eMedicine Specialties > Dermatology > Connective Tissue Diseases

Dermatomyositis

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Updated: Apr 13, 2009

Introduction

Background

Dermatomyositis (DM) is an idiopathic inflammatory myopathy (IIM) with characteristic cutaneous findings. Dermatomyositis is a systemic disorder that frequently affects the joints, the esophagus, the lungs, and, less commonly, the heart.[1,2]

In 1975, Bohan and Peter[3] first suggested a set of criteria to aid in diagnosing and classifying dermatomyositis and polymyositis (PM). Of the 5 criteria, 4 relate to the muscle disease; these include progressive proximal symmetrical weakness, elevated muscle enzyme levels, abnormal findings on electromyograms, and abnormal findings from muscle biopsy. The fifth criterion is compatible cutaneous disease.

Bohan and Peter suggested 5 subsets of myositis: dermatomyositis, polymyositis, myositis with cancer, childhood dermatomyositis/polymyositis, and myositis overlapping with another collagen vascular disorder. In a subsequent publication, Bohan and Peter[4] noted that cutaneous disease might precede the development of the myopathy; however, only recently was another possible subset of patients with disease that affects only the skin recognized; this condition is known as amyopathic dermatomyositis (ADM), or dermatomyositis sine myositis. The association between dermatomyositis (and possibly polymyositis) and cancer has long been recognized.[5,6,7,8]

Dermatomyositis sine myositis, also known as amyopathic dermatomyositis, is diagnosed in patients with typical cutaneous disease in whom no evidence of muscle weakness exists and in whom serum muscle enzyme levels are repeatedly normal for a 2-year period in the absence of disease-modifying therapies such as corticosteroids, immunosuppressive agents, or both. When studied, some patients with amyopathic dermatomyositis have abnormal ultrasound, MRI or magnetic resonance spectroscopy, or muscle biopsy findings. These patients have muscle involvement, and their condition may be better classified as hypomyopathic dermatomyositis. Patients with these variations may also reflect an underlying malignancy, and some develop severe pulmonary disease, particularly persons from Asian countries.

Patients exist in whom myositis resolves following therapy but whose skin disease remains as an active, important feature of the disease. These patients are not classified as having amyopathic dermatomyositis, despite the fact that, at this point in time, the skin is the major and often only manifestation of the disease. Sontheimer[9] has suggested the term postmyopathic dermatomyositis for these patients.

Rare cutaneous manifestations include vesiculobullous, erosive lesions, and an exfoliative erythroderma. Biopsy samples from patients reveal an interface dermatitis similar to that of biopsy samples of heliotrope rash, Gottron papules, poikiloderma, or scalp lesions. These cutaneous manifestations may be more common in patients with an associated malignancy than in those without a malignancy.

Also see the eMedicine Rheumatology article Dermatomyositis and the Neurology article Dermatomyositis/Polymyositis.

Pathophysiology

Studies of the pathogenesis of the myopathy have demonstrated that the myopathy in dermatomyositis and polymyositis are pathogenetically different.[10] Dermatomyositis-associated myopathy appears to be due to vascular inflammation. The pathogenesis of the cutaneous disease is poorly understood, but it is believed that similarities exist with that of cutaneous lupus erythematosus, in which T-cells are involved and antibody-mediated cell cytotoxicity plays a role.

Frequency

United States

The estimated incidence of dermatomyositis/polymyositis is 5.5 cases per million population. However, the incidence appears to be increasing.

Mortality/Morbidity

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Mortality/Morbidity

Dermatomyositis may cause death because of muscle weakness or cardiopulmonary involvement. Patients with an associated cancer may die from the malignancy. Most patients with dermatomyositis survive, in which case they may develop residual weakness and disability. In children with severe disease, contractures can develop if they do not receive physical therapy. Calcinosis may be a complication, particularly in children.

Race

Whites are more frequently affected. However, the rise in the incidence in African Americans is greater than that in whites.

Sex

Women are affected twice as often as men.

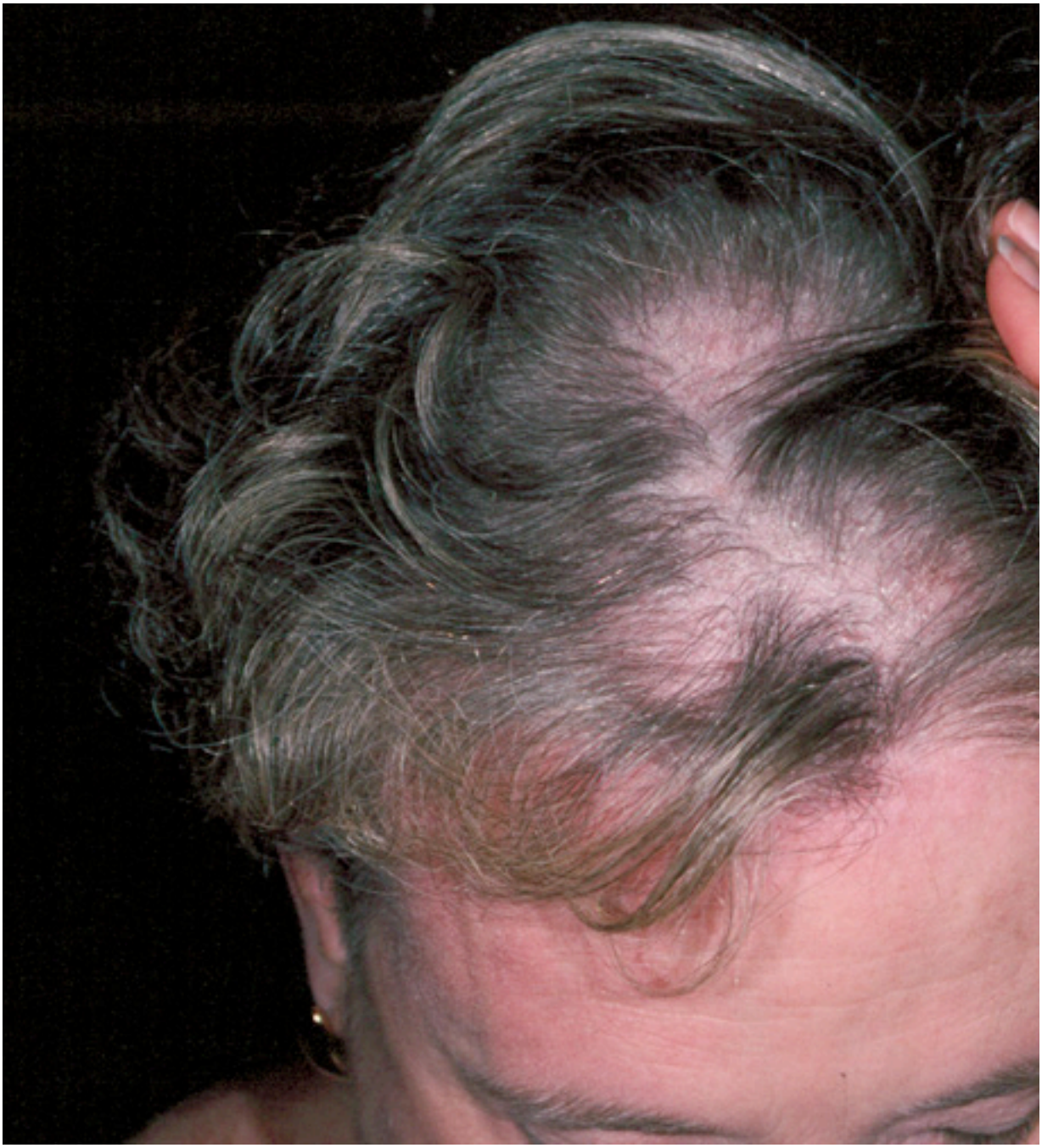
Age

Dermatomyositis can occur in persons of any age, but the most common age at onset is in the fifth and sixth decades of life.

Clinical

History

- Patients often present with skin disease as one of the initial manifestations. In as many as 40% of patients, the skin disease may be the sole manifestation at the onset. Muscle disease may occur concurrently, it may precede the skin disease, or it may follow the skin disease by weeks to years.
- Patients often notice an eruption on exposed surfaces. The disease is often pruritic, and, sometimes, intense pruritus may disturb sleep patterns. Patients may also complain of a scaly scalp or diffuse hair loss[11] (see Media File 5).



A diffuse alopecia with a scaly scalp dermatosis is common in dermatomyositis.

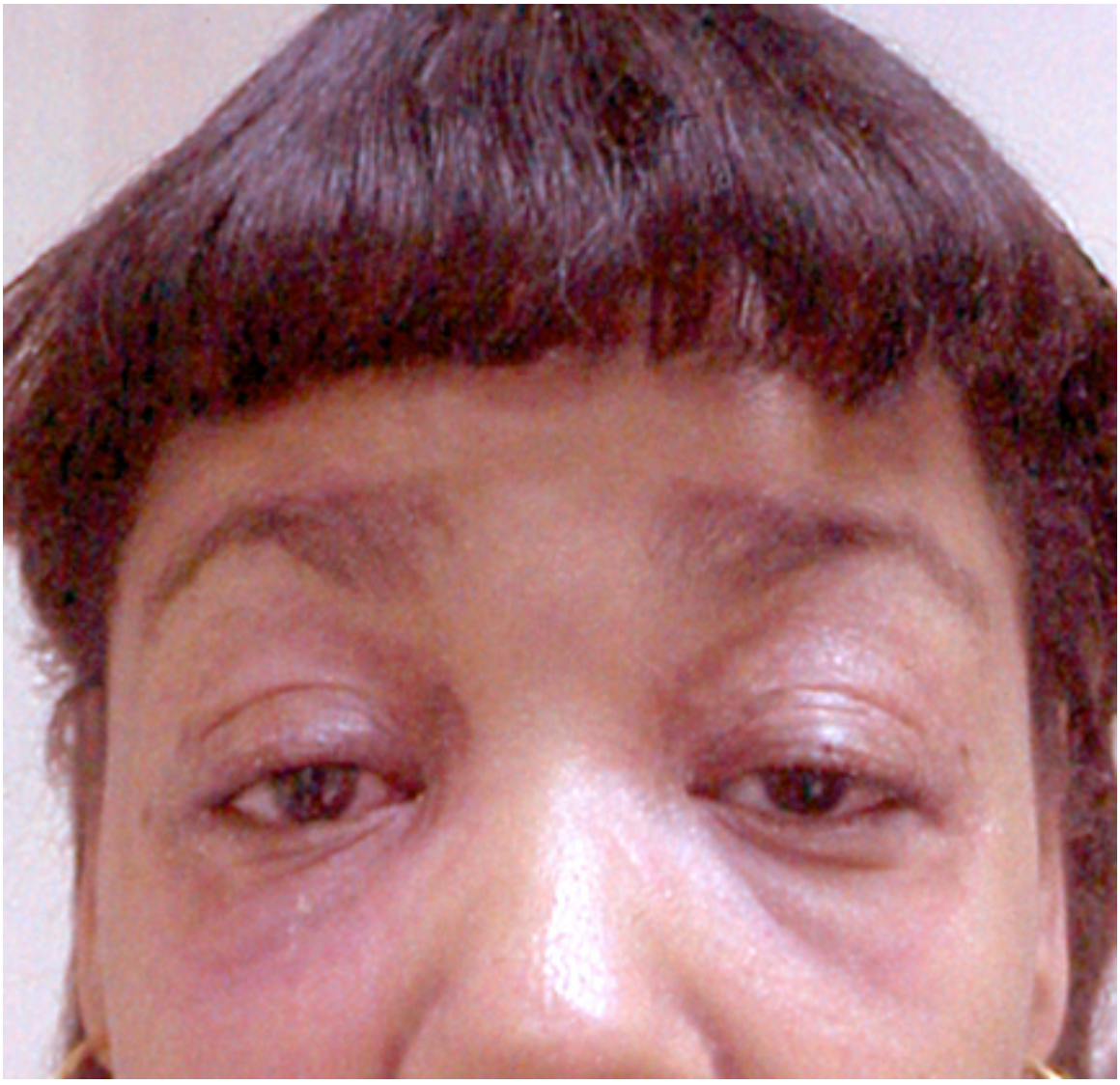
- Muscle involvement manifests as proximal muscle weakness. Patients often begin to note fatigue of their muscles or weakness when climbing stairs, walking, rising from a sitting position, combing their hair, or reaching for items in cabinets that are above their shoulders. Muscle tenderness may occur, but it is not a regular feature of the disease.
- Systemic manifestations may occur; therefore, a review of systems should assess for the presence of arthralgias, arthritis, dyspnea, dysphagia, arrhythmias, and dysphonia.
- Malignancy is possible in any patient with dermatomyositis, but it is much more common in adults older than 60 years. Only a handful of children with dermatomyositis and malignancy have been reported. The history should include a thorough review of systems, as well as an assessment for previous malignancy.

- Children with dermatomyositis may have an insidious onset that hides the true diagnosis until the dermatologic disease is clearly observed and diagnosed. Calcinosis is a complication of juvenile dermatomyositis, but it is rarely observed at the onset of disease. African Americans and patients in lower socioeconomic groups are more likely to have a delay in their diagnosis. The prognosis in children with dermatomyositis is worse in those in whom diagnosis is delayed.
- Several reports describe drug-induced dermatomyositis or existing dermatomyositis exacerbated by certain drugs, including statins and interferon therapy,

Physical

Dermatomyositis is a disease that primarily affects the skin and the muscles, but it might also affect other organ systems.

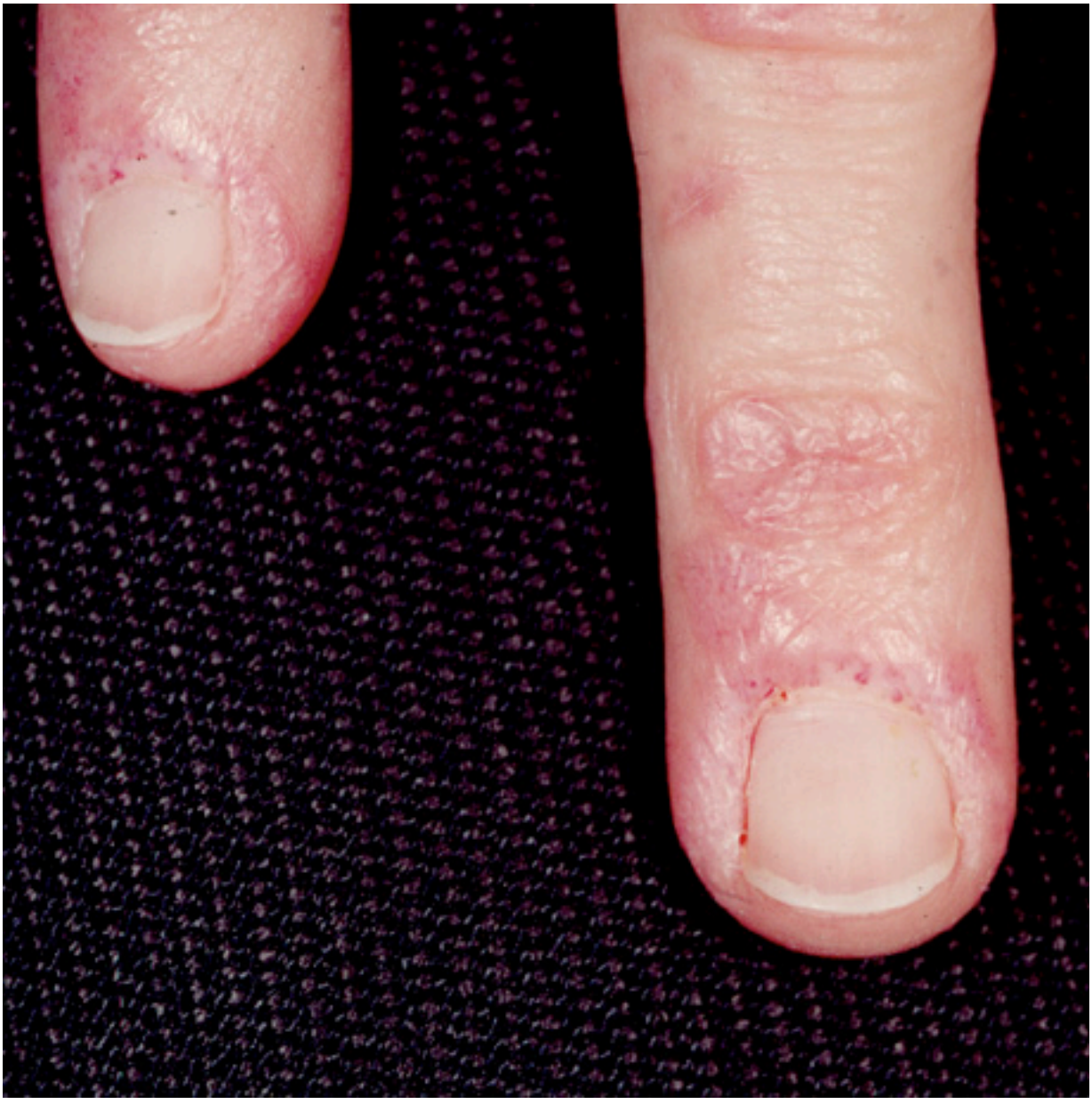
- The characteristic and possibly pathognomonic cutaneous features of dermatomyositis are the heliotrope rash and Gottron papules (see Media File 2). Several other cutaneous features are characteristic of the disease despite not being pathognomonic. They include malar erythema, poikiloderma in a photosensitive distribution, violaceous erythema on the extensor surfaces, and periungual and cuticular changes.



Heliotrope rash in a woman with dermatomyositis.

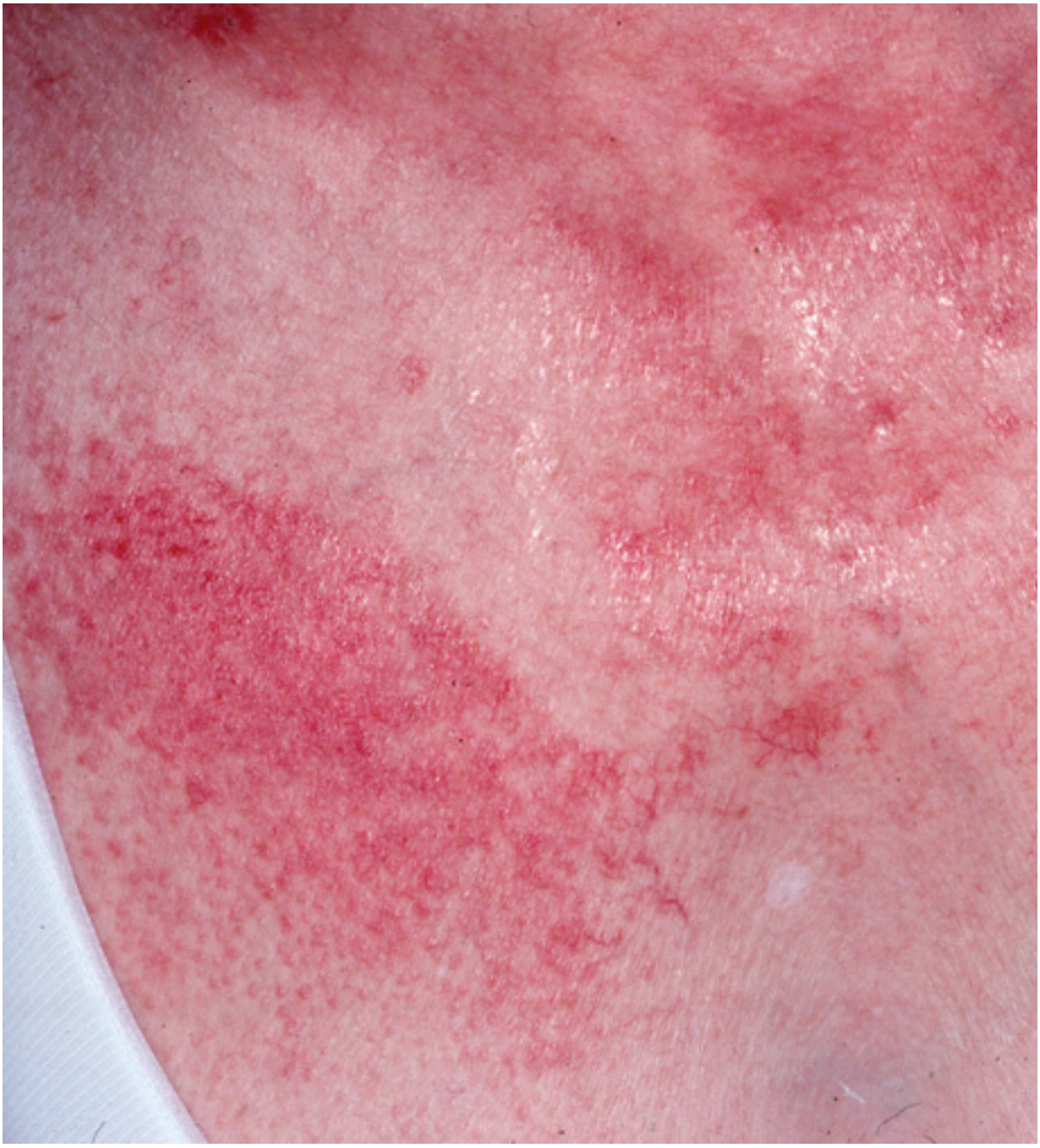
- The heliotrope rash consists of a violaceous to dusky erythematous rash with or without edema in a symmetrical distribution involving the periorbital skin. Sometimes, this sign is subtle and may consist of only a mild discoloration along the eyelid margin. Similar to other areas, scale may be present on the eyelids. A heliotrope rash is rarely observed in other disorders; therefore, its presence is highly suggestive of dermatomyositis.
- Gottron papules are found over bony prominences, particularly the metacarpophalangeal joints, the proximal interphalangeal joints, and/or the distal interphalangeal joints. They may also be found overlying the elbows, the knees, and/or the feet. The lesions consist of slightly elevated, violaceous papules and plaques. A slight scale may be present, and, occasionally, a thick psoriasiform scale is observed. These lesions may resemble lesions of lupus erythematosus, psoriasis, or lichen planus (LP).

- Nail fold changes consist of periungual telangiectases and/or a characteristic cuticular change with hypertrophy of the cuticle and small, hemorrhagic infarcts in this hypertrophic area (see Media File 3). Periungual telangiectases may be clinically apparent, or they may be appreciated only by capillary microscopy.



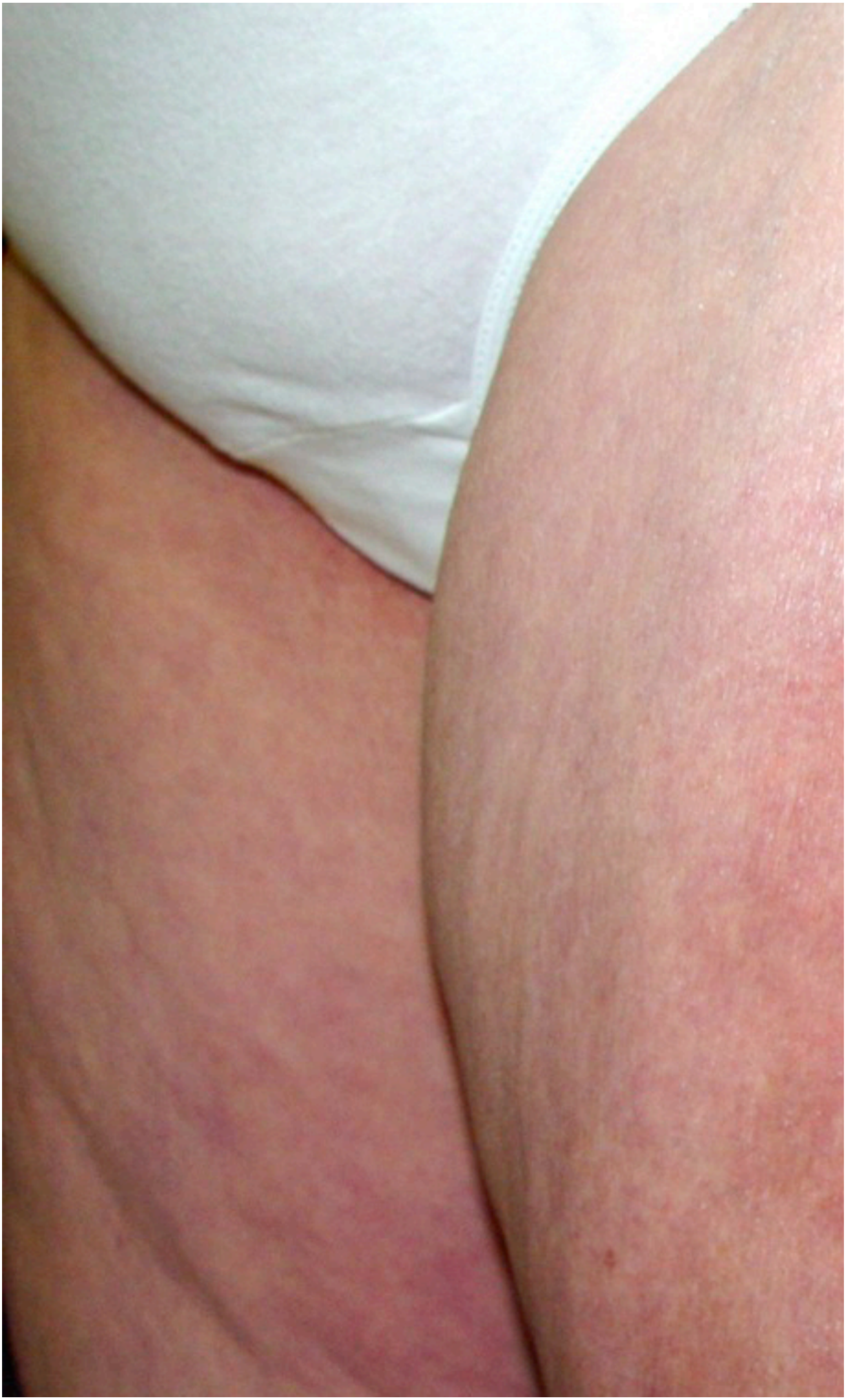
Gottron papules and nail fold telangiectasia are present in this patient.

- Poikiloderma may occur on exposed skin, such as the extensor surfaces of the arm, the V of the neck (see Media File 6), or the upper part of the back (Shawl sign).



Dermatomyositis is often associated with a poikiloderma in a photodistribution.

- With the exception of the heliotrope rash, the eruption of dermatomyositis is photodistributed and photoexacerbated. Patients rarely complain of photosensitivity, despite the prominent photodistribution of the rash.
- Facial erythema may also occur in dermatomyositis. This change must be differentiated from lupus erythematosus, rosacea, seborrheic dermatitis, or atopic dermatitis. A study from Japan highlighted the finding of disease on the face that mimicked seborrhea.[12]
- Scalp involvement in dermatomyositis is relatively common and manifests as an erythematous to violaceous, psoriasiform dermatitis. Clinical distinction from seborrheic dermatitis or psoriasis is occasionally difficult. In some patients, nonscarring alopecia may occur and often follows a flare of systemic disease.
- Other cutaneous lesions have been described in patients with dermatomyositis or polymyositis that do not reflect the interface changes observed at histopathologic examination with pathognomonic or characteristic lesions. These include panniculitis (see Media File 9) and urticaria, as well as changes of hyperkeratosis of the palms known as mechanic's hands. Other findings include cutaneous mucinosis, follicular hyperkeratosis, hyperpigmentation, ichthyosis, white plaques on the buccal mucosa, cutaneous vasculitis, and a flagellate erythema.



Calcifying panniculitis in a patient with dermatomyositis.

- Calcinosis of the skin or the muscle is unusual in adults, but it may occur in as many as 40% of children or adolescents with dermatomyositis. Calcinosis cutis manifests as 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.[13]
- Muscle findings include weakness and, sometimes, tenderness.
    - Muscle disease manifests as a proximal symmetrical muscle weakness. Patients may have difficulty rising from a chair or squatting and then raising themselves from this position. Sometimes, in an effort to rise, patients use other muscles that are not as affected. The careful examiner may note this finding.
    - Testing of the muscle strength is part of each assessment of the patient. Often, the extensor muscles of the arms are more affected than the flexor muscles.
    - Distal strength is almost always maintained. Muscle tenderness is a variable finding.
- Other systemic features include joint swelling, changes associated with Raynaud phenomenon, and abnormal findings on cardiopulmonary examination.
    - Joint swelling occurs in some patients with dermatomyositis. The small joints of the hands are the most frequently involved. The arthritis associated with dermatomyositis is nondeforming.
    - Patients with pulmonary disease may have abnormal breath sounds.
    - Patients with an associated malignancy may have physical findings relevant to the affected organs.

Causes

- The cause of dermatomyositis is unknown. Factors that have been implicated are listed below.
    - A genetic predisposition may exist. Rarely, dermatomyositis manifests in multiple family members. However, a link to certain HLA types may exist. Polymorphisms of tumor necrosis factor may be involved; specifically, the presence of the -308A allele is linked to photosensitivity in adults and calcinosis in children.[13,14,15]
    - Immunologic abnormalities are common in patients with dermatomyositis. Patients frequently have circulating autoantibodies. Abnormal T-cell activity may be involved in the pathogenesis of both the skin disease and the muscle disease. In addition, family members may manifest other diseases associated with autoimmunity.
    - Infectious agents, including viruses (particularly coxsackievirus, echovirus, human T-lymphotropic virus 1 [HTLV-1], and human immunodeficiency virus [HIV]), *Toxoplasma* species, and *Borrelia* species, have been suggested as possible triggers of the disease.
    - Several cases of drug-induced disease have been reported. dermatomyositis-like skin changes have been reported with hydroxyurea in patients with chronic myelogenous leukemia or essential thrombocytosis.[16,17] Other agents that may trigger the disease include penicillamine, statin drugs, quinidine, and phenylbutazone.
    - Dermatomyositis may be initiated or exacerbated by silicon breast implants or collagen injections. However, this evidence is anecdotal and has not been verified in case-control studies.

Differential Diagnoses

CREST Syndrome
Graft Versus Host Disease
Lichen Myxedematosus
Lichen Planus
Lupus Erythematosus, Acute
Lupus Erythematosus, Discoid
Lupus Erythematosus, Subacute Cutaneous
Morphea
Multicentric Reticulohistiocytosis
Parapsoriasis
Pityriasis Rubra Pilaris
Polymorphous Light Eruption
Psoriasis, Plaque
Rosacea
Sarcoidosis
Tinea Corporis
Urticaria, Chronic

Workup

Laboratory Studies

- Muscle enzyme levels are often abnormal at some time in patients with dermatomyositis, except in those with the amyopathic variant. The most common enzyme level to obtain is the creatine kinase level. However, an aldolase level test and other tests, such as aspartate aminotransferase and lactate dehydrogenase tests, may also yield abnormal results. At times, the elevation of the enzyme levels precedes clinical evidence of myositis. Therefore, if a patient who is presumably stable develops an elevation in an enzyme level that was previously normal, the clinician should assess the possibility of a flare of the muscle disease.
- Several serologic abnormalities have been identified, but their routine use has not yet been delineated. As a group, these antibodies have been termed myositis-specific antibodies (MSAs).
    - A positive antinuclear antibody result is common in patients with dermatomyositis.
    - Anti-Mi-2 is highly specific for dermatomyositis, but it lacks sensitivity because only 25% of patients with dermatomyositis demonstrate this abnormality.
    - Anti-Jo-1 and other antisynthetase antibodies are associated with pulmonary involvement, but it is more common in patients with polymyositis than dermatomyositis.
    - Other MSAs include antisignal recognition protein and anti-Ku.

Imaging Studies

- MRI with T2 weighting or magnetic resonance spectroscopy may be useful for assessing the presence of an inflammatory myopathy in patients without weakness. It is also useful in differentiating a steroid myopathy from a continued inflammation. Lastly, it may serve as a guide for selection of a site for muscle biopsy.
- Chest radiography should be obtained at the time of diagnosis and when symptoms develop.
- The barium swallow test allows evaluation of esophageal dysmotility.
- Ultrasonography of the muscles has been suggested for evaluation, but its use has not been widely accepted.

Other Tests

- Pulmonary function studies, including diffusion studies, and electrocardiography may be performed.
- Esophageal manometry or other esophageal studies may be performed in selected patients.
- Electromyography is a means of detecting inflammation of the muscles. At times, it has been useful for the selection of a site for muscle biopsy. This test is less commonly obtained now by dermatologists caring for patients with typical skin lesions.

Procedures

- An age-appropriate evaluation for a possible malignancy should be performed at the time of diagnosis and then annually for the first 3 years. Female patients should be carefully screened for ovarian cancer.[18] After that time, patients should be evaluated for malignancy at intervals similar to any other person of the same age and sex.[19]
- Muscle biopsy, either open biopsy or needle biopsy, may enhance the ability of the clinician to diagnose dermatomyositis. It is also sometimes useful in differentiating steroid myopathy from active inflammatory myopathy when patients have been on corticosteroid therapy but are still weak.

Histologic Findings

Skin biopsy samples reveal an interface dermatitis that is difficult to differentiate from lupus erythematosus. Often, the histologic features of dermatomyositis and lupus erythematosus are identical. Both may contain excessive mucin, and both demonstrate an interface vacuolar dermatitis. Well-formed lesions of discoid lupus erythematosus differ from those of dermatomyositis, but often dermatomyositis and subacute cutaneous lupus erythematosus cannot be differentiated.[20]

Treatment

Medical Care

The therapy for dermatomyositis involves general measures, measures to control the muscle disease, and measures to control the skin disease. In addition, in some patients, treating other systemic manifestations or complications may be necessary.

Therapy of the muscle component involves the use of corticosteroids with or without an immunosuppressive agent. The skin disease is treated by avoiding sun exposure and by using sunscreens, topical corticosteroids, antimalarial agents,[21] and/or methotrexate or mycophenolate mofetil.

- Several general measures are helpful in the care of patients with dermatomyositis. Bedrest is often valuable for those with severe inflammation of the muscles. In patients with muscle weakness, a program of physical therapy is useful in preventing contractures that can be a complication when patients do not fully move their joints. For patients with dysphagia, elevating the head of their bed and having them avoid eating prior to bedtime are helpful. These simple maneuvers may prevent aspiration pneumonitis.
- The mainstay of therapy for the muscle disease is systemically administered corticosteroids. Traditionally, prednisone (0.5-1 mg/kg/d) up to a dose of 60 mg/d is given as initial therapy. The drug should be slowly tapered to avoid relapse of the disease. Because most patients develop steroid-related toxic effects, many authorities administer an immunosuppressive or cytotoxic agent early in the course.[22]
    - Use of drugs such as methotrexate, azathioprine, cyclophosphamide, cyclosporin, mycophenolate mofetil, and chlorambucil has been reported to be steroid sparing in some patients or in small open-label studies.[23,24,25]
    - For conditions that do not improve, the use of monthly high-dose intravenous immune globulin has proved to be beneficial.[26]
    - Rituximab is currently being tested in a large multicenter study sponsored by the US National Institutes of Health (RIM study), and perhaps this agent will be shown to be effective.
- Therapy for the cutaneous disease is often difficult. Patients who present primarily with skin disease (amyopathic dermatomyositis) and those in whom the muscle component is controlled but who still have significant skin disease exist. The first-line of therapy is recognizing that the patient is photosensitive and advising the patient to avoid sun exposure and to use sun protective measures, including broad-spectrum sunscreens. Hydroxychloroquine and chloroquine have been beneficial in small open-label case studies.[27] Methotrexate is also useful.[28] Mycophenolate mofetil has been reported to be useful.[29] Intravenous immune globulin not only benefited the muscle but also cleared the skin lesions in the patients in whom it was used. Rituximab has been used for skin disease, but the results are mixed.[30]
- Efalizumab has been used and may have some benefit.[31] Efalizumab (Raptiva), a drug indicated for psoriasis, is being **withdrawn from the US market** and will no longer be available after June 8, 2009, because of potential risk for progressive multifocal leukoencephalopathy (PML). PML is a rapidly progressive infection of the central nervous system caused by the JC virus that leads to death or severe disability. Demyelination associated with PML is a result from the JC virus infection. JC virus belongs to the genus *Polyomavirus* of the Papovaviridae. PML should be considered in any patient presenting with new-onset neurologic manifestations who have taken efalizumab. For more information, see the Food and Drug Administration MedWatch Safety Alert.
- Aggressive early treatment of the myositis may aid in the prevention of calcinosis. Once established, the process is debilitating in many patients. Although spontaneous remission is possible, it often occurs after many years. The use of the calcium channel blocker diltiazem (240 mg bid) is reportedly associated with gradual resolution of calcinosis in a small number of cases.[32] In addition, the use of an oral bisphosphonate might be helpful.[33]

Surgical Care

- Surgical care is usually not necessary.
- Some patients with local areas of calcinosis may wish to have them surgically removed.

Consultations

- Rheumatologist
- Internal medicine or pediatric specialist, depending on the patient's age
- Neurologist

- Oncologist, medical or surgical, for patients with cancer

Diet

- A well-balanced diet is helpful. Patients with severe inflammation of the muscles may need extra protein to balance their loss.
- Feeding should be avoided prior to bedtime in patients with dysphagia.

Activity

- Activity should be maintained as best as possible. Vigorous physical training should be avoided. Exercises should be used to maintain the patient's range of motion.
- Patients with skin lesions should avoid sun exposure and use sun protective measures.

Medication

The mainstay of therapy for patients with dermatomyositis is systemic corticosteroids.

Corticosteroids

These agents may be used topically for cutaneous disease. Systemic corticosteroids are a mainstay of primary therapy for patients with muscle involvement. Patients with cutaneous disease have a variable response to systemic corticosteroids. Patients with pulmonary involvement may respond, but those with esophageal dysfunction do not respond. Patients with cardiac involvement may respond.

Prednisone (Deltasone, Meticorten, Orasone)

First-line therapy for dermatomyositis. May decrease inflammation by reversing increased capillary permeability and suppressing PMN activity.

Dosing

Adult

1-2 mg/kg/d PO; may use IV pulses on occasion

Pediatric

Administer as in adults; pulsed IV methylprednisolone may be beneficial and may be associated with a lower frequency of calcinosis

Interactions

Ketoconazole, erythromycin, clarithromycin, estrogens, and birth control pills may increase levels
Aminoglutethimide, phenytoin, PB, rifampin, cholestyramine, and ephedrine may decrease levels
Increased drug levels occur with potassium-depleting diuretics (potentiates K+ loss and digitalis toxicity) and cyclosporine
Decreased drug levels occur with isoniazid, insulin (resistance is induced), and salicylates
Monitor anticoagulant therapy and theophylline levels

Contraindications

Absolute: Systemic fungal infection; herpes simplex keratitis; hypersensitivity (usually with corticotropin; occasionally with IV preparations)
Relative: Hypertension; active TB; CHF; prior psychosis; positive intermediate purified protein derivative test; glaucoma; severe depression; dermatomyositis; active PUD; cataracts; osteoporosis; recent bowel anastomosis; pregnancy

Precautions

Pregnancy

B - Fetal risk not confirmed in studies in humans but has been shown in some studies in animals

Precautions

Use lower dose in hypothyroidism, liver disease, obesity (decreased cortisol-binding globulin and increased free fraction of steroid)
Perform general medical assessment of patient before treatment (DEXA scan may be useful); check blood pressure; ophthalmologic evaluation may assess and prevent ocular complications; skin tests and/or chest radiographs detect potential for tuberculosis reactivation; abrupt discontinuation of glucocorticoids may cause adrenal crisis; hyperglycemia, edema, osteonecrosis, myopathy, peptic ulcer disease, hypokalemia, osteoporosis, euphoria, psychosis, myasthenia gravis, growth suppression, and infections may occur

Immunosuppressives

These agents should be used early in the course as steroid-sparing agents. They lower the risk of steroid-related complications.

Methotrexate (Folex, Rheumatrex)

Benefits both muscle and skin disease. Unknown mechanism of action in treatment of inflammatory reactions; may affect immune function. Ameliorates symptoms of inflammation (eg, pain, swelling, stiffness).
Antimetabolite that inhibits DNA synthesis and cell reproduction in malignant cells; may suppress immune system. Satisfactory response seen in 3-6 wk following administration. Adjust dose gradually to attain satisfactory response.

Dosing

Adult

10-30 mg/wk PO/IM

Pediatric

10-25 mg/wk PO/IM

Interactions

Salicylates, NSAIDS, dipyridamole, probenecid, retinoids, ethanol, triamterene, pyrimethamine, sulfonamides, TCN, chloramphenicol, penicillin or other broad-spectrum antibiotics, trimethoprim, dapsone, theophylline, phenytoin, phenothiazines, barbiturates, and nitrofurantoin (impair folic acid absorption), ascorbic acid, phenylbutazone, cyclosporin, aminoglycosides

Contraindications

Absolute: Pregnancy or desire to get pregnant, active peptic ulcer, alcoholism, primary/secondary immunodeficiency, blood dyscrasias, active hepatitis, cirrhosis, chronic renal failure, and active infections
Relative: History of excessive ethanol intake or substance abuse, increased LFT results, recent hepatitis, diabetes mellitus, obesity, history of heritable liver disease, unreliable patient, CrCl <50 mL/min, males contemplating conception (must discontinue for 3 mo)

Precautions

Pregnancy

D - Fetal risk shown in humans; use only if benefits outweigh risk to fetus

Precautions

Avoid pregnancy during therapy and probably for at least 3 mo after cessation of therapy; stop excessive alcohol intake; need to monitor therapy with repeated liver biopsies is controversial; monitor CBC counts and liver enzyme levels during therapy; discontinue if blood cell counts significantly decrease; aspirin, NSAIDs, or low-dose steroids may be concomitantly administered with MTX (possibility of increased toxicity with NSAIDs, including salicylates, has not been tested); caution in obesity

Azathioprine (Imuran)

Antagonizes purine metabolism and inhibits synthesis of DNA, RNA, and proteins. May decrease proliferation of immune cells, which results in lower autoimmune activity. Respiratory and muscular symptoms respond but skin lesion response has not been consistent. Slow acting, with therapeutic effect not seen for 6-8 wk. Metabolites accumulate slowly, and maximal immunosuppression not reached until 8-12 wk.

Dosing

Adult

1 mg/kg/d qd or bid (empiric) or by TPMT level (see below); increase dose by 0.5 mg/kg/d after 6-8 wks if necessary; increase q4wk; not to exceed 2 mg/kg/d for most dermatologic purposes; supplied as 25-, 50-, 75-, and 100-mg tab and 100-mg vial

Pediatric

Administer as in adults

Interactions

Allopurinol increases risk of pancytopenia; captopril/ACE inhibitors may increase risk of anemia and leukopenia; increased dose of warfarin may be necessary; may need increased dose of pancuronium for adequate paralysis; live virus vaccines, co-trimoxazole (increased risk of hematologic toxicity); rifampicin (transplants possibly rejected); clozapine (increased risk of agranulocytosis)

Contraindications

Absolute: Documented hypersensitivity, pregnancy or attempting pregnancy, and clinically significant active infection
Relative: Concurrent use of allopurinol; prior treatment with alkylating agents (cyclophosphamide, chlorambucil, melphalan, others) (high risk of neoplasia)
Pediatric: Safety and efficacy in not established

Precautions

Pregnancy

D - Fetal risk shown in humans; use only if benefits outweigh risk to fetus

Precautions

TPMT testing is not entirely reliable; it involves testing the activity of TPMT activity in RBCs, which correlates with systemic TPMT activity; functional enzyme test has been shown to have variability between test sites, and kits may contain varying amounts of enzyme inhibitor; starting at low doses, monitoring for pancytopenia, and then increasing dose is alternative; if clinical response is not good, patient may be a homozygote for high activity and may need an increased dose

Possible increased risk of lymphoproliferative disorders with long-term therapy; increases risk of neoplasia; caution with liver disease and renal impairment; hematologic toxicities may occur

Dosing by TPMT level

TPMT <5 U: No treatment

5-13.7 U: Up to 0.5 mg/kg/d

13.7-19 U: Up to 1.5 mg/kg/d

>19 U: Up to 2.5 mg/kg/d

Mycophenolate (CellCept)

Useful for skin and muscle disease. Inhibits inosine monophosphate dehydrogenase and suppresses de novo purine synthesis by lymphocytes, thereby inhibiting their proliferation. Inhibits antibody production.

Dosing

Adult

1-1.5 g PO bid

Pediatric

Not established; 15-23 mg/kg PO bid suggested

Interactions

Levels of acyclovir or ganciclovir may increase; Antacids with magnesium or aluminum may decrease absorption (take at different times); cholestyramine decreases enterohepatic recirculation, thus blood levels; effect on oral contraceptive pills unknown so use 2 forms of effective birth control; any drug eliminated by active renal tubular secretion (levels of both increase)

Contraindications

Absolute: Documented hypersensitivity, pregnancy, allergy to polysorbate 80 (only IV CellCept); Lesch-Nyhan or Kelly Seegmiller syndrome, phenylketonuria (oral susp only; contains phenylalanine)

Relative: Breastfeeding, PUD/digestive system disease, hepatic disease, renal disease, azathioprine (concurrent; both can suppress bone marrow), drugs that interfere with enterohepatic recirculation (cholestyramine), and hepatic/renal/cardiopulmonary disease

Precautions

Pregnancy

D - Fetal risk shown in humans; use only if benefits outweigh risk to fetus

Precautions

May increase risk of lymphoma in patients on long-term therapy; gastrointestinal intolerance may occur with higher doses; increases risk for infection; increases toxicity in patients with renal impairment; caution in active peptic ulcer disease

Antimalarials

These agents may be used as a steroid-sparing agent for the treatment of the skin disease. Hydroxychloroquine is preferred; chloroquine and quinacrine (100 mg/d) are second-line agents. However, antimalarial-induced drug eruptions are reportedly more common in patients with dermatomyositis than in patients with LE. Quinacrine may suppress bone marrow and is distributed by the Centers for Disease Control and Prevention; blood cell counts should be regularly obtained.

Hydroxychloroquine (Plaquenil)

For patients with skin disease as primary manifestation, may allow partial or, in some cases, complete control of disease. Anecdotal evidence suggests morbilliform drug reactions are more common in patients with dermatomyositis than in other collagen-vascular diseases. Inhibits chemotaxis of eosinophils, inhibits locomotion of neutrophils, and impairs complement-dependent antigen-antibody reactions.

Dosing

Adult

200-400 mg/d PO; not to exceed 6.5 mg/kg/d

Pediatric

Administer as in adults; not to exceed 6.5 mg/kg/d

Interactions

Cimetidine increases levels; kaolin and magnesium trisilicate decrease levels; levels of chloroquine and digoxin may increase; increased retinal toxicity with chloroquine (do not administer together)

Contraindications

Absolute: Hypersensitivity and retinopathy from any cause
Relative: Pregnancy/lactation, retinal/visual-field changes, severe blood dyscrasias, psoriasis; G-6-PD deficiency (caution advocated, but routine G-6-PD screening not recommended (associated with hemolysis, but not in usual dosage range), significant hepatic dysfunction, myasthenia gravis, significant neurologic disease, long-term therapy in children

Precautions

Pregnancy

C - Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus

Precautions

Crosses placenta and may cause ocular, CNS, or ototoxicity in fetus; may be excreted in breast milk; pediatric use should be limited to established doses to avoid potential fatality; perform regular ophthalmologic examinations; caution in hepatic disease, G-6-PD deficiency, psoriasis, and porphyria

Chloroquine (Aralen)

Inhibits growth by concentrating within acid vesicles of parasite, which increases internal pH of organism. Also inhibits hemoglobin utilization and metabolism of parasite. Anti-inflammatory activity by suppressing lymphocyte transformation. May have photoprotective effect.

Dosing

Adult

250-500 mg/d PO

Pediatric

10 mg/kg PO on day 1 (not to exceed 600 mg), then 5 mg/kg PO (not to exceed 300 mg) 6 h later; 5 mg/kg PO on days 2 and 3
5 mg/kg IM, repeat in 6 h; total 25 mg/kg

Interactions

Cimetidine increases levels; kaolin and magnesium trisilicate decrease levels; levels of digoxin may increase; increased retinal toxicity with hydroxychloroquine (do not administer together)

Contraindications

Absolute: Hypersensitivity and retinopathy from any cause
Relative: Pregnancy/lactation, retinal/visual-field changes, severe blood dyscrasias, psoriasis; G-6-PD deficiency (caution advocated, but routine G-6-PD screening not recommended (associated with hemolysis, but not in usual dosage range), significant hepatic dysfunction, myasthenia gravis, significant neurologic disease, long-term therapy in children

Precautions

Pregnancy

C - Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus

Precautions

Caution in hepatic disease, G-6-PD deficiency, psoriasis, and porphyria; not recommended for long-term use in children; perform periodic ophthalmologic examinations; test for muscle weakness; retinopathy, tinnitus, nerve deafness, skin eruption, headache, anorexia, nausea, vomiting, and diarrhea may occur

Immune globulins

High-dose IV immunoglobulin has been reported to be useful for patients with recalcitrant dermatomyositis.

Immune globulin intravenous (Sandoglobulin, Gammagard, Gamimune, Gammar-P)

For patients in whom corticosteroids and immunosuppressives have failed. Neutralize circulating myelin antibodies through anti-idiotypic antibodies; down-regulates proinflammatory cytokines, including INF-gamma; blocks Fc receptors on macrophages; suppresses inducer T and B cells and augments suppressor T cells; blocks complement cascade; promotes remyelination; may increase CSF IgG (10%).

Dosing

Adult

1 g/kg IV on 2 consecutive days monthly

Pediatric

Administer as in adults

Interactions

Antibodies in globulin preparation may interfere with response to live viral vaccines (eg, MMR); defer using live viral vaccines until approximately 11 mo after immunoglobulin administration; no known drug interactions

Contraindications

No absolute contraindication other than documented hypersensitivity; patients who are IgA deficient should receive IVIG preparations with no IgA; anti-IgE/IgG antibodies, severe thrombocytopenia, or coagulation disorders
Gammagard S/D contains only trace amounts of IgA and is not indicated in patients with selective IgA deficiency in whom the IgA deficiency is the only abnormality of concern, and it should be given with caution to patients with antibodies to IgA or IgA deficiencies that are a component of an underlying primary immunodeficiency disease for which IVIG therapy is indicated; in such instances, a risk of anaphylaxis may exist despite the fact that Gammagard S/D contains only trace amounts of IgA

Precautions

Pregnancy

C - Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus

Precautions

Consider checking serum IgA before IVIG and using IgA-depleted IVIG (G-Gard-SD) if indicated; IVIG may increase serum viscosity and thromboembolic events

Reported adverse effects include migraine attacks; 10% increased risk of aseptic meningitis; and increased risk of urticaria, pruritus, or petechiae 2-5 d postinfusion that may last up to 1 mo; increased risk of renal tubular necrosis in older patients, in patients with diabetes, in patients with volume depletion, and in patients with preexisting kidney disease

IVIG can lead to elevated antiviral or antibacterial antibody titers for 1 mo and 6-fold increase in ESR for 2-3 wk; apparent hyponatremia

Monoclonal antibodies

Rituximab is an anti-CD20 antibody specific in targeting the antibody-producing B cells.

Rituximab (Rituxan)

Antibody genetically engineered. Chimeric murine/human monoclonal antibody directed against the CD20 antigen found on surface of B-lymphocytes. Being used in refractory patients in an NIH-sponsored trial.

Dosing

Adult

375 mg/m^2 IV qwk for 4 wk

Pediatric

Not established

Interactions

Coadministration with cisplatin is known to cause severe renal toxicity including acute renal failure; may interfere with immune response to live virus vaccine (MMR) and reduce efficacy (do not administer within 3 mo of vaccine)

Contraindications

Documented hypersensitivity; IgE-mediated reaction to murine proteins

Precautions

Pregnancy

C - Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus

Precautions

Monitor CBC and platelet counts regularly during and few months post treatment for occurrence of cytopenia; monitor human antichimeric antibody development (approximately 1% patients); monitor and treat associated infections (30% probability)

Severe infusion reactions have occurred, typically during first infusion, with time to onset of 30-120 min; signs and symptoms may include urticaria, hypotension, angioedema, hypoxia, or bronchospasm and may require interruption of infusion; most severe manifestations and

sequelae include pulmonary infiltrates, acute respiratory distress syndrome, myocardial infarction, ventricular fibrillation, cardiogenic shock, and anaphylactic and anaphylactoid events; factors most commonly associated with fatal outcomes are female sex pulmonary infiltrates, and chronic lymphocytic leukemia or mantle cell lymphoma; infusions should be interrupted for severe infusion reactions and medication and supportive care measures provided; in most cases, infusion can be resumed at 50% reduction in rate when symptoms have completely resolved

Tumor lysis syndrome (TLS), rapid reduction in tumor volume followed by acute renal failure, hyperkalemia, hypocalcemia, hyperuricemia, or hyperphosphatemia, has been reported within 12-24 h after first infusion; risks greater in patients with high numbers of circulating malignant cells (>25,000/μ L) or high tumor burden; following complete resolution of the complications of TLS, rituximab has been tolerated when re-administered in conjunction with prophylactic therapy for TLS

Hepatitis B virus (HBV) reactivation with related fulminant hepatitis, other viral infections, hepatic failure, and death have been reported in some patients with hematologic malignancies; most patients received rituximab in combination with chemotherapy; median time to diagnosis of hepatitis was approximately 4 months after initiation of therapy and approximately 1 mo after last dose; patients who develop viral hepatitis should have rituximab and any concomitant chemotherapy discontinued, and appropriate treatment should be initiated; limited data regarding the safety of resuming rituximab in patients who develop hepatitis subsequent to HBV reactivation

Follow-up

Further Inpatient Care

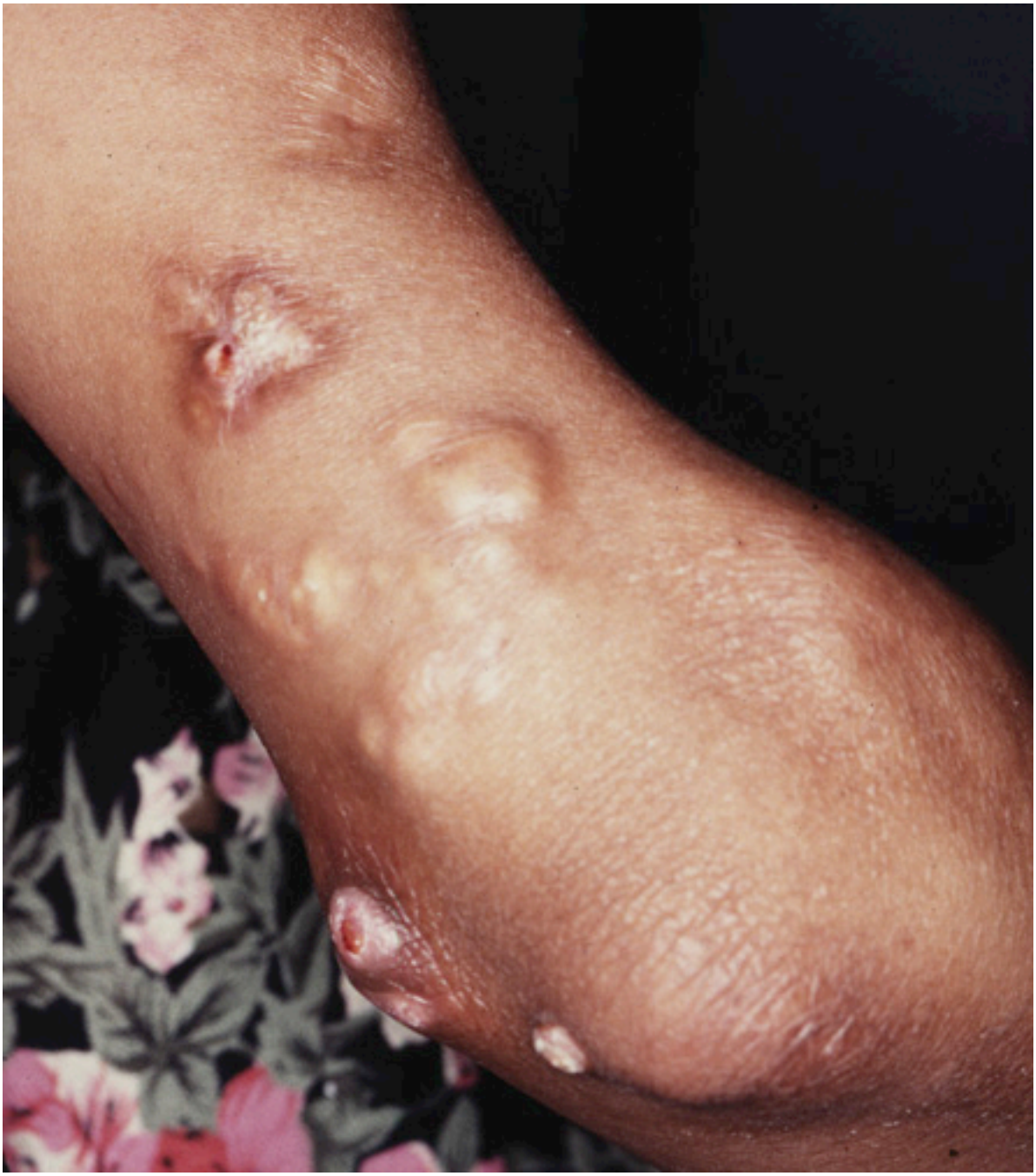
- Inpatient care is needed for patients with fulminant disease.

Further Outpatient Care

- Monitoring of the activity of the disease is necessary on at least a monthly basis. Repeat measurements of muscle enzyme levels may aid in the assessment of the activity of the myositis, along with clinical assessment of strength. Machines are available that can aid in the quantification of the strength, but they are not widely used.
- An assessment of the skin disease is by a physical examination in conjunction with a history. A new validated measure, known as the Cutaneous Dermatomyositis Area and Severity Index (C-DASI), for assessing skin disease might be useful, particularly when performing clinical studies in the future.[34]
- Annual physical examinations are useful to monitor for potential toxicity from therapy or for a malignancy.
    - Malignancy evaluations should be conducted for at least the first 3 years following diagnosis and at other times if symptoms develop or the patient's disease is poorly responsive to therapy. The testing selected should be chosen based on the patient's age, sex, race, and other symptoms or findings. After 3 years, patients should be monitored as any other person of the same age, race, and sex.
    - Women should be screened for ovarian cancer.[18]

Complications

- Calcinosis may be a complication in children and adolescents with dermatomyositis (see Media File 8). Its presence has been linked to a delay in diagnosis and to therapy that is less aggressive.



Calcinosis due to dermatomyositis in childhood can be seen in this patient who had active dermatomyositis 15 years prior to the time of this photograph.

- Contractures can occur if the patient is immobile.

Prognosis

- The prognosis depends on the severity of the myopathy,[35] the presence of a malignancy, and/or the presence of cardiopulmonary involvement.

- Patients with dermatomyositis who have malignancy, cardiac involvement, or pulmonary involvement and those with dermatomyositis who are elderly (>60 y) have a poorer prognosis.
- The disease may spontaneously remit in as many as 20% of patients.
- About 5% of patients have a fulminant progressive course, with eventual death. Therefore, many patients require long-term therapy.

Patient Education

- Physical therapy and rehabilitative measures are necessary in selected patients.
- Sun protective measures are necessary for patients with skin disease.
- The Myositis Association of America is a resource on inflammatory myopathies for patients and the medical community.

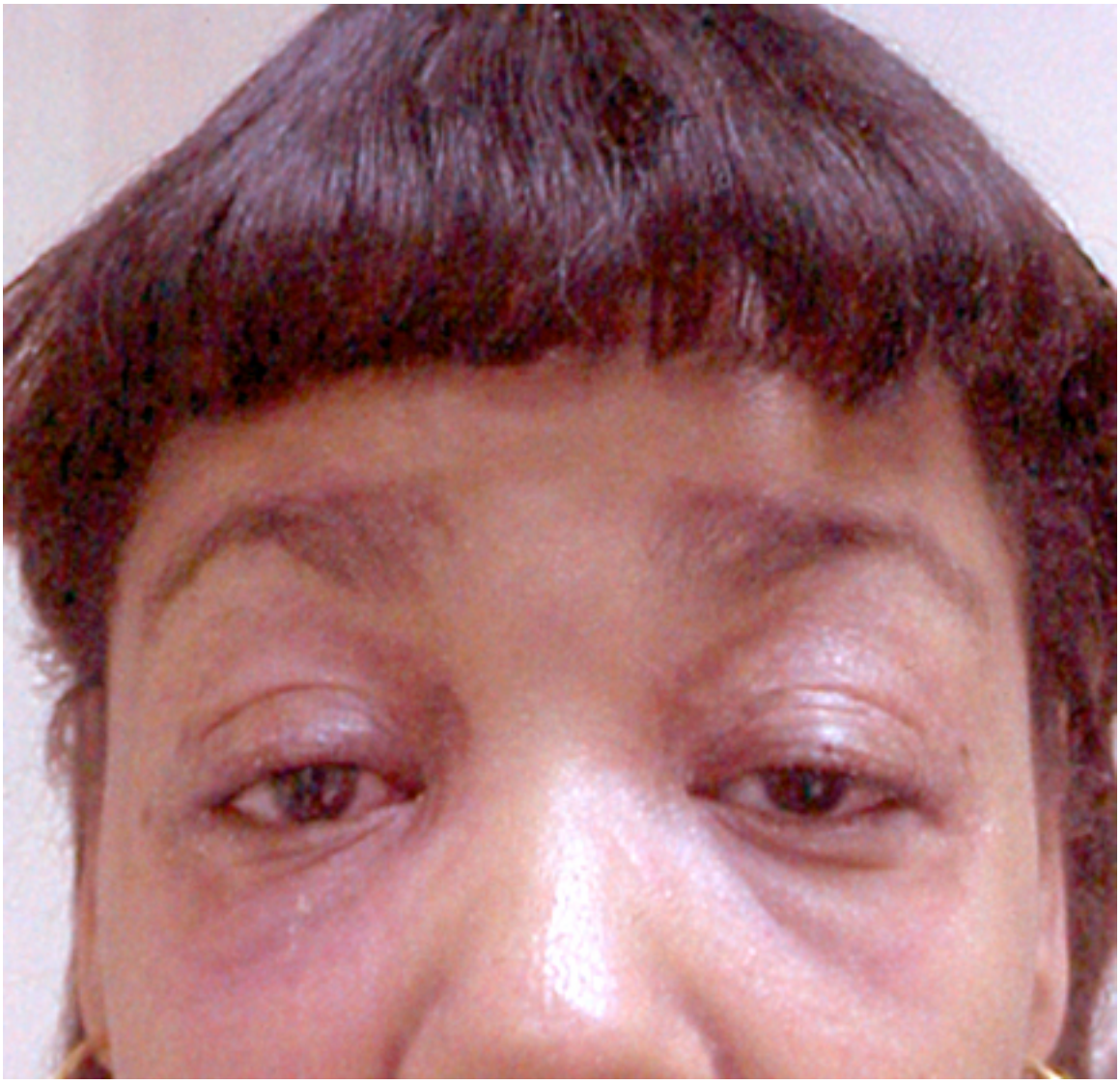
Miscellaneous

Medicolegal Pitfalls

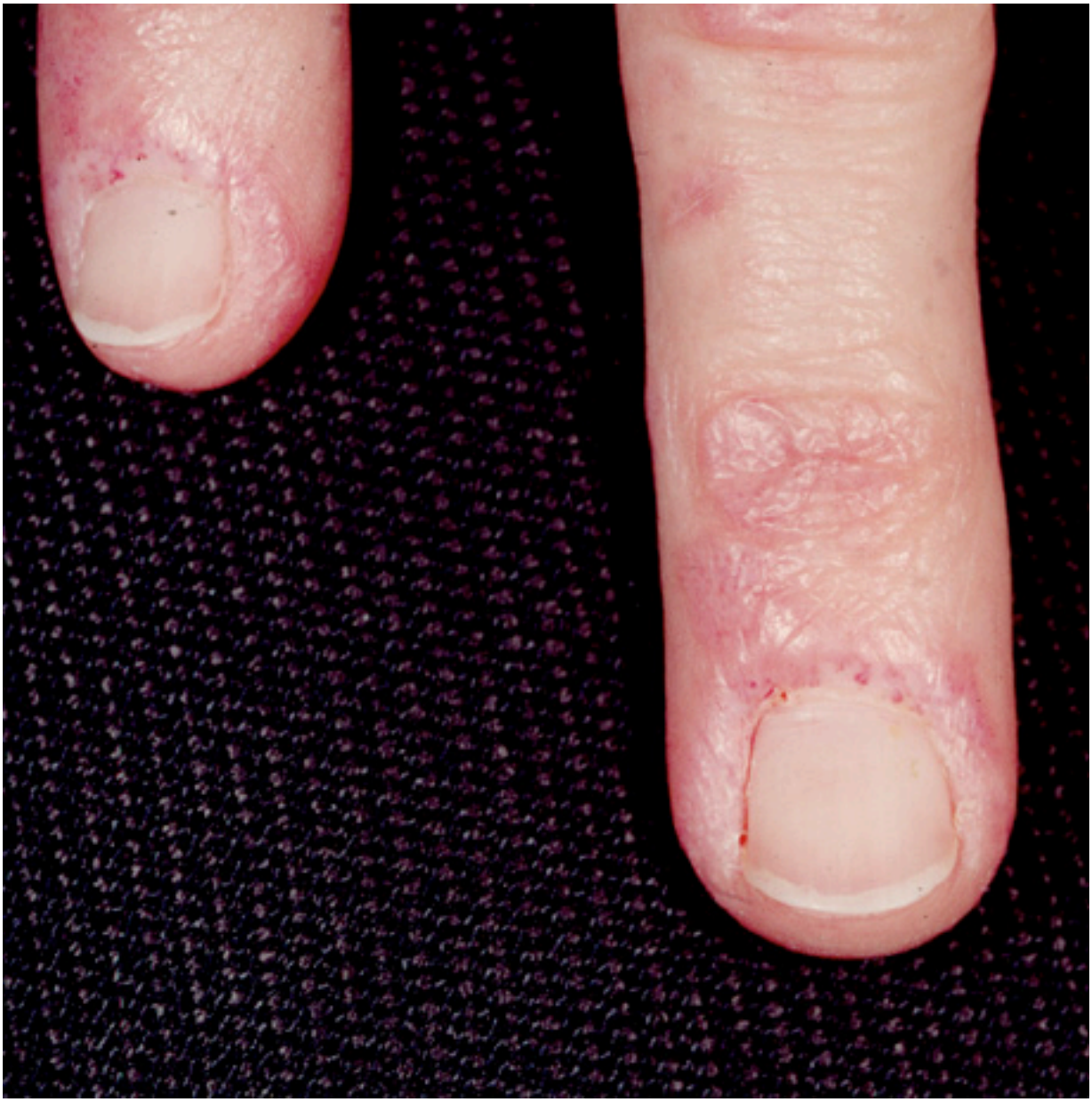
- Failure to diagnose (Early in the course, the skin disease may be misdiagnosed as eczema, psoriasis, or lupus erythematosus.)
- Failure to recognize an associated malignancy
- Failure to inform about or monitor for potential toxicity of therapies

Multimedia

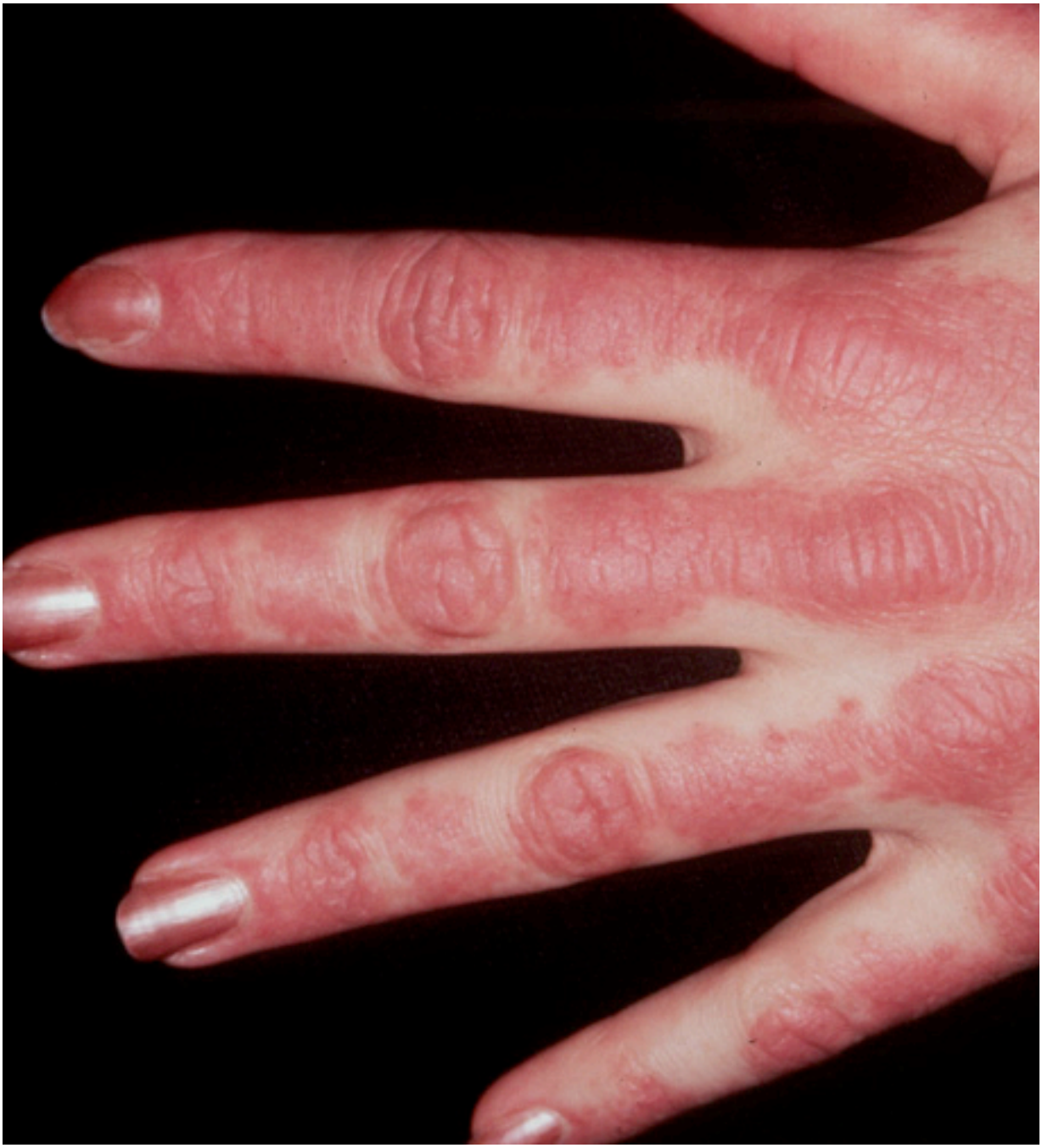
Media file 1: The heliotrope rash is a characteristic and possibly pathognomonic cutaneous feature of dermatomyositis. The heliotrope flower from which the manifestation is named is pictured.



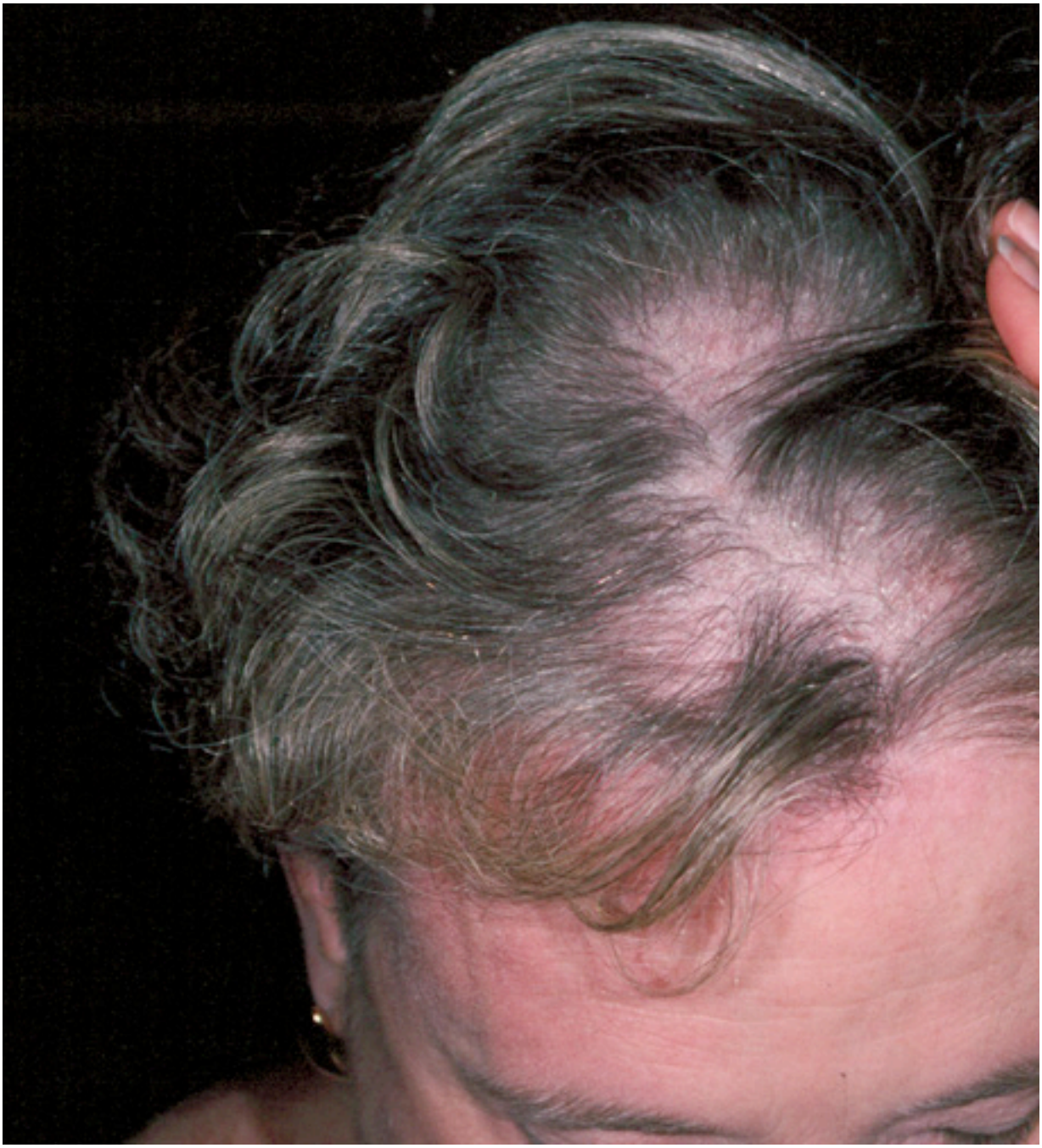
Media file 2: Heliotrope rash in a woman with dermatomyositis.



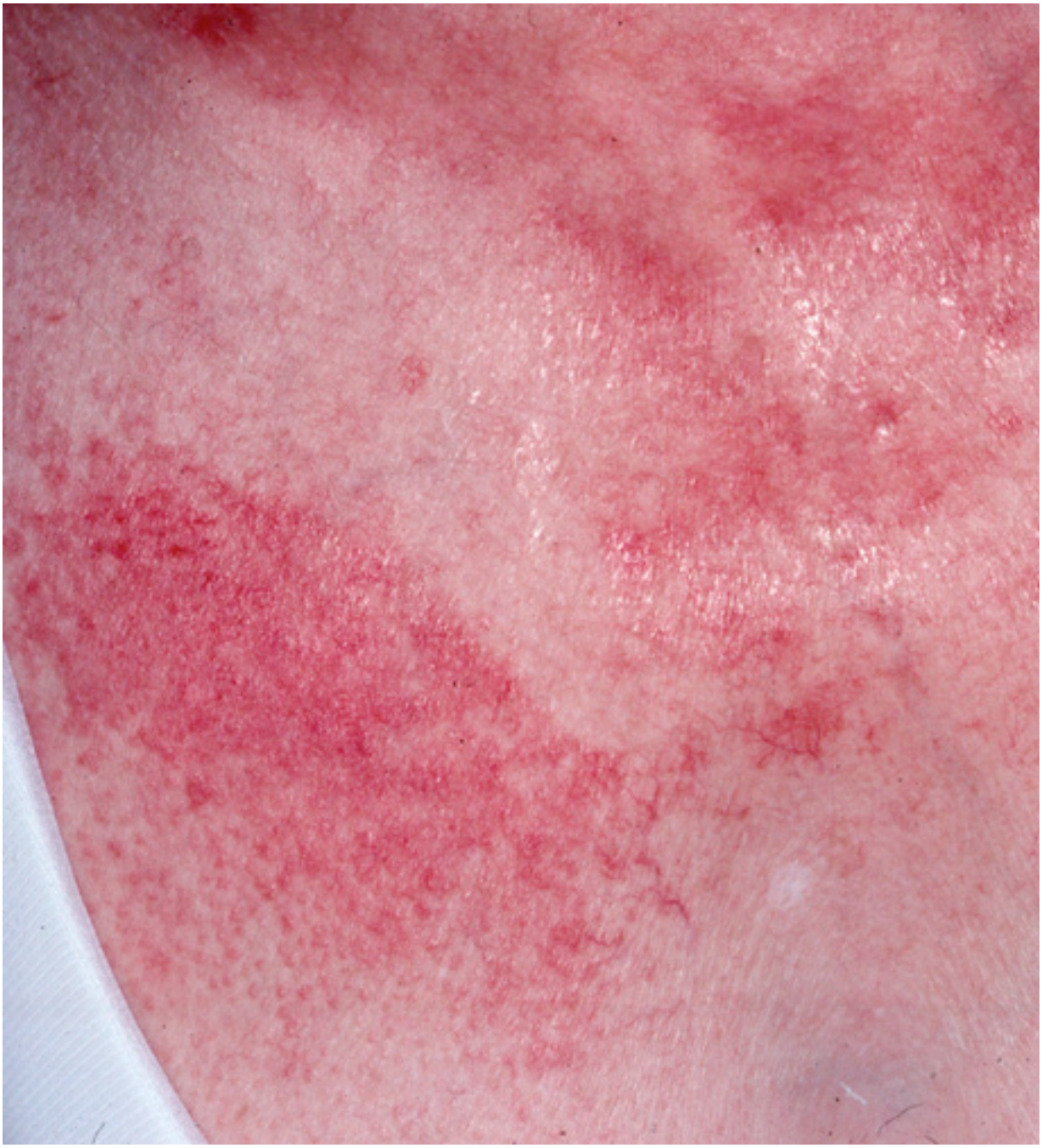
Media file 3: Gottron papules and nail fold telangiectasia are present in this patient.



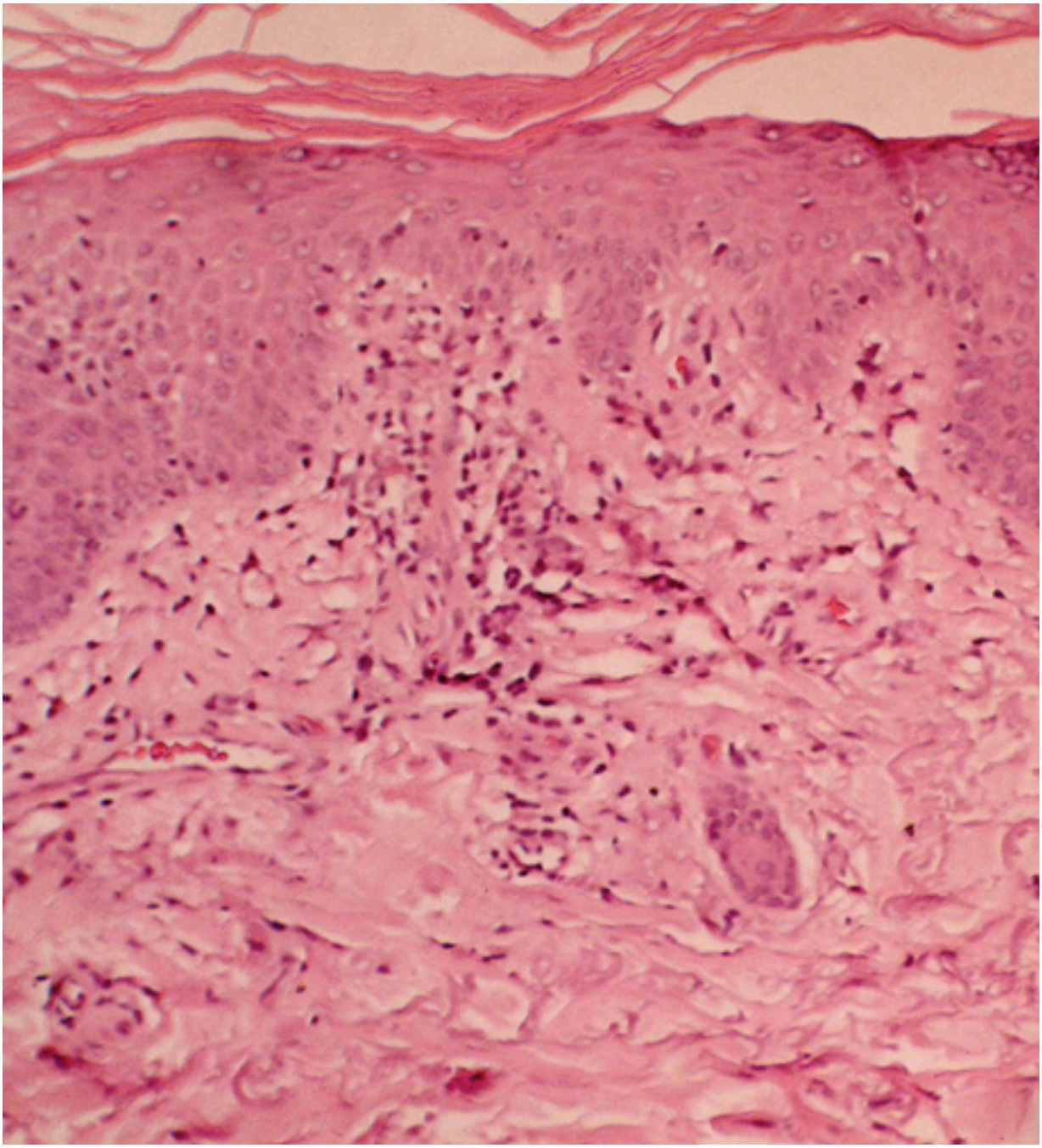
Media file 4: The lesions on the dorsal aspect of the hand demonstrate the photodistribution of dermatomyositis. Note the sparing of the interdigital web spaces.



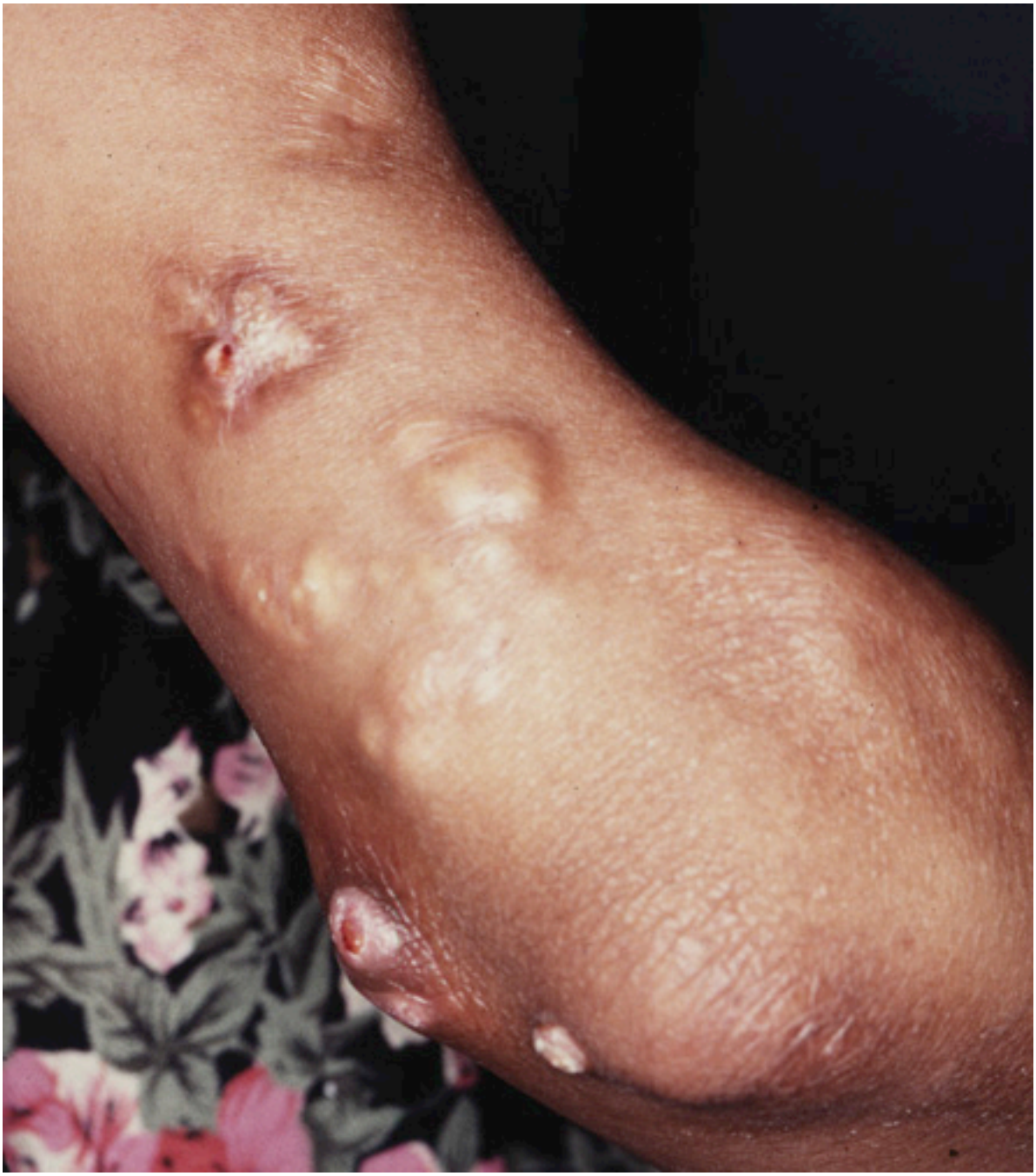
Media file 5: A diffuse alopecia with a scaly scalp dermatosis is common in dermatomyositis.



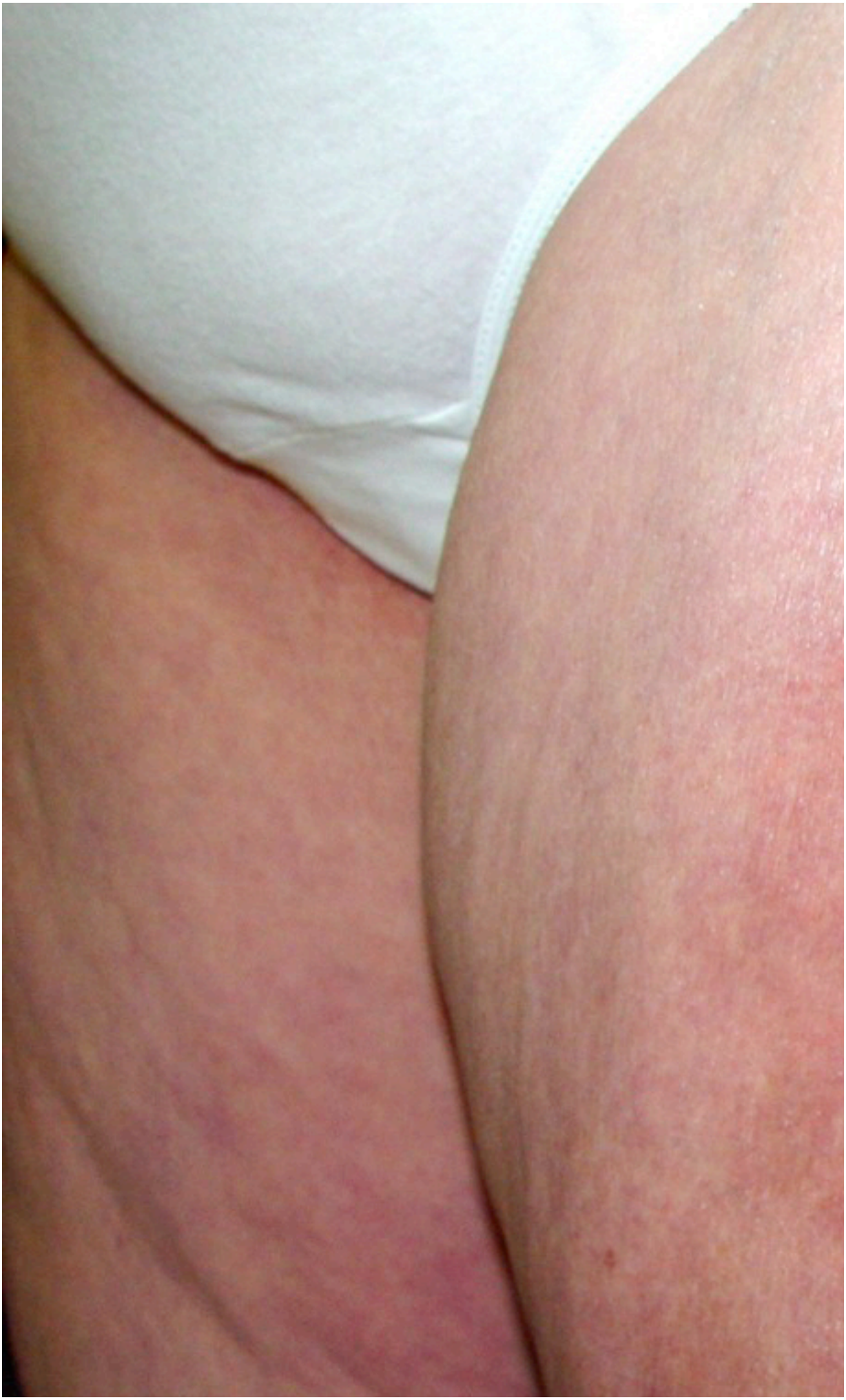
Media file 6: Dermatomyositis is often associated with a poikiloderma in a photodistribution.



Media file 7: The histopathologic feature of dermatomyositis is an interface dermatitis.



Media file 8: Calcinosis due to dermatomyositis in childhood can be seen in this patient who had active dermatomyositis 15 years prior to the time of this photograph.



Media file 9: Calcifying panniculitis in a patient with dermatomyositis.

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