Disabling pansclerotic morphea
Clinical presentation in two adults

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Disabling pansclerotic morphea involves all layers of the skin, extending through the dermis and subcutaneous tissues to involve muscle, tendon, and bone. It is distinguished from generalized scleroderma by its lack of systemic involvement. Onset usually occurs before the age of 14 years. We describe adult-onset disabling pansclerotic morphea in two previously healthy young men. In both cases, the onset of disease was explosive, with rapid progression, widespread cutaneous involvement, and severe disablement caused by mutilating contracture deformities. Increased susceptibility of sclerodermatous tissue to recalcitrant ulceration and malignant transformation with development of nonmelanoma skin cancers was also observed. Treatment of this disease continues to present a therapeutic dilemma with only sporadic remission despite multimodality therapy. (J Am Acad Dermatol 2005;53:S115-9.)

Disabling pansclerotic morphea (DPM) is a rare form of morphea that involves all layers of the skin, extending through the dermis and subcutaneous tissues to muscle, tendon, and bone. It is distinguished from generalized scleroderma by its lack of systemic involvement. Unlike the relatively benign localized, linear, and generalized variants of morphea, DPM has an aggressive, mutilating course that results in severe functional and psychologic impairment of those affected. Painful ulcerations and contracture deformities occur as a result of the pansclerotic process. Poor response to treatment is a hallmark of this disease.

In most previously reported cases of DPM, onset is in childhood, usually before the age of 14 years. Herein we describe adult-onset DPM in two previously healthy young men. In both patients, the onset of disease was explosive, with rapid progression, widespread cutaneous involvement, and severe disability.

CASE REPORTS

Case 1

A 26-year-old man presented to our institution in October 1998 with a 2.5-year history of rapidly progressive “tightening” of the skin involving his upper and lower extremities, starting distally and extending proximally. The process did not involve the digits. Within months of disease onset, contracture deformities of the hands developed that prevented him from performing his normal activities of daily living. The process completely spared his head, neck, and torso. He had no history of trauma or excessive physical activity preceding the onset of symptoms. There was no personal or family history of autoimmune or connective tissue disease. There was no history of Raynaud’s phenomenon.

On physical examination, confluent hypopigmented and hyperpigmented sclerotic plaques involved his upper and lower extremities, with clawlike contracture deformities of his hands (Fig 1). On the left foot was an 8-mm ulcer (Fig 2).

An excisional biopsy specimen from a representative area of the left thigh showed pansclerosis extending from the papillary dermis through the panniculus and into fascia. Results of direct immunofluorescence of involved skin were negative. Laboratory data were remarkable for peripheral eosinophilia (1.35 × 10⁹/L [reference range, 0.05-0.50 × 10⁹/L]), hypergammaglobulinemia (4.13 g/dL [reference range, 0.7-1.7 g/dL]), and mild elevation of the erythrocyte sedimentation rate (38 mm/h [reference range, 0-29 mm/h]). Analyses for antinuclear antibody, antihistone antibody, extractable nuclear antigen antibodies (ribonucleoprotein,
Smith, SS-A, SS-B, Scl-70), and rheumatoid factor were negative. Findings on chest radiography were normal. Pulmonary function testing yielded a positive methacholine challenge result, attributed to a life-long history of asthma. Upper gastrointestinal tract endoscopy and esophageal manometry did not show esophageal dysmotility, although the patient had reflux symptoms.

Therapy with hydroxychloroquine (400 mg/d) was initiated and maintained for approximately 5 months. Physical therapy was recommended. Subsequently methotrexate, in a dose escalated from 10 to 22.5 mg weekly, and prednisone (10-20 mg/d) were added to treatment with hydroxychloroquine. In the ensuing months, the degree of sclerosis improved gradually, with softening of the skin.

Despite response of the sclerotic process to therapy, the patient’s course was complicated during subsequent months by the development of extensive leg ulcerations. The lower extremity ulcerations progressed to involve the entire back and sides of both feet with extension onto the distal calves (Fig 3). They were extremely painful, requiring narcotic analgesia. Arterial and venous studies showed no serious vasculopathy; values on transcutaneous pulse-oximetry measurement were slightly decreased.

With maintenance of triple-drug therapy (hydroxychloroquine, methotrexate, and prednisone) for 2 years, “burn-out” of the sclerotic process has occurred with considerable softening of the skin. No new areas of involvement have developed. However, the lower extremity ulcers have been recalcitrant and progressive despite multimodality intensive wound care, including systemic antibiotics for methicillin-sensitive *Staphylococcus aureus* infection, topical agents, compression boots, arterial pneumatic compression pump, hyperbaric oxygen, and

**Fig 1.** Case 1. **A** and **B**, Confluent hypopigmented and hyperpigmented sclerotic plaques involving extremities with sparing of torso. **C**, Clawlike contracture deformities of hands.
placement of tissue-engineered skin (Apligraf; Novartis Pharmaceutical Corp, East Hanover, NJ). Biopsy specimens from the edges of the ulcerations showed no evidence of malignancy. Most recently, pinch grafting was performed with some evidence of healing. Pain control has been maintained with morphine and opiates. Because of the debilitating nature of this process, the patient is wheelchair dependent.

**Case 2**

A 32-year-old man with a 14-year history of DPM presented to our institution in July 2001. Before the onset of his disease, he had been a healthy, fit distance runner. The sclerosis of his skin started on his feet and evolved rapidly over approximately 6 months to involve all his skin, including extremities, trunk, neck, face, and scalp. Painful contracture deformities of the hands, wrists, elbows, hips, and feet developed, resulting in severe disability. He had no history of trauma or excessive physical activity before onset of the sclerotic process. He had not participated in any of his usual running activities for several months before disease onset. There was no personal or family history of autoimmune or connective tissue disease. There was no history of Raynaud's phenomenon.

Skin biopsy specimen findings were consistent with DPM with extension through the dermis and panniculus into fascia. There was no evidence of systemic involvement, dyspnea, and dysphagia. Pulmonary function testing did not reveal parenchymal disease; however, results did demonstrate a restrictive pattern secondary to chest wall constriction attributable to the pansclerotic process. Over the course of his disease, he had recurrent painful ulceration of the distal extremities. These ulcers, in addition to the contracture deformities, have been debilitating and severely limiting to his activities of daily living and functional independence.

In 1998 (12 years after onset of disease), a small lesion developed on the right side of the patient’s lower lip; it enlarged slowly during the ensuing 18 months. Biopsy specimen findings were consistent with a diagnosis of squamous cell carcinoma, treated with excision. Since that time, several squamous cell carcinomas have occurred on the skin and oral mucosa.

His disease had been treated with multiple systemic agents before presentation at our institution, including penicillamine, methotrexate, azathioprine, thalidomide, and prednisone. He had little or no clinical or functional improvement with these agents.

On physical examination, there was generalized sclerosis with a "bound-down" appearance of the skin involving the extremities, trunk, neck, face, and scalp. Polymorphous, large, confluent hypopigmented and hyperpigmented sclerotic plaques were widespread over the body (Fig 4). He had bilateral ectropion, scalp alopecia (Fig 5), and superficial ulcers involving the hands, feet, and sacrum.

Laboratory findings were normal, including serum protein electrophoresis; erythrocyte sedimentation rate; analyses for antinuclear antibody, antidouble-stranded DNA antibody, and extractable nuclear antigen antibodies (ribonucleoprotein, Smith, SS-A, SS-B, Scl-70); serologic analyses for hepatitis; and HIV testing. Results of noninvasive arterial and venous studies were normal.

Therapy with hydroxychloroquine (400 mg/d) was initiated. Triamcinolone 0.1% cream was used topically.

After 4 months of therapy, there was minimal slowing of the sclerotic process. Daily narcotic analgesics have been required to control pain caused by progressive contracture deformities, ulcers, and digital necrosis that required amputation. Routine physical and occupational therapy have been instrumental in helping the patient maintain minimal independent functional capacity. The patient is now wheelchair dependent for mobility.
DISCUSSION

Both patients, previously healthy young men, had explosive onset of the sclerotic process, resulting in severe disability and impairment. Remarkably, in case 1, skin involvement was purely acral, involving only the extremities, excluding the digits, and completely sparing the rest of the body. In case 2, the disease began acrally but rapidly generalized. Neither patient had evidence of systemic involvement. Specifically, there were no signs of primary renal, pulmonary, or gastrointestinal tract involvement.

On serologic evaluation, autoantibody analyses were negative in both patients. Peripheral eosinophilia, elevated \( \gamma \)-globulin level, and elevated erythrocyte sedimentation rate were observed in case 1. This pattern of laboratory findings is similar to that observed in the patients described by Diaz-Perez et al.\(^1\)

For both patients (Table I), the sclerotic process led to the development of severe, recalcitrant, and extraordinarily painful skin ulcers. Results of non-invasive arterial and venous studies were normal in our patients. Ulcers arising in the setting of DPM have been observed commonly.\(^1-6\) Despite control of the sclerotic process, these ulcers are often recalcitrant to therapy. Given the normal results of vascular studies in these patients, it is difficult to understand why these ulcerations occurred. In neither patient did medications have any effect on decreasing the occurrence or promoting healing of these ulcers.

In case 2, squamous cell carcinomas arose in ulcerated and nonulcerated sclerodermatous skin and even involved the lips. Increased susceptibility of sclerodermatous tissue to malignant transformation has been described previously.\(^2,7,9\) Such factors as recalcitrant ulcerations, scar tissue formation, and treatment with immunosuppressive agents further increase the likelihood of malignant transformation. Chronic infection also plays a role. Wollina et al\(^9\) described squamous cell carcinoma presenting as malignant ulcers in pansclerotic morphea of childhood in a 16-year-old boy. Parodi et al\(^2\) described a case of metastatic squamous cell carcinoma arising in a recalcitrant ulceration in a 20-year-old man with an 18-year history of DPM. In both patients amputations were performed; however, both patients died.

Treatment of this disease continues to present a therapeutic dilemma. The usual course of disease is relentless progression despite aggressive therapy. Used in combination, hydroxychloroquine, prednisone, and methotrexate seemed to slow disease progression in case 1. There has been limited success with penicillamine, antimalarials, corticosteroids, and cytotoxic agents, including methotrexate, cyclophosphamide, and azathioprine.\(^1,10,11\) Used singly, these agents cannot halt or reverse the sclerotic
process. There have been reports of disease response to UVA-1 phototherapy.3,12,13 Wollina et al14 reported softening of sclerotic plaques and healing of ulcerations with intravenous immunoglobulin infusion in a patient with childhood DPM.

In summary, adult-onset DPM without evidence of systemic involvement occurred in two previously healthy young men. In both patients, the disease has had devastating physical and psychologic effects. Fulminant progression has led to severe disability within a short time. Remarkable associations of recalcitrant ulcerations and development of nonmelanoma skin cancers were observed. These patients demonstrate that this disease may have onset in postadolescent years. Early, aggressive therapeutic intervention may prevent this disease from progressing to the extent observed in these two patients.

REFERENCES


Table I. Summary of clinical characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Case 1</th>
<th>Case 2</th>
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<tr>
<td>Sex</td>
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<tr>
<td>Age at disease onset, y</td>
<td>26</td>
<td>18</td>
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<tr>
<td>Extent of involvement</td>
<td>Extremities only</td>
<td>All skin</td>
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<td>Biopsy specimen finding</td>
<td>Pansclerotic morphea</td>
<td>Pansclerotic morphea</td>
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<td>Systemic involvement</td>
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<td>None</td>
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<tr>
<td>Noninvasive lower extremity arterial</td>
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<tr>
<td>and venous studies</td>
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<td>Laboratory findings</td>
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<td>Autoantibodies (ANA, ENA, anti–SCL-70)</td>
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<td>Response to therapy</td>
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<td>Degree of disability caused by disease</td>
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<td>Narcotics required for pain</td>
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</tr>
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<td>Raynaud’s phenomenon</td>
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ANA, Antinuclear antibody; ENA, extractable nuclear antigen; SCC, squamous cell carcinoma.