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Morphea

Kendra G Bergstrom, MD, Private Practice, Manhattan Dermatology

Updated: Aug 3, 2009

Introduction

Background

Morphea, also known as localized scleroderma, is a disorder characterized by excessive collagen deposition leading to thickening of the dermis, subcutaneous tissues, or both. Morphea is classified into plaque, generalized, linear, and deep subtypes according to the clinical presentation and depth of tissue involvement. Unlike systemic sclerosis, morphea lacks features such as sclerodactyly, Raynaud phenomenon, and internal organ involvement. Saleh et al discuss a new variant, termed superficial morphea, which is characterized clinically by hyperpigmented or hypopigmented patches of skin that lack induration.¹

Pathophysiology

Overproduction of collagen by fibroblasts in affected tissues is common to all forms of morphea, although the mechanism by which these fibroblasts are activated is unknown. Proposed factors involved in the pathogenesis of morphea include endothelial cell injury, immunologic (eg, T lymphocyte) and inflammatory activation, and dysregulation of collagen production. An autoimmune etiology is supported by the frequent presence of autoantibodies in affected individuals.

Studies have shown increased levels of circulating intercellular adhesion molecule-1 and fibrogenic T-helper 2 cytokines such as interleukin (IL)-4 and transforming growth factor-beta (TGF-beta) in patients with morphea. These cytokines recruit eosinophils and other inflammatory cells (which are present in early morphea lesions and in eosinophilic fasciitis) and induce fibroblasts to synthesize excessive collagen and connective-tissue growth factor. The latter is a soluble mediator that enhances and perpetuates the profibrotic effects of TGF-beta.^{2,3,4,5}

Frequency

United States

The incidence of morphea has been estimated as approximately 25 cases per million population per year. The actual incidence is likely higher because many cases may not come to medical attention. Two thirds of adults with morphea present with plaque-type lesions, with generalized, linear, and deep variants each accounting for approximately 10% of cases. Up to half of all cases of morphea occur in pediatric patients. In this group, linear morphea predominates (two thirds of cases), followed by the plaque (25%) and generalized (5%) subtypes. Of note, as many as half the patients with linear morphea have coexistent plaque-type lesions.

Mortality/Morbidity

Morphea typically has a benign, self-limited course. Survival rates for morphea patients are no different from those of the general population. However, linear and deep morphea subtypes can cause considerable morbidity, especially in children when they interfere with growth. Joint contractures, limb-length discrepancy, and prominent facial atrophy result in substantial disability and deformity in a quarter to half of all patients with linear or deep morphea. Neurologic and ophthalmologic manifestations can also occur in those with craniofacial lesions (eg, en coup de sabre, Parry-Romberg syndrome). Such complications are more common in pediatric cases.

Race

Although morphea occurs in persons of all races, it appears to be more common in whites than in African Americans.

Sex

Women are affected approximately 3 times as often as men for all forms of morphea except the linear subtype, which only has a slight female predominance.

Age

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Age

Linear morphea commonly manifests in children and adolescents, with two thirds of cases occurring before age 18 years. Other morphea subtypes have a peak incidence in the third and fourth decades of life.

Clinical

History

- Morphea is usually asymptomatic, and the development of lesions is typically insidious. One exception is the acute, painful onset of eosinophilic fasciitis.
- Arthralgias, usually localized to an affected extremity, may be reported by patients with morphea. Linear and deep lesions can also be associated with arthritis, myalgias, carpal tunnel syndrome, and other peripheral neuropathies.
- Patients with craniofacial linear morphea can present with seizures (typically complex partial), headaches, cranial nerve palsies, trigeminal neuralgia, hemiparesis/muscle weakness, eye pain, and visual changes.

Physical

Physical findings in morphea are localized to the affected skin and underlying tissues, with varying configurations (eg, oval, linear, ill defined) and depths of involvement in the subtypes. Although subdivision of morphea by subtype is useful with regard to differences in epidemiology, anatomic site, and course of disease, it is important to recognize that continuous clinical and histologic transitions exist among all the variants within the morphea spectrum.

Plaque-type morphea is the most common and benign morphea subtype and includes guttate and keloidal (nodular) variants (see Media File 1). These lesions are relatively superficial, primarily involving the dermis.



Inflammatory plaque-type morphea on the abdomen, characterized by induration, erythema, and a surrounding lilac ring.

Generalized morphea is a more extensive and severe form of plaque-type disease.

Linear morphea includes the en coup de sabre and Parry-Romberg variants (see Media File 2). It often qualifies as deep morphea (albeit in a linear pattern), involving the deep dermis, subcutaneous fat, muscle, bone and even underlying meninges and brain.



A hyperpigmented band of linear morphea involving the right part of the trunk and thigh.

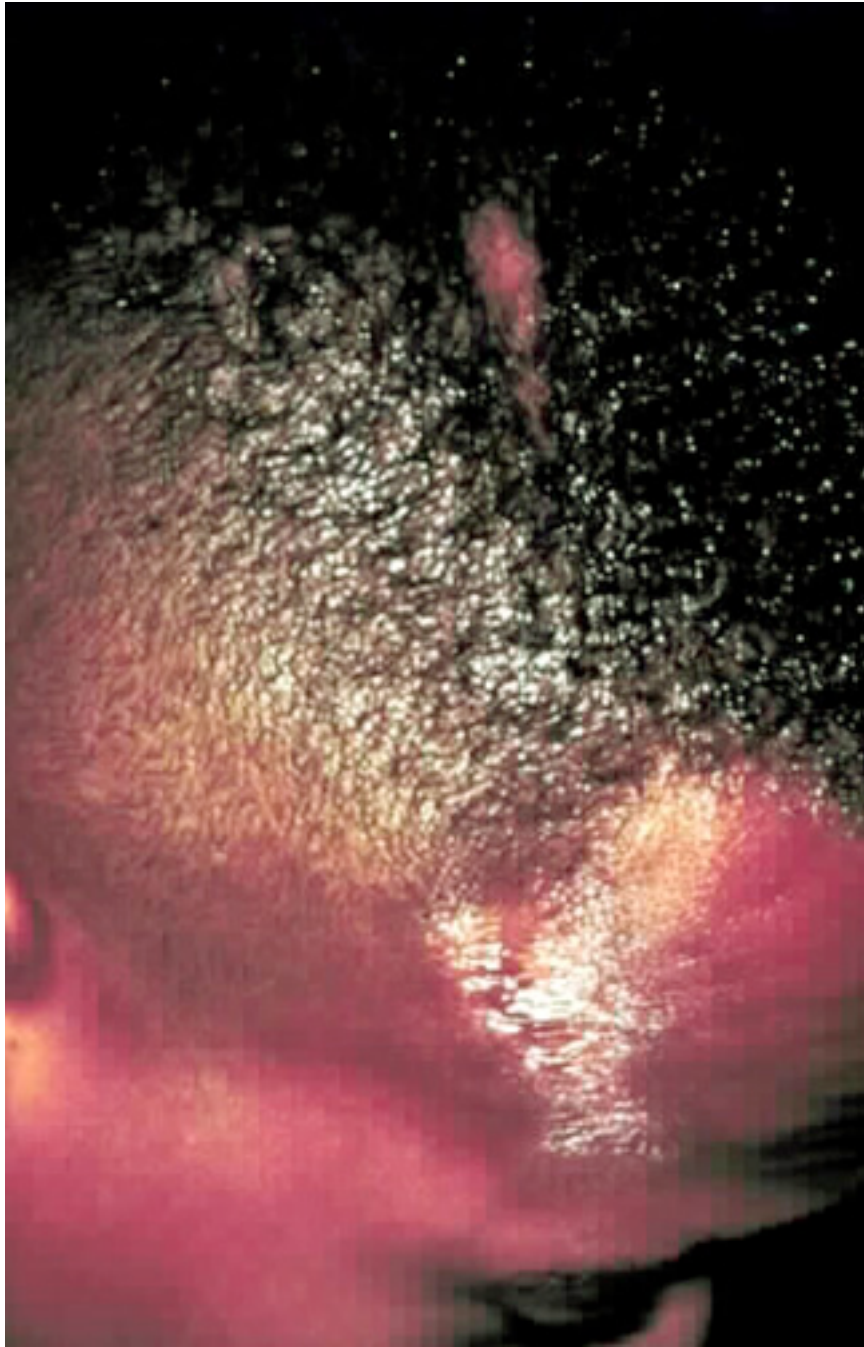
Deep morphea, also referred to as subcutaneous morphea or morphea profunda, primarily involves the subcutaneous fat and underlying structures such as fascia (see Media File 4). Variants of deep morphea include eosinophilic fasciitis and disabling pansclerotic morphea of children.



Morphea profunda involving the left lower extremity, with thickened, taut, bound-down skin.

- Types of skin lesions

- Plaque-type morphea lesions are characterized as circumscribed, indurated plaques that range from 1 cm to more than 20 cm in diameter. They often begin as erythematous to violaceous patches or slightly edematous plaques. With disease progression, sclerosis develops centrally as the lesions undergo peripheral expansion. The surface becomes smooth and shiny over time, with loss of hair follicles and sweat glands. The margins are often surrounded by a zone of violaceous color or telangiectasias. Over a period of months to years, the skin softens and the dermis becomes atrophic.
- Guttate morphea lesions are small (<10 mm in diameter) and superficial, with less induration and a sharply demarcated border. The clinical appearance overlaps with that of lichen sclerosus, but true guttate morphea lacks epidermal atrophy and follicular plugging.
- Keloidal (nodular) morphea is a rare variant characterized by nodules resembling keloids in the presence of typical plaque-type morphea.
- Atrophoderma of Pasini and Pierini is thought to represent an abortive form of morphea and resembles "burnt-out" plaque-type lesions. It is characterized by hyperpigmented, slightly depressed areas with well-defined "cliff-drop" borders and no obvious induration. Similar hyperpigmented patches with minimal induration are seen in persons with superficial morphea, which, unlike atrophoderma of Pasini and Pierini, is characterized histologically by sclerosis of the upper dermis.
- Bullous morphea is a rare variant in which tense subepidermal bullae develop overlying plaque-type, linear, or deep morphea lesions. This phenomenon may result from stasis of lymphatic fluid due to the sclerodermatous process or coexisting lichen sclerosus.
- Linear morphea features discrete, indurated linear bands.
- Frontoparietal linear morphea, called en coup de sabre, is characterized by a linear, atrophic depression suggestive of a stroke from a sword. Such lesions may extend deep into underlying tissues (see Media File 3).



Linear atrophic depression of an en coup de sabre lesion on the right side of the forehead and the frontal part of the scalp.

- Parry-Romberg syndrome (progressive hemifacial atrophy) is thought to represent a severe, segmental form of craniofacial linear morphea. Unlike en coup de sabre, the primary abnormality occurs in the subcutaneous fat, muscle, and bone. Although the skin is typically not indurated or bound down, some patients also exhibit primary cutaneous sclerosis reminiscent of en coup de sabre.
- Deep morphea is characterized by ill-defined, bound-down, sclerotic plaques with a "cobblestone" or "pseudo-cellulite" appearance. The "groove sign" (a depression along the course of a vein, between muscle groups, or both) may be evident later in the course of disease.

- Eosinophilic fasciitis (Shulman syndrome) involves primarily the fascia and is characterized by an acute onset of symmetric pain and edema of the extremities, followed by progressive induration with an appearance similar to deep morphea.
- Disabling pansclerotic morphea of children has generalized involvement that extends throughout the tissues from dermis to bone.
- Color of skin lesions
 - Plaque-type morphea often begins as a discrete area of erythema. With progression of sclerosis, the center of the lesion gradually develops a waxy, ivory color. In active phases of the disease, a violaceous border (lilac ring) may surround the indurated region. Hyperpigmentation often ensues as lesions evolve and eventually involute. The sclerotic lesions of guttate morphea are typically whitish in color, and the clinical appearance may overlap with that of extragenital lichen sclerosus. The patches of atrophoderma of Pasini and Pierini are hyperpigmented.
 - The multiple, coalescent lesions of generalized morphea are often hyperpigmented to silvery.
 - Deep morphea lesions are frequently hyperpigmented, but, because of the deeper level of inflammation, they lack the other color changes typical of plaque-type morphea.
- Shape of skin lesions
 - Plaque-type morphea lesions are typically oval or round.
 - Linear morphea occurs as a linear band.
 - Deep morphea lesions tend to be ill defined.
- Palpation of skin lesions
 - Well-developed morphea lesions are typically indurated and firm to palpation.
 - Linear and deep morphea lesions are often fixed to underlying structures, reflecting their extension down to muscle or bone. Older lesions may be either atrophic or sclerotic.
- Arrangement of skin lesions
 - Patients can present with single or multiple plaque-type morphea lesions. Oval plaques on the trunk are often oriented with their long axes in a horizontal direction and typically have an asymmetric distribution. Guttate morphea lesions are multiple.
 - Linear morphea lesions are most often single and are unilateral in 95% of cases. If both the upper and lower extremities are involved, lesions are usually homolateral. Although a few cases of linear morphea following Blaschko lines have been described, most lesions do not obviously correspond to Blaschko lines.^{6,7} Linear morphea usually extends along the length of an extremity, but sometimes a band surrounds a limb or finger circumferentially, resembling ainhum (a constriction band that can lead to amputation of a digit).
 - Deep morphea is characterized by diffuse thickening of subcutaneous tissues with ill-defined borders. Distribution of lesions is often symmetric.
- Areas of distribution
 - Plaque-type morphea is more common on the trunk (especially the lower aspect) than on the extremities, and the face is usually spared. Guttate morphea primarily involves the neck and the upper portion of the trunk. Atrophoderma of Pasini and Pierini usually occurs on the back, whereas superficial morphea favors intertriginous sites such as the axillae and inner thighs.
 - Generalized morphea occurs when morphea plaques become confluent or multiply and affect a significant portion of 3 or more major anatomical regions, often involving the chest, abdomen, lower back, buttocks, and thighs. In a rare variant of almost universal morphea, the whole body, from the top of the head to the feet, is involved; unlike diffuse systemic scleroderma, patients lack sclerodactyly, Raynaud phenomenon, or internal involvement.
 - Linear morphea most often occurs on the lower extremities, followed in frequency by the upper extremities, frontal portion of the head, and anterior trunk. En coup de sabre is the term used for linear morphea affecting the frontoparietal aspect of the face and scalp. Paramedian lesions are more common than median lesions.
 - Eosinophilic fasciitis most often affects the extremities, sparing the fingers and toes; the trunk is occasionally involved. Disabling pansclerotic morphea of children begins on the extensor extremities and progresses to the trunk, flexor extremities, face, and scalp, eventually sparing only the fingertips and toes.
- Hair and nails
 - Scalp involvement results in scarring alopecia, as seen in en coup de sabre. Loss of eyebrows and eyelashes can also occur in this variant.

- Nail dystrophy may develop when linear lesions involve the nail matrix and in pansclerotic morphea.
- General examination
 - Extensive truncal morphea may lead to restricted respiration.
 - When linear or deep morphea lesions cross joint lines, they can cause restricted mobility, contractures, and deformity. In children, such lesions can result in growth impairment and severe atrophy of affected limbs.
 - Muscle weakness may occur in patients with central nervous system abnormalities related to craniofacial linear morphea and in those with peripheral nerve involvement by morphea on an extremity.⁸ Signs of carpal tunnel syndrome may be evident in patients with deep morphea affecting the wrist (especially eosinophilic fasciitis).
 - Ocular manifestations of craniofacial morphea include ptosis, extraocular muscle dysfunction, anterior uveitis, episcleritis, glaucoma, xerophthalmia, and keratitis.
 - Oral findings in patients with craniofacial morphea include altered dentition, malocclusion, and asymmetry of the tongue.

Causes

The cause of morphea is unknown. To date, investigations have not uncovered any consistent etiologic factors. Different morphea subtypes often coexist in the same patient, suggesting that the underlying processes are similar.

- Radiation therapy: Morphea can occur at the site of previous supervoltage radiation therapy for breast cancer and other malignancies, developing from 1 month up to more than 20 years after irradiation.
- Infection or vaccination
 - Infections, such as Epstein-Barr virus infection, varicella, measles, and borreliosis, have been reported to precede the onset of morphea and have been proposed as possible triggers.
 - The most extensive literature focuses on *Borrelia burgdorferi* as a possible etiologic agent for morphea. Some studies have detected *Borrelia* DNA within morphea lesions from a subset of European and Japanese patients (representing *Borrelia afzelii* and *Borrelia garinii* rather than *B burgdorferi sensu stricto*, the predominant subtype in the United States); however, to date, this has not been demonstrated in patients from the United States.^{9,10,11} Several more studies found no serologic or polymerase chain reaction–based evidence of *Borrelia* infection in patients with morphea.^{12,13}
 - Morphealike lesions have also been reported to occur after BCG and tetanus vaccinations.
- Trauma: Some morphea patients report a history of local trauma directly preceding the onset of disease. Excessive physical exertion triggers eosinophilic fasciitis in approximately half the cases.
- Genetics: A few familial cases of morphea have been reported, most commonly the disabling pansclerotic subtype. No significant HLA associations have been described.

Differential Diagnoses

Amyloidosis, Primary Systemic
Ataxia-Telangiectasia
Atrophoderma of Pasini and Pierini
Eosinophilia-Myalgia Syndrome
Eosinophilic Fasciitis
Graft Versus Host Disease
Keloid and Hypertrophic Scar
Lichen Sclerosus et Atrophicus

Nephrogenic Fibrosing Dermopathy
Niemann-Pick Disease
Phenylketonuria
POEMS Syndrome
Porphyria Cutanea Tarda
Scleredema
Werner Syndrome
Winchester Syndrome

Other Problems to Be Considered

Linear melorheostosis

Linear lupus erythematosus panniculitis

Linear atrophoderma of Moulin

Lipodermatosclerosis

Radiation fibrosis

Reflex sympathetic dystrophy

Scleromyxedema

Cheiroarthropathy due to diabetes mellitus

Carcinoid syndrome

Muckle-Wells syndrome

Stiff skin syndrome

Restrictive dermopathy

Progeria

Morpheaform dermatofibrosarcoma protuberans

Scleroderoid conditions caused by chemical/toxin exposures (ie, polyvinyl chloride, epoxy resins, pesticides, dry cleaning solvents, silica dust)

Scleroderoid conditions caused by iatrogenic agents (ie, bleomycin, taxanes, gemcitabine, uracil-tegafur, melphalan isolated limb perfusion, L-tryptophan, vitamin K injections, pentazocine injections, silicone or paraffin implants)

Some of the entities in the differential diagnosis above often manifest with a scleroderoid (ie, diffuse sclerosis) rather than morpheaform (ie, discrete areas of sclerosis) morphology.

Atrophoderma of Pasini and Pierini and eosinophilic fasciitis are generally viewed as part of the morphea spectrum.¹⁴ Lichen sclerosus and morphea can coexist, with clinical and histologic findings of both conditions present in the same patient and even within the same lesion.¹⁵ In addition, lichen sclerosus, discrete morpheaform plaques, diffuse scleroderoid changes, and eosinophilic fasciitis all can occur as manifestations of chronic graft versus host disease.

The differential diagnosis for early, erythematous lesions of plaque-type morphea may include the following:

- Inflammatory granuloma annulare
- Interstitial and granulomatous dermatitis
- Erythema migrans
- Fixed drug eruption
- Annular lichenoid dermatitis of youth
- Sweet syndrome (early)
- Interstitial mycosis fungoides

Workup

Laboratory Studies

- Laboratory tests have a limited role in the evaluation of patients with morphea. The following studies can be considered on a case-by-case basis (eg, to monitor disease activity) but generally are not required.
- CBC count
 - CBC count results are usually normal.
 - Peripheral eosinophilia is most often present in patients with eosinophilic fasciitis and other forms of deep morphea, but it may be observed in those with early, active morphea of any type.
 - Anemia and thrombocytopenia occasionally develop in patients with eosinophilic fasciitis.
- Erythrocyte sedimentation rate: This is usually normal, but it may be elevated in patients with eosinophilic fasciitis or extensive, active morphea.
- Immunoglobulin G and immunoglobulin M: Polyclonal increases in both antibody types may occur, especially in patients with linear and deep morphea. This finding correlates with disease activity and the development of joint contractures in linear morphea.
- Autoantibodies: Serum autoantibodies are commonly present in all types of morphea.
 - Rheumatoid factor is positive in 15-40% of morphea patients, most often children with linear morphea.
 - Antinuclear antibodies are present in approximately 50% of morphea patients, typically with a homogeneous pattern. The prevalence is higher in those with linear and deep subtypes.

- Anti–single-stranded DNA antibodies are present in 25% of patients with plaque-type morphea, in 75% of those with generalized morphea, and in 50% of those with linear morphea; levels correlate with extensive, active disease and joint contractures.
- Antihistone antibodies are present in 50% of morphea patients overall and in 85% of those with generalized morphea, correlating with the number of plaque-type lesions and the total area affected; titers do not correlate with the presence or number of linear lesions.
- Anticentromere, anti-Scl70, and anti–double-stranded DNA antibodies are present in less than 5% of morphea patients.
- Antiphospholipid antibodies are present in some morphea patients. Immunoglobulin M and immunoglobulin G anticardiolipin antibodies are present in 60% and 25% of patients with generalized morphea, respectively. Lupus anticoagulant can also be detected in approximately 50% of this subgroup of patients.
- Antitopoisomerase 2- α antibodies are present in 75% of morphea patients.
- Anti-Cu/Zn-superoxide dismutase antibodies are present in 90% of morphea patients.

Imaging Studies

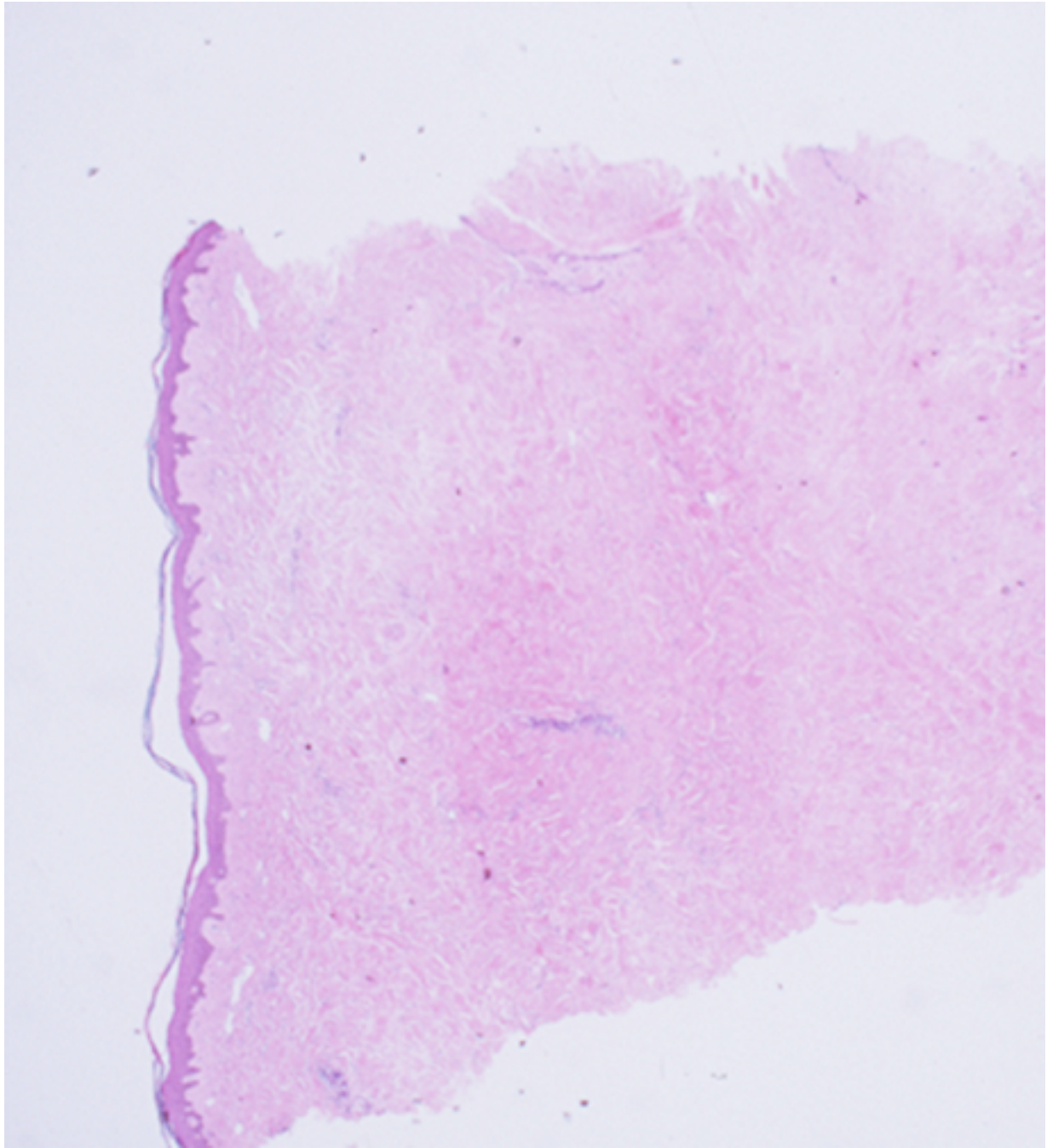
- Radiography: Radiography may be helpful in cases of linear (including en coup de sabre) or deep morphea in which involvement of the underlying bone is suspected. It can also be used to monitor pediatric patients for potential growth defects.
- Magnetic resonance imaging
 - MRI of the brain and skull in patients with en coup de sabre and Parry-Romberg syndrome may reveal abnormalities such as cortical atrophy, subcortical calcifications, white matter lesions, ventricular dilatation, leptomeningeal enhancement, anomalous intracranial vasculature, and skull atrophy, even in the absence of neurological symptoms.
 - MRI is useful in the diagnosis of eosinophilic fasciitis. Typical findings include diffuse edema of the subcutaneous tissues with thickening, increased signal intensity on T2-weighted images, and contrast enhancement of the fascial planes.
- Ultrasonography: The 20-MHz ultrasound can measure skin thickness, which correlates with disease activity. Li and Liebling suggest that ultrasonography can be of great benefit in the evaluation of localized scleroderma.¹⁶
- Electroencephalography: Abnormalities may be observed in patients with craniofacial linear morphea, usually localized to areas of the brain underlying affected skin, and sometimes without a history of clinical seizure activity.

Procedures

- Although a presumptive diagnosis of morphea can frequently be made based on clinical findings, a biopsy can be used to confirm the diagnosis and delineate the depth of involvement.
 - For plaque-type and generalized morphea, a deep punch biopsy (including subcutaneous fat) is usually sufficient. Importantly, note whether the biopsy specimen was taken from the sclerotic center or the inflammatory border of the lesion.
 - For linear and deep morphea, an incisional biopsy extending down to muscle is required.

Histologic Findings

The histologic findings of morphea and systemic sclerosis are similar, with a fundamental process of thickening and homogenization of collagen bundles. The depth of involvement is important for categorization into the morphea subtypes. The sclerotic process in plaque-type morphea is centered in the lower reticular dermis, whereas other variants are characterized by replacement of the subcutaneous fat and underlying tissues by collagen (see Media File 5).



Histopathology of mature scleroderma; full-thickness sclerosis of the dermis. Photomicrograph courtesy of Dirk Elston, MD.

The epidermis is usually normal, but rete ridges may become flattened later in the disease course.

In the early inflammatory stage, a perivascular and interstitial infiltrate of lymphocytes admixed with plasma cells and occasional eosinophils is observed in the reticular dermis and/or the fibrous trabeculae of the subcutaneous tissues. Blood vessel walls demonstrate endothelial swelling and edema, and thickening of preexisting collagen bundles and deposition of fine, wavy fibers of newly formed collagen occur.

Khandpur et al describe an unusual case of linear morphea in a 7-year-old boy with histological finds of mucin deposition in the reticular dermis.¹⁷ Pugashetti et al described mucin deposition in scleroderma and suggested it as an indicator of venous insufficiency.¹⁸

In the late sclerotic stage, the inflammatory infiltrate typically disappears. Collagen bundles in the reticular dermis and subcutis become thick, closely packed, and deeply eosinophilic. Atrophic eccrine glands appear to be trapped within the middle of the thickened dermis as subcutaneous fat is replaced by collagen. A paucity of blood vessels is seen, and adnexal structures are progressively lost. Depending on the subtype, the process of sclerosis may extend into the fascia and even underlying muscle; in contrast, thickened collagen bundles are restricted to the upper dermis in the plaque-type variant referred to as superficial morphea.

Treatment

Medical Care

No definitive treatments are available for morphea. Although several regimens have shown benefit in case series, few controlled trials have been performed. In general, therapy aimed at reducing inflammatory activity in early disease is more successful than attempts to decrease sclerosis in well-established lesions.

- Plaque-type morphea often undergoes gradual spontaneous resolution over a 3- to 5-year period. Treatment of active lesions with superpotent topical or intralesional corticosteroids may help reduce inflammation and prevent progression. Therapy with topical calcipotriene may also be beneficial, especially when nightly occlusion (eg, with plastic wrap) is used to increase penetration of the medication.¹⁹ Other topical agents shown to decrease lesional erythema and induration in small series of morphea patients include tacrolimus 0.1% ointment (under occlusion) and imiquimod 5% cream.²⁰
- Patients with potentially disabling generalized, linear, or deep morphea typically require more aggressive therapy.
 - Systemic corticosteroids can be helpful in the inflammatory phases of morphea and eosinophilic fasciitis, but they have little benefit for established sclerosis.
 - Successful treatment of severe and/or rapidly progressive morphea with systemic corticosteroids (eg, high-dose intravenous methylprednisolone in monthly pulses or oral prednisone at various intervals) in combination with weekly low-dose methotrexate (MTX) has been reported in several case series. MTX alone can also be effective.^{21,22,23,24}
 - Despite promising results in case series involving both adults and children, oral calcitriol did not lead to significant improvement in a double-blinded placebo-controlled trial.^{25,26,27} Scattered reports have described responses of severe morphea to second-line systemic agents, including cyclosporine, mycophenolate mofetil, and oral retinoids.
 - The use of hydroxychloroquine and antibiotics such as penicillin, azithromycin, and tetracyclines to treat morphea has been advocated by some clinicians, but little documentation of success is present in the medical literature.^{28,29}
 - Prolonged treatment (eg, >1 y) with penicillamine, a penicillin breakdown product that inhibits the cross-linking of collagen fibers, has been reported as beneficial in small series; however, its use is limited by adverse effects such as renal toxicity.
- Broadband UVA (320–400 nm, low-dose), long-wavelength UVA (UVA1; 340–400 nm, low- or medium-dose), and psoralen plus UVA (oral or bath) photochemotherapy have produced marked clinical improvement of morphea lesions in multiple case series and a recent randomized controlled trial. Because UVA1 wavelengths penetrate deeper into the dermis, this modality is particularly effective in the treatment of morphea. Unfortunately, the availability of UVA1 is currently limited. Narrowband UVB therapy, although less potent owing to its limited dermal penetration, can also be beneficial. Regimens combining UV therapy with topical corticosteroids or calcipotriene may be superior to either method alone.^{30,31}
- In one case report, treatment of plaque-type morphea with the 585-nm pulsed dye laser led to substantial improvement.³²
- Photodynamic therapy using topical 5-aminolevulinic acid was also effective in a small series.

Surgical Care

- Orthopedic surgery may be indicated if patients develop deformities of the joints and bones as sequelae of linear or deep morphea. Such surgical interventions include release of joint contractures and limb-lengthening procedures.

- Plastic surgery can help to correct deformities due to atrophy of subcutaneous tissues. Reconstruction of the face and scalp may be beneficial to patients with en coup de sabre and Parry-Romberg syndrome, with possible use of tissue expansion and implants of autologous bone, fat, or synthetic materials (eg, polyethylene).

Consultations

- Referral to a dermatologist can help establish the diagnosis and initiate appropriate treatment of morphea.
- Consultation with a physical therapist and a program of physical therapy are of utmost importance in maintaining range of motion and function of the extremities in patients with linear or deep morphea that crosses joint lines. Programs typically include passive stretching, muscle strengthening, and resting splints.
- An evaluation by an ophthalmologist is indicated for craniofacial morphea that involves the periocular area.
- Consultation with a neurologist is helpful for patients with craniofacial morphea who present with neurologic symptoms or have abnormalities detected via MRI of the brain.
- Consultation with a dentist is required when craniofacial morphea leads to altered dentition or malocclusion.

Medication

In general, therapy aimed at reducing inflammatory activity in early disease is more successful than attempts to decrease sclerosis in well-established lesions. The approach to treatment of the various subtypes of morphea is described in Medical Care. Note that phototherapy represents another important modality.

Corticosteroids

These agents reduce inflammation and suppress collagen synthesis.

Triamcinolone acetonide (Aristocort, Kenalog)

Medium-potency corticosteroid that reduces inflammation and may prevent progression of sclerosis.

Dosing

Adult

Apply 0.1% ointment topically to lesions bid; alternatively, inject 0.2-1 mL of a 5-mg/mL susp intralesionally (eg, into active margins) q3-4wk

Pediatric

Administer as in adults

Interactions

None reported

Contraindications

Documented hypersensitivity; viral, bacterial, and fungal skin infections

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

Application over large areas or with occlusive dressings may result in systemic absorption; long-term systemic absorption can lead to reversible HPA-axis suppression and Cushing syndrome; intralesional or prolonged topical use may cause skin atrophy, striae, and hypopigmentation

Clobetasol propionate 0.05% cream or ointment (Temovate)

Superpotent topical corticosteroid that reduces inflammation and may prevent progression of sclerosis.

Dosing

Adult

Apply topically bid for up to 4 wk; not to exceed 50 g/wk

Pediatric

Administer as in adults

Interactions

None reported

Contraindications

Documented hypersensitivity; viral, bacterial, and fungal skin infections

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

Application over large areas or with occlusive dressings may result in systemic absorption; long-term systemic absorption can lead to reversible HPA-axis suppression and Cushing syndrome; prolonged use may cause skin atrophy, striae and hypopigmentation

Prednisone (Deltasone, Orasone)

Reduces inflammation and prevents progression of sclerosis. Systemic corticosteroid therapy (often used in combination with MTX; see below) is appropriate for patients with active inflammatory disease that is widespread, severe, and/or potentially disfiguring/disabling.

Dosing

Adult

0.5-1 mg/kg/d PO for several wk, followed by slow taper

Pediatric

Administer as in adults

Interactions

Coadministration with estrogens may decrease clearance; when used with digoxin, digitalis toxicity secondary to hypokalemia may increase; phenobarbital, phenytoin, and rifampin may increase metabolism of glucocorticoids (consider increasing maintenance dose); monitor for hypokalemia with coadministration of diuretics

Contraindications

Documented hypersensitivity; viral, bacterial, mycobacterial, and fungal infections; peptic ulcer disease; hepatic dysfunction

Precautions

Pregnancy

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

Precautions

Short-term adverse effects include mood changes/insomnia, gastritis, salt and water retention, increased appetite/weight gain, hyperglycemia, and acneiform eruptions; long-term use may also lead to Cushing syndrome, HPA-axis suppression, hypertension, hypokalemic alkalosis, peptic ulcer disease, osteoporosis, myopathy, posterior subcapsular cataracts, glaucoma, and growth retardation; regardless of the dosing schedule, avascular necrosis of long bones, usually the femoral head, can occur

Vitamin D analogs

These agents inhibit fibroblast activity and TGF-beta production and have anti-inflammatory effects.

Calcipotriene 0.005% ointment (Dovonex)

Synthetic vitamin D-3 analog that can lead to softening of morphea lesions.

Dosing

Adult

Apply topically bid; occlusion (eg, with plastic wrap) can increase penetration and efficacy; not to exceed 100 g/wk

Pediatric

Administer as in adults

Interactions

Incompatible with topical ammonium lactate cream

Contraindications

Documented hypersensitivity; hypercalcemia; vitamin D toxicity

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

Avoid use on face; may result in skin irritation and transient hypercalcemia (especially if >100 g applied/wk); discontinue treatment if substantial skin irritation occurs, if serum parathyroid hormone level is low, or if serum calcium level is abnormally high

Calcitriol (Rocaltrol)

May produce skin softening and improved joint mobility in patients with morphea. Increases blood calcium levels by promoting intestinal absorption and renal retention.

Dosing

Adult

0.50-0.75 mcg/d PO

Pediatric

Initial: 15 ng/kg/d PO

Maintenance: 5-40 ng/kg/d PO

Interactions

Cholestyramine and colestipol decrease absorption; magnesium-containing antacids and thiazide diuretics can increase effects/toxicity

Contraindications

Hypercalcemia; malabsorption syndrome

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

Because of dose-dependent effect on calcium metabolism, monitoring of serum and urine calcium, inorganic phosphate, and creatinine values is recommended.

Antirheumatic agents

These agents can reduce inflammation associated with morphea.

Methotrexate (Rheumatrex, Trexall)

Antimetabolite that inhibits dihydrofolate reductase, thereby hindering DNA and RNA synthesis in lymphocytes and other immune cells. This and other mechanisms lead to an anti-inflammatory effect, which is reflected in reduced levels of circulating cytokines such as IL-2, IL-6, and IL-8 (indicators of disease activity) in morphea patients. Response is often delayed until 1-3 mo after initiation of therapy.

Dosing

Adult

15-25 mg/wk PO/IM; folic acid 1 mg/d is given concomitantly

Pediatric

0.3-0.6 mg/kg/wk PO/IM/SC; folic acid 1 mg/d is given concomitantly

Interactions

Oral aminoglycosides may decrease absorption and blood levels of concurrent oral MTX; charcoal lowers levels; coadministration with etretinate may increase hepatotoxicity of MTX; folic acid or its derivatives contained in some vitamins may decrease response to MTX

Probenecid, NSAIDs, salicylates, procabazine, and sulfonamides (including TMP-SMZ) can increase plasma levels; may decrease phenytoin plasma levels; may increase plasma levels of thiopurines

Contraindications

Documented hypersensitivity; alcoholism; hepatic insufficiency; documented immunodeficiency syndromes; preexisting blood dyscrasias (eg, bone marrow hypoplasia, leukopenia, thrombocytopenia, significant anemia); renal insufficiency

Precautions

Pregnancy

X - Contraindicated; benefit does not outweigh risk

Precautions

Monitor CBC counts monthly, and liver and renal function q1-3mo during therapy (monitor more frequently during initial dosing, dose adjustments, or when risk of elevated MTX levels, eg, dehydration); although low-dose MTX is generally well-tolerated, it can have toxic effects on hematologic, hepatic, renal, GI, pulmonary, and neurologic systems; discontinue if significant drop in blood cell counts occurs; fatal reactions have been reported when administered concurrently with NSAIDs

Follow-up

Complications

- In the linear and deep morphea subtypes, joint contractures, subcutaneous atrophy, and growth failure can be deforming and disabling.

Prognosis

- Plaque-type morphea is a self-limited condition that tends to slowly involute with time; the duration of disease activity averages 3-5 years, although it may last as long as 25 years.
- Linear lesions tend to persist for longer than plaque-type lesions, but they often improve over the years. However, linear morphea, especially the en coup de sabre subtype, may remit and reactivate, remain unchanged, or become more extensive with time. In addition, patients with linear lesions may develop limb atrophy and contractures that result in limited movement and permanent disability. Neurologic and ocular sequelae represent other potential complications of craniofacial linear morphea. Long-term follow-up and serial imaging may be indicated.
- Disabling pansclerotic morphea of children is a rare, aggressive, and mutilating variant of deep morphea that begins before age 14 years and has a disease course of relentless progression and severe disability.

Miscellaneous

Special Concerns

- Extracutaneous manifestations of morphea are more common in the pediatric population, most often affecting the joints, central nervous system, and eyes.

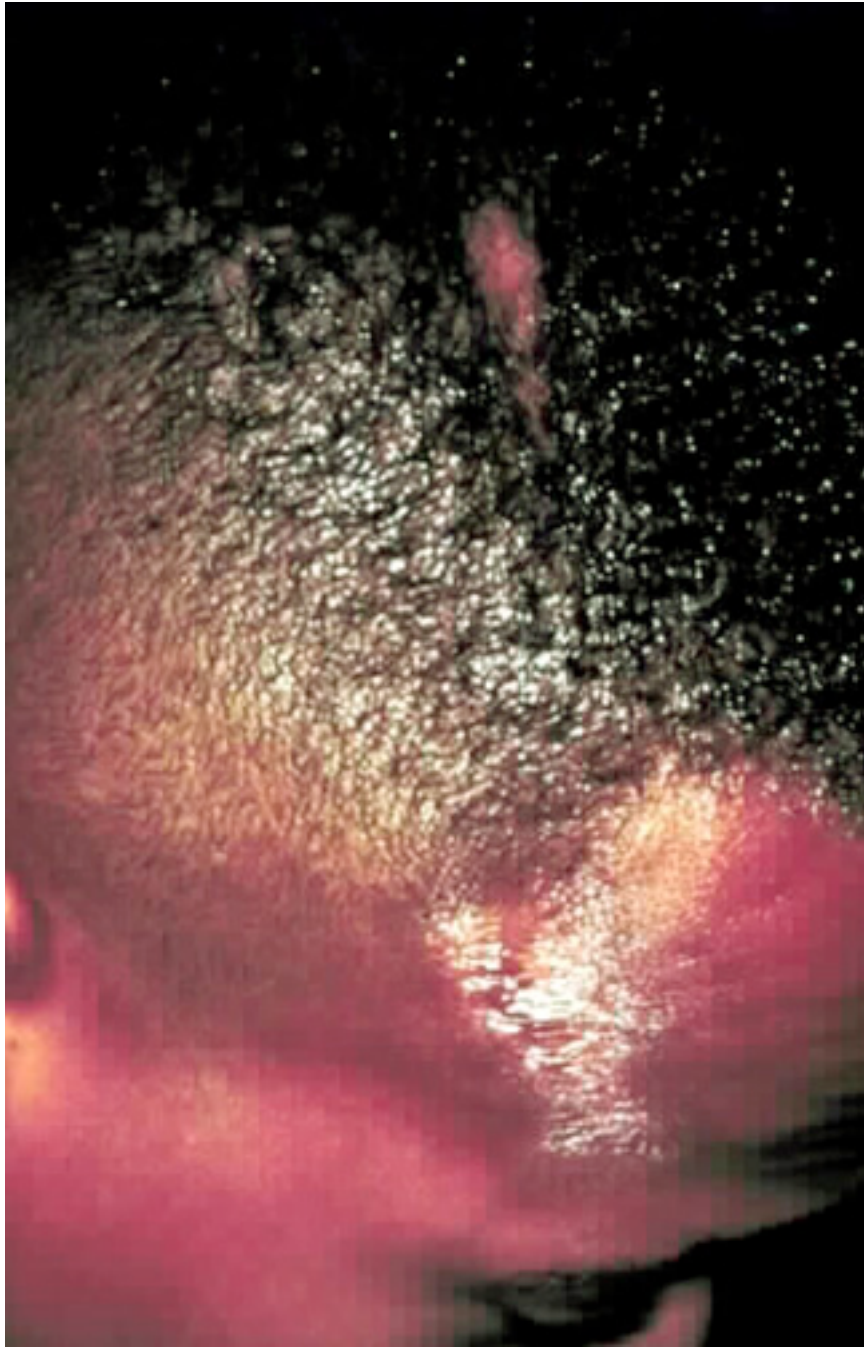
Multimedia



Media file 1: Inflammatory plaque-type morphea on the abdomen, characterized by induration, erythema, and a surrounding lilac ring.



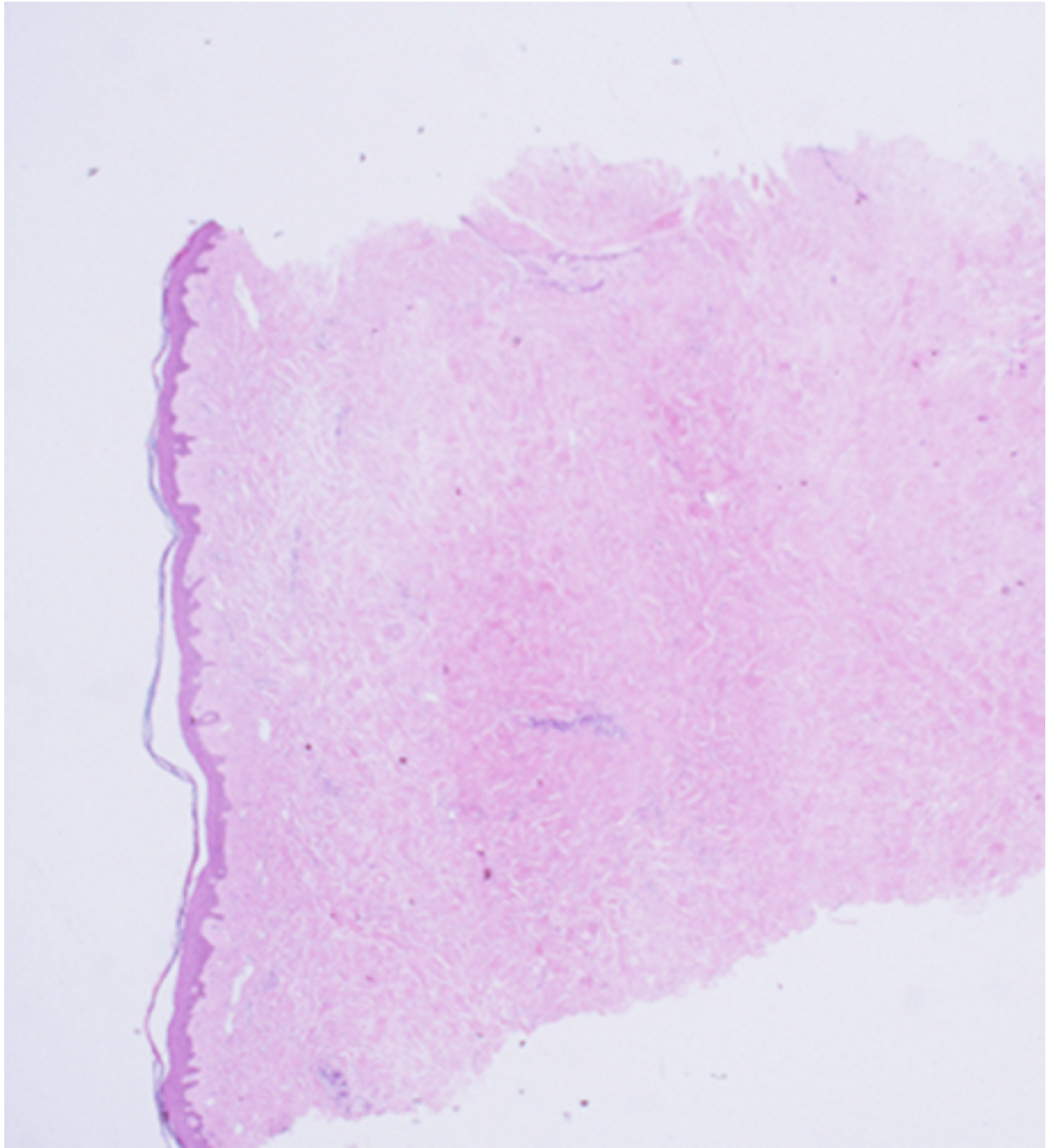
Media file 2: A hyperpigmented band of linear morphea involving the right part of the trunk and thigh.



Media file 3: Linear atrophic depression of an en coup de sabre lesion on the right side of the forehead and the frontal part of the scalp.



Media file 4: Morphea profunda involving the left lower extremity, with thickened, taut, bound-down skin.



Media file 5: Histopathology of mature scleroderma; full-thickness sclerosis of the dermis. Photomicrograph courtesy of Dirk Elston, MD.

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