reflected those expected for age and sex, though ovarian

cancer was over-represented in women with dermatomyositis, and both groups of patients displayed a greater-than-expected occurrence of non-Hodgkin lymphoma.<sup>29</sup>

There is still no consensus as to the extent of screening for malignancy in patients with myositis.<sup>13,30</sup> The minimum approach is a thorough history and physical exam, with standard laboratory tests and health maintenance screening exams (Papanicolaou smear, pelvic exam, mammography, prostate-specific antigen testing, chest radiography), pursuing any abnormalities discovered.<sup>13</sup>

However, some experts, mindful of the increased frequency of ovarian cancer and non-Hodgkin lymphoma, suggest pursuing a more rigorous workup with computed tomographic scanning of the chest, abdomen, and pelvis.<sup>29</sup>

We must also bear in mind that malignancy may not be diagnosed until 1 or more years after the onset of inflammatory myopathy. Hill et al<sup>29</sup> concluded that dermatomyositis is strongly associated with a wide range of cancers for the 5 years following diagnosis of the myositis, and that polymyositis is associated with a modest increase in the overall risk of cancer.

Therefore, even if an initial evaluation for malignancy at the time of presentation of myositis is unrevealing, the clinician should be alert to signs and symptoms of new malignancy in the first several years of follow-up. ❏

Be alert to signs of cancer in first few years of follow-up

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