

Understanding the idiopathic inflammatory myopathies

Polymyositis and dermatomyositis can manifest with similar signs and symptoms. Look for the diagnostic markers that can help you make the correct diagnosis.

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Polymyositis (PM) is one of a group of skeletal muscle diseases known as *idiopathic inflammatory myopathies*. When PM manifestations include a cutaneous rash, the disease is referred to as *dermatomyositis* (DM). In patients with both PM and DM, proximal symmetric muscle weakness develops slowly over weeks to months. Typically, both conditions also respond to corticosteroid treatment. PM and DM are associated with a wide variety of malignancies. Despite these similarities, some clinical features—in addition to the characteristic dermatologic findings—differentiate the two diseases.

PM and DM are rare disorders; prevalence rates are estimated at about 1 per 100,000 in the general population, with a female to male predominance of approximately 2:1. Peak incidence is in the fifth decade. The two diseases more commonly affect African-Americans. The estimated incidence of PM in African-Americans compared to whites is 5:1 and of DM, 3:1. The 5-year mortality rate is 20%; elderly patients and persons with cardiac and/or pulmonary involvement or dysphagia have a higher mortality rate compared to other persons with either disease.¹

SIGNS AND SYMPTOMS

Despite the similar manifestations, PM and DM have clinical and pathological differences. Clinically, DM manifests as one of several skin conditions. DM is associated with a higher incidence of malignancy. Pathologically, DM is associated with immune complex deposition in the vessels, whereas PM appears to reflect a direct T-cell mediated muscle injury. Both conditions are idiopathic; however, PM can be a manifestation of another T-cell disorder, chronic graft-versus-host disease after bone marrow transplant.²

Clinical manifestations Bohan and Peter proposed five diagnostic criteria for PM/DM: (1) symmetric proximal muscle weakness; (2) elevated serum levels of muscle enzymes; (3) myopathic changes on electromyography; (4) characteristic muscle biopsy findings; and (5) appearance of a distinct rash, which will differentiate the diagnosis as DM.³ The diagnosis is made based on the presence of a constellation of symptoms rather than the presence of only one symptom. However, many patients who meet the Bohan and Peter cri-

teria may actually have a different inflammatory myopathy, including rhabdomyolysis, muscular dystrophy, inclusion body myositis, or myositis associated with connective tissue disease.⁴ Viral and bacterial muscle infections also produce histologic evidence of muscle inflammation.

An alternative to the Bohan and Peter classification incorporates both clinical and serologic factors, which allows for a more accurate prediction of disease course and treatment response.⁵ This approach classifies inflammatory myopathies as PM; DM; overlap myositis, defined as myositis with an additional feature other than rash and/or the presence of myositis-specific autoantibodies, such as an antisynthetasis, signal recognition protein, and one of the scleroderma-associated autoantibodies; and cancer-associated myositis.

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FIGURE 1. Heliotrope rash

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Muscle weakness The most common symptom of PM/DM is muscle weakness. Onset is normally insidious, with gradual worsening over weeks to months. In some cases, however, the onset may be very abrupt. The distribution of weakness is normally symmetric and proximal. Any distal muscle involvement is usually mild and does not cause specific muscle impairment. Myalgias and muscle tenderness occur in up to 50% of cases. These symptoms tend to be mild, unlike the more severe muscle pain seen in infectious myositis, the inherited metabolic myopathies, polymyalgia rheumatica, or fibromyalgia.

Muscle atrophy is not normally seen early in the course of the disease but may become profound in long-standing cases. Weakness of the oropharyngeal muscles or the striated muscle of the upper third of the esophagus may lead to dysphagia, nasal regurgitation, or aspiration. Esophageal involvement is more common in the elderly and may explain the higher incidence of bacterial pneumonia often seen in elderly patients with PM/DM.⁶

Rash DM manifests as one of several distinct rashes. Often the rash is transient and disappears before the onset of muscle weakness. The *heliotrope rash* is a symmetric, confluent, purple-red, macular eruption of the eyelids and periorbital tissue (see Figure 1, page 42). Edema is often present. Although considered the most specific skin manifestation of DM, heliotrope rash is rarely encountered.

Gottron's sign, the most commonly occurring rash, is a symmetric, scaly, violaceous, erythematous eruption over the extensor surfaces of the metacarpophalangeal and interphalangeal joints of the fingers (see Figure 2). Lesions may also occur over the extensor surfaces of the elbows and knees, often mimicking psoriasis. Skin biopsy of these lesions reveals vascular ectasia alternating with areas of vascular dropout.

The *shawl sign* is a violaceous and erythematous, confluent macular eruption that appears over the deltoids, posterior part of the shoulders, and neck. The *V sign* is a similar eruption occurring on the "V" area of the anterior neck and upper part of the chest. Finally, *mechanic's hands* manifests as periungual erythema, abnormal nail bed capillaries, and an often painful roughening and cracking of the skin on the tips and lateral aspects of the fingers (see Figure 3).

“EMG can differentiate between the inflammatory myopathies and other disorders that can cause muscle weakness.”

Extramuscular symptoms Often patients with severe cases of PM/DM present with fever and weight loss. Nonerosive inflammatory polyarthritis, Raynaud's phenomenon, and cardiopulmonary abnormalities also may be present. Interstitial lung disease (ILD) is another clinical finding in patients with PM/DM. The presence of ILD indicates a poor prognosis for patients because of its potentially rapidly progressive nature.⁷ These patients experience dyspnea and cough before the onset of muscle weakness. Myocardial involvement leading to heart failure is not a frequent occurrence. Signs and symptoms of PM/DM can overlap with the signs and symptoms of other connective-tissue diseases such as scleroderma, systemic lupus erythematosus, rheumatoid arthritis, and Sjögren's syndrome.

DIAGNOSTIC MARKERS

Muscle enzymes Creatine kinase (CK), aldolase, lactate dehydrogenase, aspartate aminotransferase, and alanine aminotransferase are the muscle enzymes routinely measured in patients presenting with myositis. At some point in the disease process, the level of at least one of these enzymes will be elevated, and most patients with PM/DM will have elevated levels of all the muscle enzymes.

Patients with PM/DM routinely have an elevated CK-myocardial band (MB) isoenzyme level either because of skeletal muscle inflammation with its antecedent expression of the CK-B chain or because of myocardial involvement. MI may be incorrectly suspected in this situation. A normal concentration of troponin I rules out cardiac involvement.

Autoantibodies Antinuclear antibodies are routinely elevated in patients with PM/DM. This finding is not specific for this disorder, however, and may overlap with myositis associated with another connective tissue disease.⁸

KEY POINTS

- Polymyositis and dermatomyositis (PM/DM) are inflammatory myopathies that manifest as symmetric muscle weakness that develops slowly over weeks to months. Typically, both diseases respond to corticosteroid treatment. Both diseases are associated with a wide variety of malignancies.
- DM is associated with immune complex deposition in the vessels, whereas PM appears to reflect a direct T-cell mediated muscle injury. Both conditions are idiopathic; however, PM can be a manifestation of chronic graft-versus-host disease after bone marrow transplant.
- The most common symptom of PM/DM is muscle weakness. Onset is normally insidious, with gradual worsening over weeks to months. In some cases, the onset may be very abrupt.
- Initial therapy for PM/DM is glucocorticoids. Prednisone, 0.5 to 1.5 mg/kg/d, has been shown to improve strength and preserve muscle function.

COMPETENCIES

- Medical knowledge
- Interpersonal & communication skills
- Patient care
- Professionalism
- Practice-based learning and improvement
- Systems-based practice

Autoantibodies directed against cytoplasmic RNA synthetases, other cytoplasmic proteins, ribonucleoproteins, and certain nuclear antigens have been noted in as many as 30% of patients with idiopathic inflammatory myopathy and are called *myositis-specific autoantibodies*.⁹ Only anti-histidyl-tRNA synthetase (anti-Jo-1 antibody) is a diagnostic marker. Anti-Jo-1 antibody is present in 20% of patients with PM/DM and is associated with ILD, arthritis, mechanic's hands, and Raynaud's phenomenon.

Electromyography The electromyogram (EMG) reveals evidence of increased membrane irritability in the form of a classic triad: increased insertional activity and spontaneous fibrillations, abnormal myopathic low amplitude and short-duration polyphasic motor unit potentials, and bizarre high-frequency discharges. These EMG findings are supportive, but not diagnostic, of PM/DM because similar findings can be seen in other infectious, toxic, or metabolic myopathies. However, EMG can differentiate between the inflammatory myopathies and other disorders that cause muscle weakness. Muscle enzyme levels must be measured before EMG because the EMG needle will falsely elevate the inflammation measured by these markers.

Muscle biopsy The definitive tool for establishing a diagnosis of PM/DM, as well as for ruling out other causes of myopathy, is the muscle biopsy. The biopsy should be obtained from a clinically weak muscle, most often the quadriceps or deltoid. Caution should be exercised to avoid sampling a severely weak muscle, atrophied muscle, or muscle from the EMG site. A biopsy specimen obtained from the muscle contralateral to the muscle found abnormal by EMG increases the diagnostic yield.

The histologic features of PM/DM include muscle fiber necrosis, degeneration and regeneration, and an inflammatory cell infiltrate. A discussion of the specific histologic findings that differentiate PM from DM is beyond the scope of this article.

Imaging studies MRI and magnetic resonance spectroscopy (MRS) are useful for evaluating myopathies.¹⁰ MRI can reveal areas of muscle inflammation and edema with active myositis and fibrosis. MRI also reduces biopsy sampling errors by visualizing severely involved or necrotic areas in the large muscles. MRS reveals the decreased muscle metabolism found in abnormal muscle.¹¹ As clinicians gain more experience with MRI and MRS, these imaging studies will replace the more invasive procedures used for diagnosing myopathies. The case study (page 47) illustrates how these markers and test results are used to come up with the diagnosis of PM/DM.

Differential diagnosis Diseases that mimic PM/DM, both with and without elevated muscle enzymes, include the motor neuron diseases (such as amyotrophic lateral sclerosis), the muscular dystrophies, myasthenia gravis, hypothyroidism-related myopathy, rhabdomyolysis, and inclusion-body myositis. Drug and alcohol induced myopathies, acute viral infections, inherited metabolic myopathies, and muscle weakness resulting from chronic disease also mimic PM/DM.



FIGURE 2. Gottron's sign

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FIGURE 3. Mechanic's hands

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TREATMENT

A prolonged duration of illness prior to diagnosis, dysphagia, increased severity of weakness, malignant disease, and respiratory and/or cardiac involvement are features associated with a poor outcome.^{12,13} Initial therapy for PM/DM is glucocorticoids. Prednisone, 0.5 to 1.5 mg/kg/d, has been shown to improve strength and preserve muscle function.¹⁴ Muscle enzyme normalization occurs in approximately 6 weeks, whereas improvements in muscle strength may take 2 to 3 months to become evident. Once sufficient muscle strength is attained, the prednisone dosage is tapered gradually; muscle enzyme levels, muscle strength, and extramuscular signs of a relapse of PM/DM, as well as signs of glucocorticoid toxicity, are monitored throughout the treatment course.

If there is no significant improvement in symptoms after 3 months, treatment failure or an alternative diagnosis should

be considered. If treatment failure is suspected, adding azathioprine or methotrexate may improve outcomes. For more resistant disease, IV immune globulin, cyclosporine, and/or tacrolimus, alone or in combination, may offer a benefit. Data on the efficacy of other agents such as cyclophosphamide, chlorambucil, tumor necrosis factor inhibitors, and B cell-depleting treatments (rituximab) are limited. Clinicians should note that these alternatives are not FDA-approved for resistant PM/DM.

PATIENT EDUCATION

Patients taking glucocorticoids for several months need counseling on an increased risk of osteoporosis, the need to avoid direct sunlight, and the importance of exercise. An early referral to a physical therapist is warranted. A weekly dose of a

bisphosphonate, in addition to calcium and vitamin D supplementation, may be appropriate when therapy begins. Patients presenting with cricopharyngeal muscle weakness should be educated about the risks of aspiration. They should elevate the head of their beds and be referred for consultation with a speech therapist. These patients need to maintain a diet of semithick foods and be aware that they may eventually require tube feeding.

Malignancy can manifest with PM/DM, so age appropriate cancer screening should begin at presentation and continue annually thereafter. The more common malignancies found in patients with PM/DM are cervical, ovarian, lung, pancreatic, bladder, gastric, and nasopharyngeal cancers and non-Hodgkin lymphoma.¹⁵

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Case study

The patient is a 57-year-old woman who presented to the emergency department with a complaint of progressively worsening dyspnea on exertion and lower extremity edema. She had been able to walk approximately 1 mile before tiring, but on presentation she could barely walk across her room. She admitted to generalized fatigue and aches that were worse in her legs. She also stated that it was becoming increasingly difficult for her to comb her hair or reach for items on her bedside table because of weakness in her upper arms. She denied wheezing but did admit to a cough that occasionally produced white-colored sputum. The patient denied fevers, chills, nausea, vomiting, constipation, or diarrhea. She also had no rash, oral lesions, Raynaud's phenomenon, or frank arthralgias. She denied any remote history of trauma, burns, or periods of immobility.

Her medical and surgical history was significant for hypertension, hysterectomy (for fibroids), and right knee arthroscopy (secondary to trauma). The patient was a retired house cleaner and stated she was careful to avoid environmental exposures. She lived with her husband and daughter and had no pets at home. She had no family history of connective tissue diseases.

Physical examination findings were temperature, 97.8°F; pulse, 98 beats per minute; respirations, 20 breaths per minute; BP, 138/67 mm Hg; pulse oximetry, 97% on room air. Results of the head, eyes, ears, nose, and throat examination were normal, with no signs of periorbital edema or rashes and no oral lesions. Lung auscultation revealed mild bibasilar crackles and normal percussion. Cardiac examination demonstrated a II/VI systolic murmur that was unchanged from previous examinations. Abdominal palpation revealed mild direct right lower quadrant tenderness with no masses, guarding, rebound, or rigidity. There was also mild discomfort with deep palpation of the lower extremity muscles. Muscle strength was graded 4/5 in the proximal upper extremities and 3/5 in the proximal quadriceps. There was no evidence of cyanosis,

clubbing, or edema in the extremities and no erythema. All the distal pulses were strong. There was no significant pain or swelling in the proximal thighs or upper extremities. No rash was appreciated.

Initial laboratory results were creatine kinase (CK), 14,711 ng/mL (normal, 35-165 ng/mL) that peaked at 18,241 ng/mL during admission; elevated CK-MB band, prompting an MI rule-out protocol; troponin I, negative $\times 3$; elevated transaminases (aspartate aminotransferase, 609 IU/L; alanine aminotransferase, 420 IU/L); thyroid-stimulating hormone, 6.125 IU/mL; and thyroxine, 10.40 IU/dL. Brain natriuretic peptide was within normal limits (9 pg/mL). Results of a viral hepatitis panel were negative. Renal function, urinalysis, CBC, and anti-Jo-1 antibody results were all normal. Erythrocyte sedimentation rate was elevated at 50 mm/h. Blood, urine, and sputum cultures had no growth.

Spiral chest CT ruled out pulmonary embolism but demonstrated a ground-glass pattern consistent with mild interstitial lung disease. Abdominal and pelvic CT was negative. Lower extremity venous duplex scanning ruled out deep venous thrombosis. Two-dimensional echocardiography revealed mild left ventricular hypertrophy, mild tricuspid regurgitation, and an estimated right ventricular systolic pressure of 55 mm Hg. MRI of the patient's lower extremities revealed a bilateral myositis pattern in the muscle bellies of her calves. Electromyography revealed increased membrane irritability with abnormal myopathic motor potentials and bizarre high frequency discharges. A muscle biopsy of her left quadriceps revealed muscle necrosis, degeneration, and regeneration with inflammatory cell infiltrates.

A diagnosis of polymyositis was made, and the patient was started on oral prednisone, 60 mg/d. Her muscle enzymes normalized in 6 weeks, and her proximal muscle strength returned to baseline in 3 months. The patient has since fully recovered.

CONCLUSION

Inflammatory myopathies are acquired muscle disorders of unknown etiology that manifest as proximal muscle weakness. The diagnostic evaluation includes measuring muscle enzyme levels and myositis-specific autoantibodies. EMG, muscle biopsy, and imaging studies are used to diagnose PM/DM and, when appropriate, to differentiate between PM/DM and other myopathies. Treatment involves glucocorticoids to reverse the inflammatory process and, when the disease does not respond to treatment, adding other pharmacotherapeutic agents as necessary. PAs should keep in mind that some malignancies are associated with PM/DM. Therefore, appropriate patient monitoring and education is an important part of the overall treatment regimen. [JAAPA](#)

Jason Astrin is a physician assistant at Mercy Medical Center, Baltimore, Maryland. He has indicated no relationships to disclose relating to the content of this article.

DRUGS MENTIONED

Azathioprine (Azasan, Imuran)
 Chlorambucil (Leukeran)
 Cyclophosphamide (Cytoxan, Neosar)
 Cyclosporine (Gengraf, Neoral, Sandimmune)
 Methotrexate (Rheumatrex, Trexall)
 Prednisone
 Rituximab (Rituxan)
 Tacrolimus (Prograf)

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