Dermatomyositis

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Abstract Dermatomyositis is one of the idiopathic inflammatory myopathies. It is characterized clinically by progressive symmetrical proximal muscle weakness and a characteristic rash. There are patients with rash who have little or no muscle disease. Although the process primarily attacks the skin and the muscles, it is a systemic disease with frequent manifestations in the gastrointestinal tract and pulmonary system. Dermatomyositis has been linked to internal malignancy in somewhere between 15% and 25%. Therapy for the muscle disease includes systemic corticosteroids with or without an immunosuppressive agent. Therapy of the skin disease begins with photoprotection and topical corticosteroids, but also includes the use of antimalarial agents and immunomodulatory therapies.

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Introduction

Dermatomyositis (DM) is one of the idiopathic inflammatory myopathies.\textsuperscript{1-3} In 1975, Bohan and Peter\textsuperscript{4} published a classic article that suggested a set of criteria to aid in the diagnosis and classification of DM and polymyositis (PM). Of the 5 criteria, 4 related to the muscle disease: (1) progressive proximal symmetrical weakness, (2) elevated muscles enzymes, (3) an abnormal electromyogram, and (4) an abnormal muscle biopsy, while the fifth was the presence of compatible cutaneous disease. It was felt that DM differed from PM only by the presence of cutaneous disease. Recent studies of the pathogenesis of the myopathy have been controversial, some suggesting that the myopathies in DM and PM are pathogenetically different with DM being due to a vascular inflammation,\textsuperscript{5} whereas other studies of cytokines suggest that the processes are similar.\textsuperscript{6-9} There has been a renewed interest in the pathogenetic mechanisms involved in the myopathy with recent studies revealing abnormal levels of nitric oxide, elevation of circulating tumor necrosis factor (TNF) receptors, elevated soluble CD40 expression, and increased expression of major histocompatibility complex class I and interleukin 1x within the muscle. The pathogenesis of the cutaneous disease is poorly understood.

The etiology of these disorders is not known. There appear to be immunogenetic markers that are correlated with DM, PM, and additionally, these patients often possess TNF-\textit{\alpha} polymorphisms.\textsuperscript{10} What triggers the onset of DM, PM, or juvenile DM has not been established; however, there is some suggestion that the onset of some of the subsets is seasonal,\textsuperscript{11} and, in children, there is evidence suggesting that the disease might follow an infection.\textsuperscript{12} It is therefore possible that DM, PM, and/or juvenile DM are due to an interaction of environmental factors including infections in an individual with an immunogenetic predisposition to develop disease.
Classification and clinical appearance

Classification

Bohan and Peter⁴ suggested 5 subsets of myositis—DM, PM, myositis with cancer, childhood DM/PM, and myositis overlapping with another collagen vascular disorder. In a subsequent publication, Bohan et al¹³ noted that cutaneous disease may precede the development of the myopathy; however, it was only recently recognized that another subset of patients with disease that only affects the skin (amyopathic DM [ADM] or DM-sine myositis) may occur.¹⁴ A seventh subset known as inclusion body myositis has been recognized in 1979.¹⁵,¹⁶ Perhaps there is an eighth group in which characteristic cutaneous disease is drug-induced.¹⁷ Finally, Sontheimer¹⁸ has proposed that other subsets exist for patients with cutaneous disease including classic DM, ADM, and at least 2 additional subsets known as hypomyopathic DM, when the skin disease is present with subtle muscle disease, evident with studies other than enzymatic analysis, and finally, a subset known as post-myopathic DM when patients with previous classic DM have the myositis resolve, but the skin disease remains active.

In a recent report, Troyanov et al¹⁹ suggested a “novel” classification based upon clinical and serologic features. They examined 100 patients using several classification schemes. This allowed them to reclassify many of their patients and they were able to predict their course and responsiveness to therapy. Specifically, only 10 of the 45 patients with PM remained with a classification of “pure PM,” whereas 20 of the 28 with DM remained with a diagnosis of “pure DM.” Forty-four of the patients who were reclassified from these 2 subsets were classified as having “overlap” myositis. With this scheme it was evident that PM is almost always chronic and had the highest level of refractoriness to corticosteroid therapy, whereas DM was chronic, but was usually responsive to corticosteroid therapy.

Cutaneous manifestations

The characteristic and possibly pathognomonic cutaneous features of DM are the heliotrope rash and Gottron’s papules. The heliotrope rash consists of a violaceous to dusky erythematous rash with or without edema in a symmetrical distribution involving periorbital skin (Fig. 1). At times the only manifestation of the heliotrope is the presence of dilated veins of the eyelids. Some have postulated that the violaceous erythema that is seen is due to inflammation of the striated muscle with dilated veins in the muscle that are able to be visualized through the thin skin of the eyelids. In addition to color changes, there is, at times, some scaling and desquamation that may also occur. Sometimes this sign is quite subtle and may involve only a mild discoloration along the eyelid margin. At other times there may be massive edema that develops (Fig. 2). A heliotrope rash is rarely observed in patients with lupus erythematosus (LE) and scleroderma. Early in their course, some patients might be diagnosed as having either angioedema or dermatitis.

Gottron’s papules are found over bony prominences, particularly the metacarpophalangeal joints, the proximal interphalangeal joints, and/or the distal interphalangeal joints (Fig. 3). They may also be found overlying the elbows, knees, and/or feet. The lesions consist of slightly elevated, violaceous papules and plaques. There may be a slight scale and, on some occasions, there is a thick psoriasiform scale. Within the lesions, there is often telangiectasia. These lesions may be clinically confused with lesions of LE, or, at times, with papulosquamous disorders, such as psoriasis or lichen planus. Routine histopathologic evaluation will aid in the differentiation from psoriasis or lichen planus, but cannot reliably distinguish the cutaneous lesions of DM from those of LE.

Several other cutaneous features are characteristic of the disease despite not being pathognomonic. They include malar erythema, poikiloderma in a photosensitive distribution, violaceous erythema on the extensor surfaces, periungual and cuticular changes, and alopecia. Facial erythema

Fig. 1 Heliotrope eruption. The periorbital changes represent the heliotrope eruption.

Fig. 2 Massive periorbital edema in a patient with DM.

Fig. 3 Typical Gottron’s papules over metacarpophalangeal joints.
in DM must be differentiated from LE, rosacea, seborrheic dermatitis, or atopic dermatitis. Poikiloderma (the combination of atrophy, dyspigmentation, and telangiectasia) may occur on exposed skin such as the extensor surfaces of the arm, the “V” of the neck (Fig. 4) or the upper back (shawl sign) (Fig. 5), and/or the upper-lateral thighs (holster sign) (Fig. 6). Patients rarely complain of photosensitivity, despite the prominent photodistribution of the rash. This photosensitive poikilodermatous eruption may be difficult to differentiate from LE. Nailfold changes consist of periungual telangiectasia and/or a characteristic cuticular change with hypertrophy of the cuticle and small, hemorrhagic infarcts within this hypertrophic area (Fig. 7). Periungual telangiectasia may be clinically apparent or may be appreciated only by capillary microscopy. Scalp involvement in DM is relatively common and is manifested by an erythematous to violaceous, psoriasiform dermatitis (Fig. 8). Clinical distinction from seborrheic dermatitis or psoriasis is occasionally difficult, but histopathologic evaluation is helpful. Nonscarring alopecia may occur in some patients and often follows a flare of the systemic disease. Lastly, recent reports have detailed the finding of gingival telangiectasia and angiokeratomas in children with DM.

Dermatomyositis-sine myositis, also known as ADM, is diagnosed in patients with typical cutaneous disease in whom there is no evidence of muscle weakness and who repeatedly have normal serum muscle enzyme levels. Some patients with “ADM” when studied will have abnormal imaging studies of muscle, for example, an abnormal ultrasound, magnetic resonance imaging, magnetic resonance spectroscopy, or muscle biopsy. These patients have muscle involvement and may be better classified as having hypomyopathic DM. Because many of the patients with ADM are not evaluated beyond clinical and enzymatic studies, many feel that the ADM in patients represents a
systemic process requiring systemic therapies. There are also a fair number of patients whose myositis resolves after therapy, but whose skin manifestations remain active, becoming the most important feature of the disease. These patients have post-myopathic DM, and the skin is the major and often the only site of manifestation of the disease. There is also a small subset of patients who never develop myositis, despite having prominent cutaneous changes, and it is these patients who can be classified as having ADM assuming that they have not received systemic corticosteroids or immunosuppressive agents.

Patients with DM are at times difficult to distinguish from patients with subacute cutaneous LE. The lesions of DM differ slightly in their distribution, occurring more over bony prominences, and they are frequently accompanied by severe pruritus, whereas LE lesions tend to occur between the knuckles and are usually asymptomatic. The facial distribution of LE and DM also differ with LE, usually sparing the nasolabial folds and eyelids, whereas DM frequently involves these areas. Routine skin biopsy is not helpful in the distinction between LE and DM. Immunofluorescence microscopy should be negative in DM and positive in LE; however, about 50% of patients with subacute cutaneous LE have a negative immunofluorescence microscopy, and immunofluorescence microscopy may be falsely positive on sun-exposed skin. Serologic testing is also imperfect because only 25% to 30% of patients with DM are Mi-2–positive, and on a single testing, only 60% to 70% of patients with subacute cutaneous LE are Ro (SS-A) antibody-positive.

The skin lesions of DM are probably photoaggravated despite the lack of symptoms suggestive of photosensitivity reported by patients. Clinical observations suggest that not only is the skin disease exacerbated by light, but muscle disease may be worsened after sun exposure. Photo-testing has however not been able to reliably reproduce the skin lesions; thus, the wavelength of light that is responsible for the clinical manifestations (action spectrum) is not known.

Rare cutaneous manifestations include vesiculobullous lesions, an eruption that simulates pityriasis rubra pilaris, vasculitis, erosive lesions, as well as an exfoliative erythroderma. In small case series, it has been suggested that some of these cutaneous manifestations may be more common in patients with an associated malignancy.

A variety of other cutaneous lesions have been described in patients with DM or PM that do not reflect the interface changes observed histopathologically with the pathognomonic or characteristic lesions. These include panniculitis, plaquelike mucinosis, scleromyxedema-like papular lesions (Fig. 9), a flagellate eruption, urticaria, as well as changes of hyperkeratosis of the palms known as mechanics hands. Lastly, children with DM may develop calcinosis, but, in addition, insulin resistance and lipodystrophy have recently been reported as a relatively common complication despite adequate therapy.

Fig. 7 Marked periungual telangiectasia and cuticular overgrowth are present in a patient with DM.

Fig. 8 Erythematous to violaceous, scaly diffuse alopecia is characteristic of DM. This eruption was extraordinarily pruritic.

Fig. 9 Papular mucinosis-like lesions in a patient with DM. Prominent papular lesions are present within the poikilodermatous eruption. Histopathology revealed deposition of massive amounts of mucin in the dermis.
Skin lesions of DM may precede the development of myopathy and may persist well after the control and quiescence of the myositis. Patients’ skin lesions may flare with sun exposure, but only some of these patients will have a flare of their muscle involvement. Thus, in many instances, the course of the skin lesions does not parallel that of the muscle disease.

**Muscle disease**

Clinical and laboratory abnormalities suggestive of muscle disease are characteristic features of DM. The myopathy primarily affects the proximal muscles, is usually symmetrical, and is slowly progressive over a period of weeks to months. Initial complaints include myalgias, fatigue, or weakness manifested as an inability to climb stairs, to raise the arms for actions like hair grooming or shaving, to rise from a squatting or sitting position, or a combination of these features. Myalgia and tenderness upon palpation of the muscles are not common. An inability to swallow and symptoms of aspiration may reflect the involvement of striated muscle of the pharynx or upper esophagus. Dysphagia or dysphonia generally signifies a rapidly progressive course and may be associated with poor prognosis.

**Systemic features**

Dermatomyositis is a multisystem disorder. Arthralgias and/or arthritis may be present in up to one fourth of patients with inflammatory myopathy. The usual picture is one of generalized arthralgias accompanied by morning stiffness. The small joints of the hands, wrists, and ankles may be involved with symmetrical non-deforming arthritis that is non-erosive.

Esophageal disease as manifested by dysphagia is estimated to be present in 15% to 50% of patients with inflammatory myopathy. The dysphagia can be of 2 types: proximal dysphagia or distal dysphagia. Proximal dysphagia is caused by involvement of striated muscle in the pharynx or proximal esophagus. This involvement correlates well with the severity of the muscle disease and is steroid-responsive. Distal dysphagia results from dysmotility due to involvement of nonstriated muscle and appears to be more frequent in patients who have an overlap with scleroderma or another collagen vascular disorder. Dysphagia is associated with a poor prognosis and correlates with the presence of pulmonary involvement.

Pulmonary disease occurs in DM and PM in approximately 15% to 65% of patients. Interstitial pneumonitis is a primary process observed in DM/PM. Kang et al have demonstrated that interstitial lung disease also occurs in patients with ADM, and in this subset of idiopathic inflammatory myopathy the survival of patients is poor. Pulmonary involvement is more frequent in patients with esophageal dysfunction. Lung disease may also occur as a direct complication of the muscle disease, such as hypoventilation or aspiration in patients with dysphagia, or may be a result of treatment, as with opportunistic infections or drug-induced hypersensitivity pneumonitis. In a retrospective review of 70 patients with myositis-associated interstitial lung disease seen at Mayo Clinic between 1990 and 1998, most presented with either symptoms of lung disease or symptoms of myositis alone, with only 15 in whom the involvement occurred simultaneously. In general, the lung disease was at first felt to be a pneumonitis that was antibiotic-resistant. Nonspecific interstitial pneumonitis or diffuse alveolar damage was observed in a majority of those who were biopsied. Only 2 patients had bronchiolitis obliterans with organizing pneumonia. It is unclear how many of the 70 patients had DM, but perhaps between 8 and 12 of the entire group with interstitial lung disease had DM. Therapy for the patients with myopathy and lung disease included corticosteroids with or without an immunosuppressive agent; however, the prognosis is poorer for patients in whom lung disease is present than unselected patients with myositis as demonstrated by a 5-year survival of only 60.4% for patients with lung disease. Patients with Jo-1 antibodies (19 of 50 who were tested) had roughly the same features and prognosis as those who did not have this antibody.

Clinically symptomatic cardiac involvement in patients with DM or PM is uncommon, but when present it is associated with a poor prognosis. Conduction defects and rhythm disturbances are the most common cardiac manifestations. Although congestive heart failure, pericarditis, and valvular disease may occur, they are much less frequent. Depending on the report, cardiac manifestations may occur in up to 50% of patients, but only a small proportion of these patients manifest symptoms. It is not known whether the identification of asymptomatic abnormalities has an effect on long-term outcome, or even if the findings are more prevalent in DM/PM than in an age-matched control group.

Calcination of the skin or muscle is unusual in adults, but may occur in up to 40% of children or adolescents with DM. Calcification is manifested by firm, yellow, or flesh-colored nodules, often over bony prominences. Occasionally, these nodules can extrude through the surface of the skin, in which case secondary infection may occur. Calcification of the muscles is often asymptomatic and may be seen only on radiologic examination. In severe forms, the calcinosis can cause loss of function, and, rarely bone formation is possible.

**Myositis and malignancy**

The relationship of DM-PM to malignancy has been recently clarified. The reported frequency of malignancy in DM has varied from 6% to 60% with most large population-based cohort studies revealing a frequency of about 20% to 25%.

Several Scandinavian studies have documented the increased frequency of malignancy in DM over the general
Although patients with PM had a slight increase in cancer frequency, it was not highly significant and could be explained by a more aggressive cancer search (known as diagnostic suspicion bias). These studies have not dealt with the ADM subset, but data from the Mayo Clinic suggest that these patients may also have an associated malignancy. Malignancies may occur before the onset of myositis, concurrently with myositis, or after the onset of DM. In addition, the myositis may follow the course of the malignancy (a paraneoplastic course) or may follow its own course independent of the treatment of the malignancy. Studies demonstrating benefits of cancer surgery on myositis as well as those showing no relationship of the myositis to the malignancy have been reported.

A wide variety of malignancies have been reported in patients with DM. Gynecologic malignancy, particularly ovarian carcinoma, may be overrepresented in DM. Asians with DM are often found to have nasopharyngeal cancer. In the recent analysis of combined data from Scandinavia, Hill et al again noted the increased association of ovarian cancer, but also noted increases in lung, pancreatic, stomach, colorectal cancer, and non-Hodgkin’s lymphoma. Malignancy is more common in older patients (>50 years), but reports on young adults and rarely even children with DM have appeared, suggesting that age alone should not dissuade the physician from a careful evaluation (see below). The site of malignancy can be predicted by the patient’s age and sex (eg, malignancy in a young man is more often testicular cancer, whereas in an elderly man, colon or prostate cancer would be more common). In the past, there was concern about whether the use of immunosuppressive therapies would predispose the patient to an excess cancer risk. This has not proven to be the case with most cancers being reported within the first 3 years after diagnosis.

Juvenile (childhood) DM

Dermatomyositis is much more common than PM in children and adolescents. Although a fulminant course may occur, most often the onset is indolent and follows a viral infection or presumed “dermatitis.” Delayed diagnosis is more common in the nonwhite population and is associated with a poorer prognosis. Major differences of juvenile DM from adult DM include the greater potential for calcinosis, the presence of vascular inflammation, and the potential for lipodystrophy accompanied by insulin resistance. A recent report detailed the chronic nature of this disease in children, with many patients requiring therapy to suppress their disease activity more than 3 years after diagnosis. In addition, it was noted that the development of calcinosis was not related to initial therapy, but was associated with a lower score on an assessment instrument of physical function. Pachman et al linked the presence of calcinosis and a prolonged course of disease with TNFα-308A allele in their patients with juvenile DM.

Drug-induced DM

The etiology of most cases of DM is unknown; however, in a small number of patients, the cutaneous manifestations are due to or are exacerbated by drugs. This has been best documented for hydroxyurea in which de-challenges and re-challenges have been performed. Quinidine, nonsteroidal anti-inflammatory drugs, T-penicillamine, isoniazid and 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors, and most recently TNF antagonists have also been linked on occasion to DM.

Diagnosis and evaluation of the patient with DM

The diagnosis of DM is suspected in patients with clinically compatible cutaneous findings. Exclusion of other possible cutaneous conditions is aided by skin biopsy and the recognition of muscle involvement. In the absence of identifiable myopathy, the differentiation from cutaneous LE may be difficult. Muscle weakness may be caused by many other disorders including toxins, infections, metabolic abnormalities, and neurologic disorders. The presence of characteristic skin lesions however allows the diagnosis to be more firmly established.

Muscle involvement is suspected clinically. Enzymatic testing will reveal enzyme elevations of creatine kinase, aldolase, lactic dehydrogenase, or alanine aminotransferase. Creatine kinase and lactic dehydrogenase are the most useful tests for following response to therapy. Additional testing including electromyography, muscle biopsy, ultrasound, or magnetic resonance imaging may be ordered in patients in whom other tests are inconclusive. Many pediatric rheumatologists will feel comfortable diagnosing juvenile DM without a muscle biopsy. Those of us in dermatology feel comfortable diagnosing DM when there are classic or compatible cutaneous findings, proximal muscle weakness, and elevated muscle-derived enzymes. In such patients, further muscle tests including electromyography and biopsy can be omitted. Many rheumatologists prefer to search for evidence of muscle inflammation using these techniques and/or magnetic resonance imaging.

Serologic tests are often ordered, but their clinical application is at best controversial. Antinuclear antibody testing is frequently positive in patients with DM. Several myositis-specific antibodies have been recognized and correlate with certain subsets. Most myositis-specific antibodies are described in patients with PM and will not be further discussed here. Anti–Jo-1 antibody (and the 6 other antisynthetase autoantibodies) is predictive of pulmonary involvement and is much more common in patients with PM than in those with DM. Anti–Mi-2 occurs in roughly 25% to 30% of patients with DM, and although
almost specific for DM, it is not sensitive. Recently, Targoff et al. described a new antibody to a 155-kd antigen or Se antigen (90-95 kd) that appears to be a marker of ADM (16 of 18 patients studied). The anti-155-kd antibody may also be associated with juvenile DM and might predict a chronic course. Anti-Ro (SS-A) antibody may occur rarely. When other antibodies such as PM-SCL or U1-RNP are present, an overlap syndrome is suggested. With some exceptions, patients with antisynthetase antibody syndromes respond only partially to therapy, but often do not gain remission. Those with anti-SRP antibodies have the worst prognosis and those with anti–Mi-2 antibodies appear to have the best prognosis. Perhaps as further studies are performed, serologic testing for myositis-specific antibodies will become clinically useful. Until then, these tests are primarily reserved for investigation.

Markers of activity in DM have not been consistent. In children with DM, it was suggested that elevated von Willebrand factor was associated with active disease. Komiya et al. analyzed von Willebrand factor in adults and found that elevated levels occurred in patients with active disease and were associated with weakness, fatigue, and fever. In a small subset of their patients the von Willebrand factor decreased with successful corticosteroid therapy.

Once the diagnosis is confirmed, the patient should have a thorough evaluation. Evaluation has several purposes: assessment of severity, prediction of prognosis, and identification of associated disorders. The severity of the myositis often correlates with enzyme levels and degree of weakness. Patients should be assessed for esophageal, pulmonary, and cardiac involvement with tests such as a swallowing evaluation and/or esophageal motility studies, chest X ray, pulmonary function studies including diffusion studies, and an electrocardiogram.

An evaluation of malignancy should be considered in all adult patients with DM. The type of evaluation is selected based upon the patient’s age and sex. The likelihood of malignancy increases with age and the sites vary depending on the patient’s age. Malignancy evaluation is repeated with new symptoms or annually for the first 3 years after diagnosis. The overrepresentation of cancer in these patients seemingly approaches normal levels after 3 years; thus, age- and sex-specific malignancy screening, along with evaluation of any new symptoms or findings, is recommended for following patients more than 3 years after the initial diagnosis.

Course and therapy

Several general measures are helpful in treating patients with DM. Bed rest is often valuable in the individual with progressive weakness; however, this must be combined with a range-of-motion exercise program to prevent contractures. Patients who have evidence of dysphagia should have the head of their bed elevated and should avoid eating meals immediately before retiring.

Corticosteroids and immunosuppressive agents

The mainstay of therapy for DM is the use of systemic corticosteroids. Traditionally, prednisone is given at a dose of 0.5 to 1 mg/kg daily as initial therapy. The treatment should continue for at least 6 weeks after the myositis has become clinically and enzymatically inactive. At this point, the dose is slowly tapered, generally over a period lasting one and a half to two times as long as the period of active treatment. Approximately 25% of patients with DM will not respond to systemic corticosteroids, and another 25% to 50% will develop significant steroid-related side effects. Therefore, early intervention with steroid-sparing, primarily immunosuppressive agents, such as methotrexate, azathioprine, cyclophosphamide, mycophenolate mofetil, chlorambucil, or cyclosporin, may be an effective means of inducing or maintaining a remission.

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Additional therapeutic options

Patients who fail to respond to these immunosuppressives may respond to pulse methylprednisolone therapy, combination immunosuppressive therapy, etanercept, infliximab, or rituximab. Early enthusiasm for plasmapheresis was followed by a placebo-controlled study that failed to demonstrate effectiveness. In a double-blind, placebo-controlled study, however, Dalakas and co-workers demonstrated the benefits of high-dose intravenous immune globulin for recalcitrant DM. Further open-label studies have demonstrated similar results. In addition, intravenous immune globulin (IVIG) has been used safely in patients with DM who became pregnant. Tachyphylaxis can however develop with repeated IVIG infusions.

Lung disease is a frequent complication of DM and in many reports has been associated with significant morbidity and mortality. Recent reports have focused on several “aggressive” therapies to manage these patients including tacrolimus, combination therapy with corticosteroids, cyclosporin and cyclophosphamide, azathioprine, and autologous peripheral blood stem cell transplantation.

Management of cutaneous disease

Therapy for cutaneous disease in patients with DM is often difficult because, although the myositis may respond to treatment with corticosteroids and/or immunosuppressive drugs, the cutaneous lesions often persist. Although

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Therapy for cutaneous disease in patients with DM is often difficult because, although the myositis may respond to treatment with corticosteroids and/or immunosuppressive drugs, the cutaneous lesions often persist. Although
cutaneous disease may be of minor importance in patients with serious fulminant myositis, in many patients, cutaneous disease becomes the most important aspect of their disorder. Most patients with cutaneous lesions are photosensitive; thus, the daily use of a broad-spectrum sunscreen with a high sun-protective factor is recommended. Topical therapy with an appropriately selected corticosteroid or nonsteroidal immunomodulators such as tacrolimus ointment (0.1%) or pimecrolimus cream (1%) may be useful adjunctive therapy.\(^9^9\) Hydroxychloroquine HCl in dosages of 200 to 400 mg/d is effective in approximately 80% of patients treated with a steroid-sparing agent.\(^9^0\) Patients who do not respond well to hydroxychloroquine can be switched to chloroquine phosphate 250 to 500 mg/d or can have quinacrine HCl 100 mg twice daily added to the regimen. Patients on continuous antimalarial therapy should have periodic ophthalmologic examinations and blood counts. It appears that patients with DM have a greater frequency of drug eruptions from antimalarials; thus, patients should be warned about this possibility.\(^9^1\)

Other nonsteroidal therapies that have been used for patients with cutaneous lesions of LE such as dapsone, clofazimine, or thalidomide have either not been tried or not been effective. Methotrexate in doses of 15 to 35 mg/wk has been reported to be useful for skin lesions of DM.\(^9^2,9^3\) These studies, however, are uncontrolled, open-label observations. The need for routine liver biopsy in the patient with DM treated with methotrexate is controversial, but patients who do not drink excessive amounts of alcohol, are not obese, nondiabetic, and have normal liver function tests probably do not require periodic liver biopsies.

Mycophenolate mofetil has recently been reported to be of use in patients with “recalcitrant” cutaneous disease in several studies.\(^9^4\) Mycophenolate mofetil is usually begun without changing concomitant therapies in a dose of 1 g twice daily and is advanced to 1.5 g twice daily if tolerated during the first several weeks. It appears to have a slow onset of action, and, therefore, the concomitant therapy should only be reduced after 4 to 8 weeks as response is noted. Mycophenolate mofetil may be used alone or, in some instances, has been used in conjunction with methotrexate (JPC, unpublished observations). A recent report by Rowin et al.\(^7^3\) demonstrated that 6 of 10 patients with DM treated with mycophenolate mofetil (MMF) were able to taper their steroid dosage. Three of their patients had opportunistic infections that led to death in 1 patient; however, their patients were on much higher doses of MMF than those of Edge et al.\(^9^4\) Other immunosuppressive agents have not been systematically studied as treatment of cutaneous lesions of DM. In addition, there is anecdotal information suggesting that some of the TNF-\(\alpha\) antagonists might be useful.\(^9^5\) The use of rituximab has not been reported to be of benefit for the cutaneous component of DM thus far,\(^9^6\) but can have a profound effect on the muscle involvement. Lastly, intravenous immune globulin administered monthly can result in the clearing of cutaneous lesions in patients.

Calcinosis is a complication of disease in children and adolescents. This process may be prevented by aggressive early treatment. Preliminary analysis of the use of intravenous methylprednisolone suggested that this therapy might lessen the frequency and severity of this process.\(^7^5\) In addition, Pachman et al.\(^7^7\) have presented data that suggest that delay in diagnosis is a major factor in the potential for the development of calcinosis. Others have suggested that immunosuppressives may similarly reduce the chance of calcinosis.\(^9^8\) Once established, calcinosis is difficult to treat. Although possible, spontaneous regression is unusual. Individual patients have been treated with low-dose warfarin or oral aluminum hydroxide; however, no studies have documented the usefulness in larger groups of patients. Recent reports of long-term administration of diltiazem are promising.\(^9^9\) Lastly, a recent report detailed the use of alendronate in a single patient.\(^1^0^0\)

**Prognosis**

The prognosis of DM varies greatly, depending on the series of patients studied. Factors that affect prognosis include the patient’s age, the severity of myositis, the presence of dysphagia, the presence of cardiopulmonary disease, the presence of an associated malignancy, and the response to corticosteroid therapy.\(^1^0^1\) It seems to be well established by retrospective reports that the use of corticosteroids and/or immunosuppressive therapies improves the prognosis.

**Conclusions**

Dermatomyositis is a condition primarily of the skin and muscles, but other systemic features may occur. Dermatomyositis is the most common presentation of inflammatory muscle disease in children. Whereas dermatomyositis also occurs in adults, individuals in this age group may also have inflammatory muscle diseases (polymyositis or inclusion body myositis) that do not have cutaneous manifestations. The pathogenesis of the muscle disease is becoming better understood, but the cutaneous disease mechanisms remain enigmatic. Dermatomyositis in adults is associated with malignancy, and, thus, a careful evaluation of each patient should be part of their initial and follow-up assessments. Patients should also be evaluated for the presence of esophageal, pulmonary, and cardiac disease. Calcinosis is more frequent in children with DM, and early aggressive therapy may limit the chance of this complication. Corticosteroids, immunosuppressives, biologic agents, and/or immune globulin are effective therapies for the myopathy of DM, whereas the skin disease is best managed with sun protection, topical corticosteroids, antimalarials, methotrexate, and/or immune globulin. The prognosis is good except for patients with malignancy, those with severe weakness,
and those with cardiac dysfunction, interstitial lung disease, or the presence of a myositis-specific autoantibody other than Mi-2.

References


68. Callen JP. When and how should the patient with dermatomyositis or amyopathic dermatomyositis be assessed for possible cancer? Arch Dermatol 2002;138:969-971.


79. Saadeh CK. Etanercept is effective in the treatment of polymyositis/dermatomyositis which is refractory to conventional therapy including steroids and other disease modifying agents. Arthritis Rheum 2000;43:S193A.


