## CASE RECORDS *of the* MASSACHUSETTS GENERAL HOSPITAL

# Case 18-2014: A 32-Year-Old Man with a Rash, Myalgia, and Weakness

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## PRESENTATION OF CASE

*Dr. Eli Miloslavsky* (Medicine): A 32-year-old man was admitted to this hospital because of a rash, muscle pain, weakness, and respiratory failure.

The patient had been well until 10 weeks before admission, when a violaceous rash developed involving the eyelids, elbows, metacarpophalangeal and proximal interphalangeal joints, and knees. One week later, intense generalized muscle pain and weakness developed, including difficulty walking, arising from a squat, and climbing stairs. Two weeks later, examination at another hospital revealed a heliotrope rash (a red-to-purple rash on the eyelids), periungual edema, erythematous papules on the fingertips, and moderate-to-severe weakness of the deltoids, triceps, hip flexors, hamstrings, and quadriceps bilaterally. Muscle bulk and tone, deeptendon reflexes, and the sensory examination were normal. Electrodiagnostic studies of muscle and nerve reportedly showed evidence of a chronic proximal myopathy with inflammatory features. Prednisone, 80 mg daily, was administered, with transient improvement in weakness and a reported decrease in the serum creatine kinase level, from 6700 U per liter to 4200 U per liter. Twenty-six days before admission, the administration of azathioprine, 150 mg per day, was begun because of the patient's progressive weakness (including difficulty raising his arms) and tenderness on deep palpation of the proximal limbs. Two days later, tests of coagulation and the blood level of total bilirubin were normal; other test results are shown in Table 1. Azathioprine was stopped after 2 days because of a rise in the creatine kinase level, and the patient was admitted to the other hospital.

Computed tomography (CT) of the chest and abdomen revealed a small left pleural effusion and anasarca. Magnetic resonance imaging (MRI) performed after the administration of gadolinium reportedly revealed enhancement and edema throughout the major muscle groups of the right thigh. Pathological examination of a biopsy specimen of skeletal muscle reportedly revealed mildly increased variation in fiber size and occasional degenerating fibers, myonecrosis, vascular injury, and fibrosis. Rituximab and a 5-day course of intravenous immunoglobulin were administered. Anemia and hypertension reportedly developed. Red cells (6 units) were transfused and antihypertensive agents were administered. Pathological examination of a biopsy specimen of the bone marrow showed normal trilineage hematopoiesis and no malignant cells. Fever developed, and a possible pulmonary infil-

trate was seen on chest radiographs; vancomycin and ceftriaxone were administered. On the 19th day, the patient was discharged to a rehabilitation hospital. He had progressive weakness and was unable to ambulate.

During the next 5 days, worsening cough and increasing sputum production developed. On the fifth day, a modified barium-swallow examina-

tion reportedly revealed aspiration of thin liquids. Oral intake was stopped and a nasogastric tube placed. The next morning, respiratory distress developed while the patient was in a supine position; the oxygen saturation decreased to 68% while he was breathing ambient air (from a previous level of ≥90%). A chest radiograph reportedly revealed air-space disease in the left lower lobe and

### Table 1. Laboratory Data.*

| Variable | Reference Range, Adults† | 1st Hospital, 24 Days before Admission to MGH | This Hospital, On Admission | This Hospital, 48th to 49th Hospital Day | 3rd Hospital (Rehabilitation), on Admission, 50 Days after Admission to MGH | 3rd Hospital (Rehabilitation), 14 Wk after Admission to MGH |
|---|---|---|---|---|---|---|
| Hematocrit (%) | 41.0–53.0 (men) | 46.8 | 31.0 | 22.8 | 21.0 | 27.9 |
| Hemoglobin (g/dl) | 13.5–17.5 (men) | 16.3 | 10.5 | 7.4 | 7.0 | 9.6 |
| White-cell count (per mm³) | 4500–11,000 | 24,000 | 17,000 | 9100 | 8000 | 8000 |
| Differential count (%) | | | | | | |
| Neutrophils | 40–70 | 93.8 | 85 | 77 | 75.4 | 66.0 |
| Band forms | 0–10 | | 1 | | | |
| Lymphocytes | 22–44 | 2.7 | 2 | 6 | 6.4 | 7.7 |
| Monocytes | 4–11 | 3.3 | 12 | 6 | 7.2 | 10.0 |
| Eosinophils | 0–8 | 0.1 | 0 | 11 | 10.8 | 16.1 |
| Basophils | 0–3 | 0.1 | 0 | 0 | 0.2 | 0.2 |
| Platelet count (per mm³) | 150,000–400,000 | 288,000 | 728,000 | 481,000 | 415,000 | 337,000 |
| Red-cell distribution width (%) | 11.5–14.5 | | 16.1 | 18.2 | 17.9 (ref 11.0–16.0) | 18.9 (ref 11.0–16.0) |
| Erythrocyte count (per mm³) | 4,500,000–5,900,000 | | 3,650,000 | 2,670,000 | 2,440,000 | 3,230,000 |
| Erythrocyte sedimentation rate (mm/hr) | 0–15 | | | | 105 | |
| Reticulocytes (%) | 0.8–1.8 | | | | 6.2 | 3.2 |
| Activated partial-thromboplastin time (sec) | 21.0–33.0 | | 30.0 | | | |
| Prothrombin time (sec) | 11.0–13.7 | | 13.9 | | | 12.6 |
| International normalized ratio for prothrombin time | | | 1.2 | | | 1.0 |
| Sodium (mmol/liter) | 135–145 | 124 | 135 | 142 | 140 | 140 |
| Potassium (mmol/liter) | 3.4–4.8 | 6.0 | 3.6 | 4.6 | 4.2 | 4.2 |
| Chloride (mmol/liter) | 100–108 | 87 | 97 | 100 | 100 | 100 |
| Carbon dioxide (mmol/liter) | 23.0–31.9 | 24 | 30.2 | 37.8 | 32 | 31 |
| Urea nitrogen (mg/dl) | 8–25 | 30 | 17 | 23 | 19 | 24 |
| Creatinine (mg/dl) | 0.60–1.50 | 1.09 | 0.38 | 0.29 | 0.4 | 0.3 |
| Glucose (mg/dl) | 70–110 | 158 | 155 | 120 | 110 | 108 |
| Total protein (g/dl) | 6.0–8.3 | 5.4 | 6.3 | | 4.7 | 5.6 |
| Albumin (g/dl) | 3.3–5.0 | 2.5 | 3.0 | | 2.2 | 2.1 |
| Alkaline phosphatase (U/liter) | 45–115 | 62 | 74 | | 117 | 302 |
| Aspartate aminotransferase (U/liter) | 10–40 | 440 | 225 | | 57 | 99 |

**Table 1. (Continued.)**

| Variable | Reference Range, Adults† | 1st Hospital, 24 Days before Admission to MGH | This Hospital, On Admission | This Hospital, 48th to 49th Hospital Day | 3rd Hospital (Rehabilitation), on Admission, 50 Days after Admission to MGH | 3rd Hospital (Rehabilitation), 14 Wk after Admission to MGH |
|---|---|---|---|---|---|---|
| Alanine aminotransferase (U/liter) | 10–55 | 128 | 63 | | 43 | 101 |
| Lactate dehydrogenase (U/liter) | 110–210 | | 468 | | 283 | |
| Creatine kinase (U/liter) | 60–400 (men) | 12,511 | 1915 | 84 | 52 | 80 |
| Creatine kinase MB isoenzyme (ng/ml) | 0.0–6.9 | 109.5 | 19.7 | | | |
| Troponin I (ng/ml) | 0.00–0.50 | 0.05 | | | | |
| Troponin T (ng/ml) | <0.03 | | 0.72 | | | |
| Fibrinogen (mg/dl) | 150–400 | | 473 | | | |
| Ferritin (ng/ml) | 30–300 | | 2324 | 2341 | | |
| Iron (μg/dl) | 45–160 | | 24 | | 22 | 59 |
| Total iron-binding capacity (μg/dl) | 230–404 | | 108 | | 158 | 151 |
| Iron saturation (%) | 30–60 | | | | 14 | 39 |
| Soluble interleukin-2 receptor α chain (U/ml) | 45–1105 (age 7 years or older) | | 3172 | | | |
| Glucose-6-phosphate dehydrogenase (IU/g hemoglobin) | 8.8–13.4 | | 14.9 | | | |
| γ-Glutamyltransferase (IU/liter) | 0–40 | | | | 237 | |
| Arterial blood gases | | | | | | |
|     Fraction of inspired oxygen | | | 1.00 | | 0.40 | 0.35 |
|     pH | 7.35–7.45 | | 7.15 | | 7.43 | 7.42 |
|     Partial pressure of carbon dioxide (mm Hg) | 35–42 | | 88 | | 52 | 47 |
|     Partial pressure of oxygen (mm Hg) | 80–100 | | 45 | | 120 | 95 |
|     Bicarbonate (mmol/liter) | 22–46 | | | | 34 | 30 |
|     Base excess (mmol/liter) | | | –0.9 | | | |

\* MGH denotes Massachusetts General Hospital, and ref reference range at the rehabilitation hospital. To convert the values for urea nitrogen to millimoles per liter, multiply by 0.357. To convert the values for creatinine to micromoles per liter, multiply by 88.4. To convert the values for glucose to millimoles per liter, multiply by 0.05551. To convert the values for iron and iron-binding capacity to micromoles per liter, multiply by 0.1791.

† Reference values are affected by many variables, including the patient population and the laboratory methods used. The ranges used at MGH are for adults who are not pregnant and do not have medical conditions that could affect the results. They may therefore not be appropriate for all patients.

a small, left-sided pleural effusion. Furosemide, vancomycin, piperacillin and tazobactam in combination, transdermal nitroglycerin ointment, and oxygen were administered, and the patient was transferred to this hospital. Medications on transfer included hydralazine, fondaparinux, cyclobenzaprine, furosemide, metoprolol, and methylprednisolone.

The patient had had a meniscal repair 10 years earlier. He was married and lived with his wife and two young children and worked in a service industry. He did not smoke or use illicit drugs. His father had hypertension, and two aunts had hypothyroidism; there was no family history of muscle, skin, or other autoimmune disease.

On examination, the patient was alert, oriented, and afebrile. The blood pressure was 175/90 mm Hg, the pulse 128 beats per minute, the respiratory rate 40 breaths per minute, and the oxygen saturation 93% while he was breathing oxygen that was administered through a nonrebreather face mask at a rate of 10 liters per minute. Breath sounds were diminished at both lung bases, and there was no wheezing. Bowel sounds were hypoactive. There were erythematous papules on the extensor surfaces of

the fingers, elbows, and knees and a heliotrope rash bilaterally. Nontender erythema of the periungual regions was present. There was pitting edema of the arms and legs. Grip strength and the strength of foot dorsiflexion and plantar flexion were 4–/5, and the patient was unable to lift his arms, legs, or head against gravity (2+/5). Red-cell indexes were normal, as were blood levels of globulin, total and direct bilirubin, magnesium, phosphorus, calcium, N-terminal pro–B-type natriuretic peptide, and CA 19-9; direct and indirect Coombs' tests and assays for antineutrophil cytoplasmic antibodies and antimitochondrial antibodies were negative; other test results are shown in Table 1. Normal saline, metronidazole, cefepime, and ciprofloxacin were administered. CT performed according to the pulmonary-embolism protocol showed air-space opacities and diffuse stranding in the superficial soft tissues, with no evidence of embolism. In the evening on the day of admission, hypoxemic and hypercarbic respiratory failure developed (Table 1). The patient was sedated, the trachea was intubated, and mechanical ventilation was begun.

During the next 2 weeks, a tracheostomy was performed and the patient was weaned from respiratory support to nocturnal pressure-support ventilation. Serum immunoglobulin levels and protein electrophoresis were normal. Examination of a specimen from a second muscle biopsy of the right quadriceps muscle showed tubuloreticular inclusions within endothelial cells, atrophy of type 2B fibers, and a small area of inflammation. A second 5-day course of intravenous immunoglobulin was administered. Stools became guaiac-positive; endoscopic examination revealed two gastric ulcers, which were cauterized. Pathological examination of biopsy specimens from the lesions showed no malignant cells or dysplasia. Testing for *Helicobacter pylori* was positive; metronidazole and clarithromycin in a 14-day course and a proton-pump inhibitor were administered. Red cells were transfused intermittently, the levels of creatine kinase returned to normal, and the dose of prednisone was tapered to 7.5 mg daily. The patient was discharged to a rehabilitation hospital on the 50th day, breathing 40% oxygen through the tracheostomy with a tracheostomy mask during the day and receiving pressure-support ventilation at night. He was able to sit on the edge of a bed with assistance and was lifted to a chair for chair rest. Prednisone was continued at 7.5 mg per day, and the monthly administration of intravenous immunoglobulin was planned.

Seven weeks after discharge from this hospital, and approximately 6 months after the onset of symptoms, new erythematous macules and papules appeared on the torso, extremities, and face. Examination of the trunk, limbs, and face revealed discrete, erythematous macules and papules that were too numerous to count (Fig. 1). These lesions were characterized by central, white, atrophic and sclerotic centers, violaceous borders, and peripheral hyperpigmentation.

A diagnostic procedure was performed.

## DIFFERENTIAL DIAGNOSIS

*Dr. Susan Burgin:* The patient's initial constellation of dermatologic findings is in keeping with the diagnosis of dermatomyositis. Gottron's papules are erythematous papules that overlie interphalangeal and metacarpophalangeal joints, elbows, and knees. They are pathognomonic for dermatomyositis. A heliotrope rash, as manifested by this patient, is seen in 30 to 60% of patients with dermatomyositis. The patient also had periungual erythema and edema, which are less specific signs that may be seen in dermatomyositis and other connective-tissue diseases, such as systemic lupus erythematosus (SLE).

During the patient's convalescence, a new and widespread eruption was seen that was different from the first eruption. On examination, white, depressed, scarlike papules with violaceous borders were seen on the face. Some crusts were also seen. On the abdomen, small, sclerotic, flat papules were less inflamed and very white. I will focus on the differential diagnosis of this new eruption, characterized by guttate, white papules.

### MALIGNANT ATROPHIC PAPULOSIS

Malignant atrophic papulosis, or Degos's disease, is a rare small-vessel vasculopathy, in which crops of erythematous cutaneous papules progress to depressed, porcelain-white scars with a varicelliform or varioliform appearance and a violaceous rim (consisting of fine telangiectasias) and then to inactive, atrophic white scars. Lesions are small, measuring between 0.5 and 1 cm in greatest dimension. New papules typically occur in crops, and lesions at differing stages are usually seen. Tens to hundreds of lesions may be seen at any given time. Classic sites of involvement are the trunk and proximal ex-

tremities; however, cases involving the face, scalp, and genitalia have been reported.[1]

In the majority of reported cases, malignant atrophic papulosis is a multisystem disease in which skin findings precede gastrointestinal and central nervous system involvement or, on rare occasions, other organ involvement by weeks to years. Abdominal pain, nausea, diarrhea, and melena signal the onset of gastrointestinal tract infarcts occurring anywhere from the mouth to the anus. Bowel perforation resulting in peritonitis is a common cause of death in these patients. Involvement of the central nervous system occurs in only 20% of patients with systemic involvement and is heralded by hemiparesis, monoplegia, sensory abnormalities, or visual changes.[1] A chronic, benign, skin-limited form of malignant atrophic papulosis has been recognized, and malignant atrophic papulosis also has been reported in families with an autosomal-dominant mode of inheritance, with variable expressivity.[2,3] Malignant atrophic papulosis can occur in association with autoimmune diseases, most often SLE, but it has also been reported in patients with progressive systemic sclerosis, rheumatoid arthritis, discoid lupus, and dermatomyositis.[4]

Porcelain-white, depressed plaques resembling malignant atrophic papulosis may also occur in patients with primary antiphospholipid syndrome or the antiphospholipid syndrome caused by lupus.[5] The antiphospholipid syndrome and dermatomyositis may occasionally coexist. It is therefore important to rule out the antiphospholipid syndrome in this case.

The pathogenesis of malignant atrophic papulosis has yet to be fully elucidated. A study of four patients showed increased expression of MxA (a type I interferon–inducible protein), signifying dysregulated interferon-$\alpha$, and C5b–C9 (membrane-attack complex) in endothelial cells, vessel walls, perivascular interstitium, inflammatory cells, and keratinocytes in involved skin,[6] suggesting that complement-mediated injury to endothelial cells may be involved in the pathogenesis of malignant atrophic papulosis.

### LIVEDOID VASCULOPATHY

Another cause of porcelain-white plaques is livedoid vasculopathy (formerly known as atrophie blanche). The plaques may be stellate and display papular telangiectasias within and at their periphery. Retiform purpura and livedo reticularis may be present. The typical site of involvement is
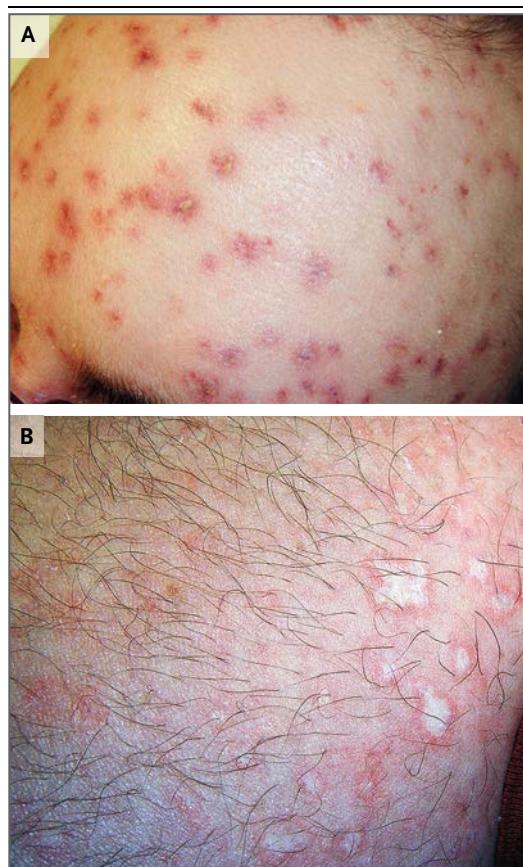


**Figure 1. Clinical Photographs of the Patient.**
Panel A shows the patient's forehead, with multiple small, white, atrophic and crusted papules with violaceous borders. In Panel B, lesions on the thigh consist of porcelain-white, slightly depressed papules.

the legs, and women are more frequently affected than men. Livedoid vasculopathy may be a primary condition, or it may be caused by varicose veins or an underlying hypercoagulable state (e.g., the antiphospholipid syndrome, factor V Leiden mutations, antithrombin III deficiency, protein C or protein S deficiency, and hyperhomocysteinemia). Although the specific morphologic features of primary lesions are common to malignant atrophic papulosis and livedoid vasculopathy, the distribution of plaques and their associations are different. On the basis of the distribution of lesions in this patient, livedoid vasculopathy is not a likely cause.

### DISCOID LUPUS ERYTHEMATOSUS

The plaques on this patient's face resemble the annular atrophic plaque variant of discoid lupus

erythematosus. The plaques associated with this variant of discoid lupus have white sclerotic centers and a red rim. In patients with classic discoid lupus, the plaques are typically seen on the face and neck (and below the neck in patients with generalized discoid lupus) and are initially well-demarcated, scaly plaques that progress to atrophic white plaques with a hyperpigmented border. A recent report detailed a case of discoid lupus with plaques resembling malignant atrophic papulosis.[7] Histopathological evaluation of the plaques revealed features of both discoid lupus and malignant atrophic papulosis, but the patient responded to treatment for discoid lupus erythematosus. Because of the multiplicity of lesions in this patient and because the lesions were seen in different stages (with crusts preceding the annular atrophic plaques, which in turn developed into lesions more typical of malignant atrophic papulosis), the diagnosis of discoid lupus is unlikely in this patient.

### PAPULAR MUCINOSIS

Scleromyxedema is a chronic disorder of unknown cause marked by an increased deposition of collagen and mucin in the dermis. Although scleromyxedema is generalized, localized forms of the disease have been recognized, including papular mucinosis, acral persistent papular mucinosis, papular mucinosis of infancy, and a nodular form. A rare variant of papular mucinosis is annular lichen myxedematosus, in which papules are flesh-colored to red in varying sizes and with a central depression. A case report details annular lichen myxedematosus in a patient with dermatomyositis.[8] Interstitial mucin deposition in the dermis is frequently seen in cutaneous-biopsy specimens in patients with dermatomyositis. The causes of mucin deposition and papular mucinosis in dermatomyositis are unknown, but elevated levels of interleukin-1 and interleukin-6 may mediate excess mucin production by fibroblasts. In this patient, the sclerotic and depressed nature of the plaques, as opposed to raised, infiltrated plaques with central depressions, makes papular mucinosis a less likely diagnosis than malignant atrophic papulosis.

### GUTTATE MORPHEA AND LICHEN SCLEROSUS

Morphea is an inflammatory disorder of unknown cause in which inflammation in the skin leads to localized sclerotic plaques. Guttate morphea is a rare subtype of morphea in which plaques are small and raindrop-like. This subtype frequently coexists with lichen sclerosus. Lichen sclerosus may involve the anogenital region and extragenital sites. Patients with extragenital involvement present with papules that are small, shiny, white, wrinkly, and flat and that may have follicular prominence. These papules progress to display sclerosis and atrophy. The papules may be discrete or confluent and commonly occur on the trunk. The plaques in this case do not resemble those of lichen sclerosus.

### ARSENIC TOXICITY

Arsenic toxicity may be recognized on the skin by the presence of arsenical keratoses (a palmoplantar keratoderma with punctate and larger papules), the presence of superficial nonmelanoma skin cancers, and a disorder of pigmentation with raindrop-like hyperpigmented and hypopigmented macules that are predominantly seen on the trunk. These macules have normal skin texture, which differentiates them from those seen in this patient.

*Dr. Nancy Lee Harris* (Pathology): Dr. Kroshinsky, would you tell us your impression when you saw this patient?

*Dr. Daniela Kroshinsky* (Dermatology): I was asked to evaluate this patient for asymptomatic lesions that began on the torso and extremities and progressed rapidly to involve the face. On examination, he had innumerable erythematous macules and papules with central atrophic, white, sclerotic centers, many with peripheral hyperpigmentation and telangiectasias (Fig. 1). The lesions on the face were similar in appearance but had violaceous borders.

The clinical findings, taken in the context of the patient's dermatomyositis, caused concern for dermatomyositis-associated atrophic papulosis, and in view of the absence of gastrointestinal symptoms at the time, it was unclear whether he had a skin-limited or a disseminated variant. A biopsy of a lesion and a coagulopathy workup were performed.

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### CLINICAL DIAGNOSIS

Malignant atrophic papulosis (Degos's disease) in a patient with dermatomyositis.

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### DR. SUSAN BURGIN'S DIAGNOSIS

Malignant atrophic papulosis (Degos's disease) in a patient with dermatomyositis.

## PATHOLOGICAL DISCUSSION

*Dr. Declan McGuone:* A muscle-biopsy specimen from the right quadriceps, obtained as part of the initial diagnostic workup, showed a mildly increased variation in fiber sizes and an occasional atrophic fiber (Fig. 2A). No fiber necrosis, regeneration, endomysial inflammation, or perifascicular atrophy was present. The density of the endomysial capillaries was within normal limits. Antibody to C5b–C9 (the membrane-attack complex) highlighted an occasional capillary (Fig. 2A, inset). Electron microscopy was unrevealing. A repeat muscle-biopsy specimen from the right quadriceps, obtained 5 weeks later, showed subtle changes of an inflammatory myopathy with minimal endomysial inflammation, occasional degenerating and regenerating fibers, and scattered capillaries that were positive for C5b–C9 (Fig. 2B). There was mild atrophy of type 2 fibers, a finding consistent with glucocorticoid therapy.

The diagnostic workup also included two concurrent skin-biopsy specimens obtained 4 months after the initial muscle biopsy. The first specimen showed deep dermal ischemic damage with eccrine gland necrosis, features consistent with Degos's disease (Fig. 2D). The second specimen showed mild interface dermatitis with vacuolation of cells in the basal epidermis, focal dyskeratosis, scattered small lymphocytes, and increased superficial dermal mucin, findings consistent with dermatomyositis (Fig. 2E).

## DISCUSSION OF MANAGEMENT

*Dr. John H. Stone:* This 32-year-old man had a devastating disease for which many therapies have been tried, but none have been shown to be effective. He had already been treated intensively for dermatomyositis when the diagnosis of Degos's disease was made. His serum creatine kinase level had normalized, but his muscle strength had not improved and there was concern that a glucocorticoid myopathy might partly explain his persistent weakness. The second muscle-biopsy specimen confirmed this diagnosis. He had also received azathioprine, rituximab, and intravenous immunoglobulin, all of which are commonly used in cases of dermatomyositis, typically with clinically significant efficacy. None of these interventions, however, had improved his muscle strength.

After the diagnosis of Degos's disease and a negative coagulopathy workup, the administration of aspirin (325 mg) was begun, which was followed by dipyridamole, without a clinically significant effect.[9,10] We then considered a range of other conventional and biologic therapies for both the ongoing profound muscle weakness and the Degos's disease, including cyclophosphamide, methotrexate, and inhibitors of tumor necrosis factor and vascular endothelial growth factor, but because of the lack of compelling evidence that they might work, we rejected them all.

As Dr. Burgin mentioned, there is some evidence that Degos's disease stems from endothelial-cell injury mediated by both interferon-α and the terminal components of complement (C5b–C9, the membrane-attack complex).[6,11,12] Although this finding requires confirmation in more cases of Degos's disease, we needed a novel approach to therapy for this patient immediately. Eculizumab is a monoclonal antibody directed against C5 that blocks the cleavage of this complement protein by C5 convertase. In theory, eculizumab might interrupt the process of complement-mediated cell destruction in Degos's disease by preventing C5b–C9 formation.[13] Eculizumab decreases the need for blood transfusions in paroxysmal nocturnal hemoglobinuria, a hemolytic anemia caused by a clonal disorder of hematopoietic stem cells that is mediated by C5b–C9 deposition on red cells.[14] Eculizumab is approved in many countries for that indication, and anecdotal evidence suggests that it may be effective in Degos's disease.[15]

We initiated treatment with eculizumab (900 mg intravenously each week). The patient received four doses of treatment. Although there was some suggestion that the lesions on his head and face improved during that time, the patient continued to note new lesions on his arms and also noted the return of crampy abdominal pain. His muscle strength showed no improvement. We therefore considered more intensive immunosuppressive therapy with cyclophosphamide and high-dose prednisone, but before pursuing that regimen, we performed an MRI-guided muscle biopsy.

*Dr. McGuone:* A muscle-biopsy specimen of the left quadriceps obtained 8 months after the patient's initial presentation showed an inflammatory myopathy with prominent perifascicular atrophy, patchy T-cell–rich lymphocytic inflammation, and multiple capillaries that were positive for C5b–C9, a finding consistent with dermatomyositis (Fig. 2C).

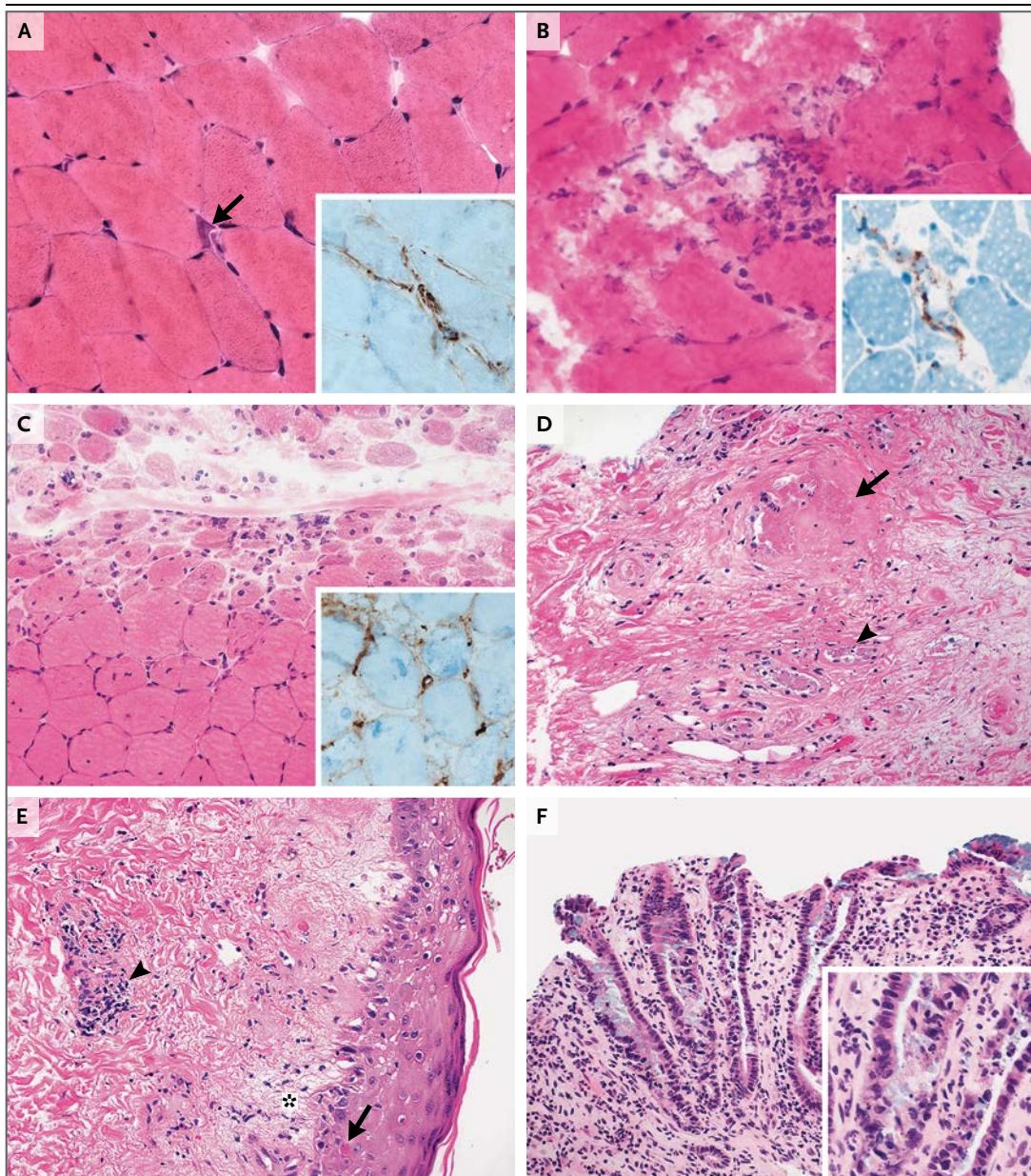*Dr. Stone:* Five days after the muscle biopsy, the

**Figure 2. Pathological Examination of Biopsy Specimens (Hematoxylin and Eosin).**

A skeletal-muscle–biopsy specimen from the right quadriceps, obtained shortly after presentation, shows slight variation in muscle-fiber diameters and an occasional atrophic fiber (Panel A, arrow). Antibody to C5b–C9 (membrane-attack complex) highlights an occasional endomysial capillary (Panel A, inset; C5b–C9 immunohistochemical stain). In a repeat skeletal-muscle–biopsy specimen obtained 5 weeks after presentation (Panel B), there is focal endomysial chronic inflammation with capillary labeling for C5b–C9 (inset, C5b–C9 immunohistochemical stain). A muscle-biopsy specimen from the left quadriceps obtained 8 months after presentation (Panel C) shows marked perifascicular atrophy and occasional lymphocytes. Many capillaries in this specimen are positive for C5b–C9 (inset, C5b–C9 immunohistochemical stain). A skin-biopsy specimen (Panel D) shows necrosis of the dermis (arrow) and necrosis of an eccrine gland (arrowhead), features that are typical of Degos's disease. There is mild vacuolation of the basal layer of the epidermis (Panel E) and an occasional dyskeratotic epidermal cell (arrow); the dermis contains scattered small lymphocytes (arrowhead), and there is accumulation of mucin in the superficial dermis (asterisk), a finding consistent with dermatomyositis. A colonic-biopsy specimen shows denuded surface epithelium (Panel F) and slightly distorted crypt architecture and apoptotic debris in the basal epithelium (inset).

patient was admitted to this hospital with diffuse abdominal pain, a temperature of 39.4°C, and a leukocytosis. CT of his abdomen was performed.

*Dr. Anuradha S. Shenoy-Bhangle:* CT of the abdomen and pelvis after the administration of oral and intravenous contrast material was performed. The CT images showed diffuse thickening of the small-bowel wall, minimal ascites, and no mesenteric inflammation (Fig. 3). There was no pneumoperitoneum or intraabdominal mass. The celiac and superior and inferior mesenteric arteries did not show thrombosis.

CT of the abdomen is important in determining both the extent of abdominal involvement and early detection of complications in cases of Degos's disease. In patients with Degos's disease, abdominal CT scans can show intestinal and extraintestinal findings. The small bowel is more commonly involved than the large bowel.[16] Bowel-wall ischemia and infarction each result in diffuse bowel-wall thickening (>3 mm when the bowel is distended with fluid or air), as seen in this patient.[17] Infarcted bowel shows no enhancement on contrast-enhanced CT images. Ischemic bowel may progress to bowel-wall hemorrhage, and resulting complications, such as intestinal perforation and pneumoperitoneum, could cause death. Extraintestinal abdominal disease includes omental infarction and ascites.[18] In the context of the clinical scenario, this patient most likely had vasculopathic changes that caused bowel-wall edema and thickening, without the associated complications of infarction, hemorrhage, or perforation.

*Dr. McGuone:* Because of ongoing diarrhea, abdominal pain, and immunosuppression, as well as the imaging findings, a colonic biopsy was performed to rule out infectious colitis. The biopsy specimen showed focal mucosal damage with disruption of crypt architecture, apoptosis in the basal epithelium, and focal denudation of surface epithelium (Fig. 2F), findings consistent with ischemic colitis. Evaluation for vasculitis could not be performed because no arterioles were present.

*Dr. Stone:* Enterococcus was identified on blood cultures. The administration of vancomycin was begun, but shortly thereafter, upper gastrointestinal hemorrhage with hypotension and shock developed, and the patient died, 10 months after the diagnosis of dermatomyositis.

*Dr. McGuone:* An autopsy was performed. The source of hemorrhage was multiple linear ulcers in the lower esophagus and associated surround-
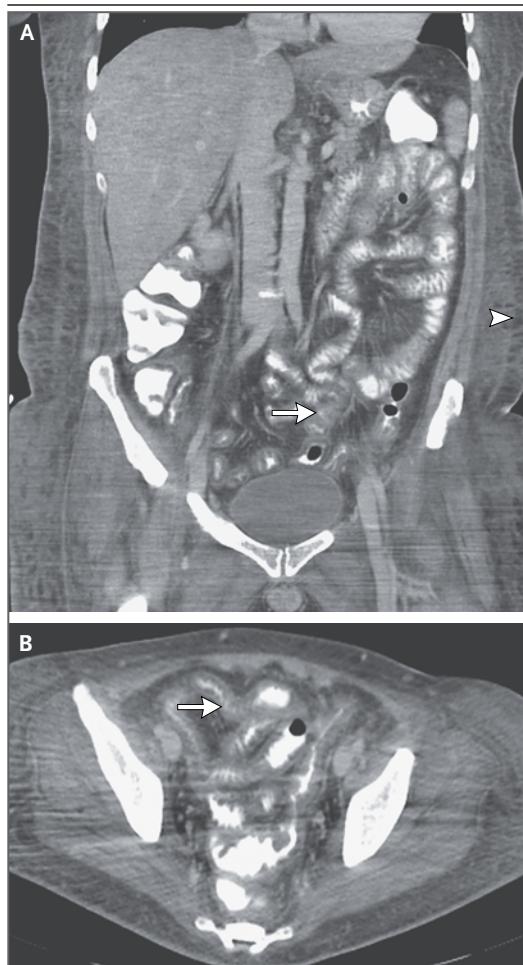


**Figure 3. CT Images of the Abdomen.**

Coronal (Panel A) and axial (Panel B) contrast-enhanced CT images of the abdomen show diffuse thickening of the small-bowel wall (arrows), a finding that is consistent with edema. Diffuse subcutaneous edema (Panel A, arrowhead) is also seen. There is no evidence of bowel-wall perforation or omental infarction.

ing mucosal erythema (Fig. 4A and 4B). There was ill-defined plum-colored discoloration of the antimesenteric surface of the small intestines and punctate foci of acute hemorrhage in the surrounding mesenteric fat. Microscopic examination confirmed a widespread obliterative vasculopathy of the gastrointestinal tract, with intimal hyperplasia, luminal stenosis, and preserved internal elastic lamina. There was no granulomatous vasculitis or fibrinoid necrosis, although several vessels contained lymphocytes in their walls and some contained fibrin thrombi (Fig. 4C, 4D, and 4E). Examination of skeletal muscle at
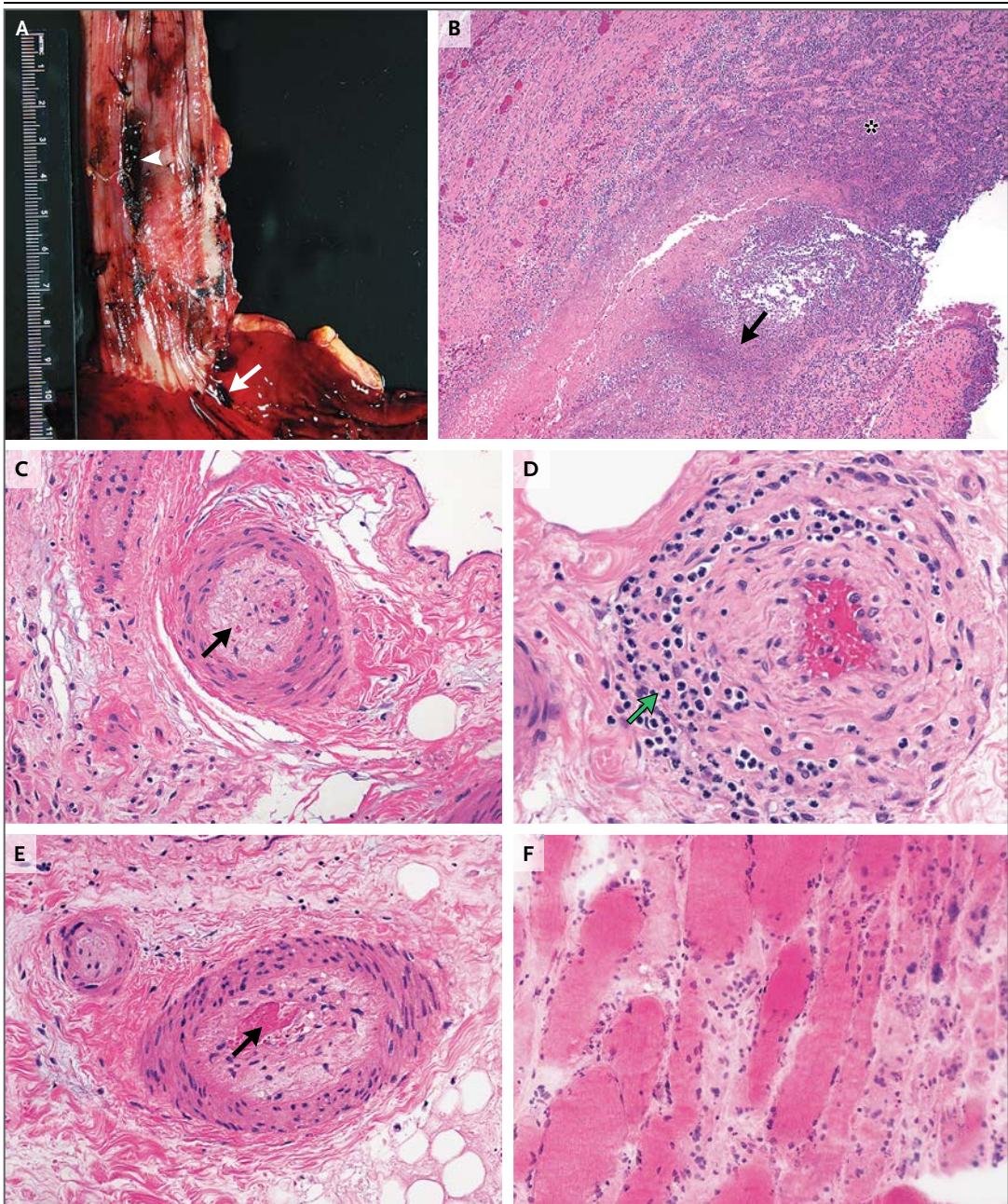
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**Figure 4.** Pathological Findings at Autopsy.

A gross photograph (Panel A) shows the gastroesophageal junction containing multiple linear hemorrhagic ulcers in the lower esophagus (arrowhead) and proximal stomach (arrow) and associated erythema of gastric mucosa. A histologic section through an esophageal ulcer (Panel B) shows mucosal necrosis (arrow), with surrounding inflammation (asterisk). There is an obliterative vasculopathy in the wall of the esophagus (Panel C) and in the wall of the small bowel (Panels D and E), with intimal thickening (Panel C, arrow), inflammation (Panel D, arrow), and focal luminal thrombus (Panel E, arrow). A section of deltoid muscle (Panel F) shows widespread muscle inflammation and fiber atrophy, which are findings consistent with dermatomyositis.

autopsy confirmed severe dermatomyositis, most severe in the deltoid muscles (Fig. 4F), next most severe in the iliopsoas, and less severe, but still striking, in the leg muscles. The peripheral nerves (sciatic and femoral) showed patchy perivascular chronic inflammation with hemosiderin pigment and scarring, features suggestive of a vasculopathy but without evidence of active vasculitis or

obstructive vasculopathy. The central nervous system was not involved.

*Dr. Harris:* Are there any questions for our discussants?

*A Physician:* Is there any understanding of why the gastrointestinal tract and the skin seem to be preferentially the focus of this endothelial membrane-attack complex?

*Dr. Stone:* Degos's disease also very typically involves the brain, so involvement is really of the skin, gut, and brain; but why those organs, we really don't know. And why a subset of patients also have muscle disease is unknown.

## ANATOMICAL DIAGNOSES

Dermatomyositis.

Malignant atrophic papulosis (Degos's disease), involving the skin and gastrointestinal tract.

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