eMedicine Specialties > Dermatology > Connective Tissue Diseases

Eosinophilic Fasciitis

Brad S Graham, MD, Consulting Staff, Dermatology Associates of Tyler
Updated: Jun 19, 2009

Introduction

Background

Eosinophilic fasciitis is an idiopathic, fibrotic disorder with the histopathologic hallmark of fascial fibrosis. The presentation of eosinophilic fasciitis is acute with painful, swollen extremities progressing to disabling cutaneous fibrosis. Joint contractures, arthritis, neuropathy, and myositis may be associated with eosinophilic fasciitis. Many authors consider eosinophilic fasciitis to be a variant of morphea; others consider it a distinct entity.

Pathophysiology

The etiology of eosinophilic fasciitis is unknown, but aberrant immune responses may play a role because hypergammaglobulinemia and antinuclear antibodies are associated. In addition, toxic, environmental, or drug exposures have been implicated in causing eosinophilic fasciitis. A 2006 case report implicated atorvastatin in a temporal relationship as the cause of a patient's eosinophilic fasciitis.[1] Simvastatin has also been reported temporally to the onset of eosinophilic fasciitis.[2]

Reports indicate that *Borrelia burgdorferi* may be a possible etiologic agent in some cases of eosinophilic fasciitis. However, one report of a patient with eosinophilic fasciitis and a review of the literature of cases in which *Borrelia* species were implicated in the pathogenesis failed to show a relationship between eosinophilic fasciitis and *Borrelia* infection. *Borrelia* species were not identified by direct microscopic examination of tissue samples or by polymerase chain reaction amplification of tissue samples in any of these reported cases of eosinophilic fasciitis. The conclusion was that positive serology alone for *Borrelia* does not implicate *Borrelia* infection in the pathogenesis of eosinophilic fasciitis in the absence of the positive demonstration of *Borrelia* by histochemical stains, immunohistochemical stains, or polymerase chain reaction amplification in tissue samples.[3]

In vitro fibroblasts from involved fascia produce increased levels of mRNA for collagen types I, III, and IV compared with adjacent dermal fibroblasts. In addition, fascial fibroblasts express transforming growth factor-beta I and connective-tissue growth factor mRNA, which may account for the clinical fibrosis. Eosinophil degranulation may lead to fibroblast activation.

Further research into eosinophilic fasciitis has shown elevations of transforming growth factor-beta and interleukin 5, which normalize with corticosteroid therapy. Another study has show that the fascial inflammatory infiltrate is predominately composed of $CD8^+$ T lymphocytes, macrophages, and fewer eosinophils, suggesting a possible cytotoxic immune reaction in response to possible infectious or environmental agents. Other studies have shown elevated serum levels of manganese superoxide dismutase and tissue inhibitor of metalloproteinase (TIMP-1).

Serum TIMP-1 may also serve as a marker of disease severity.[4,5]

One report describe of diffuse eosinophilic fasciitis developing after local radiation therapy for breast cancer, implicating radiation injury as a possible traumatic trigger for the development of eosinophilic fasciitis.[6]

Frequency

International

Eosinophilic fasciitis is uncommon.

Mortality/Morbidity

The end stage of the fibrotic process leads to substantial morbidity due to skin sclerosis and joint contractures. In addition, arthritis, neuropathies, and myositis may be present. Ten percent of cases may result in myelodysplasia, such as aplastic anemia, which portends a poor prognosis. Spontaneous resolution is possible, and treatment with corticosteroids usually results in recovery; however, skin sclerosis and joint contractures may alvato da Windows Internet Explorer 8> Subject: Eosinophilic Fasciitis: [Print] - eMedicine Dermatology Date: Fri, 4 Sep 2009 00:52:59 +0200 MIME-Version: 1.0 Content-Type: multipart/related; type="text/html"; boundary="----=_NextPart_000_0223_01CA2CFA.0C373030" X-MimeOLE: Produced By Microsoft MimeOLE V6.00.2900.5579 This is a multi-part message in MIME format. ------=_NextPart_000_0223_01CA2CFA.0C373030 Content-Type: text/html; charset="Windows-1252" Content-Transfer-Encoding: quoted-printable Content-Location: http://emedicine.medscape.com/article/1065199-print

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A 2007 study reported that the risk of residual fibrosis/contractures after therapy was much higher with an age younger than 12 years at presentation, trunk involvement, associated morphealike, and dermal fibrosis in addition to the subcutaneous fat/fascial fibrosis.[7]

Race

Whites are primarily affected by eosinophilic fasciitis.

Sex

Eosinophilic fasciitis occurs equally in males and females.

Age

Most eosinophilic fasciitis patients are in their third to sixth decades of life; however, cases in children have been reported.

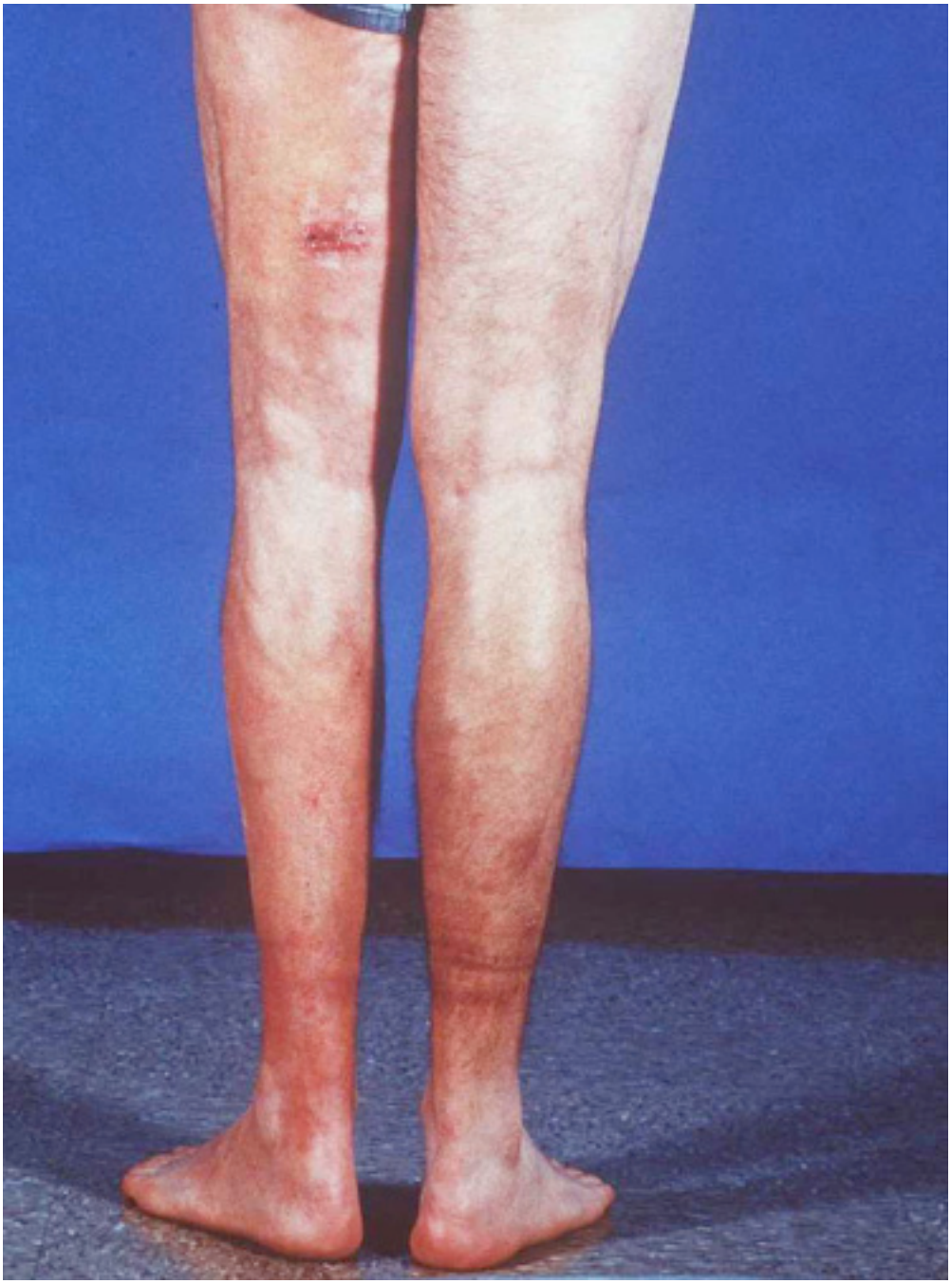
Clinical

History

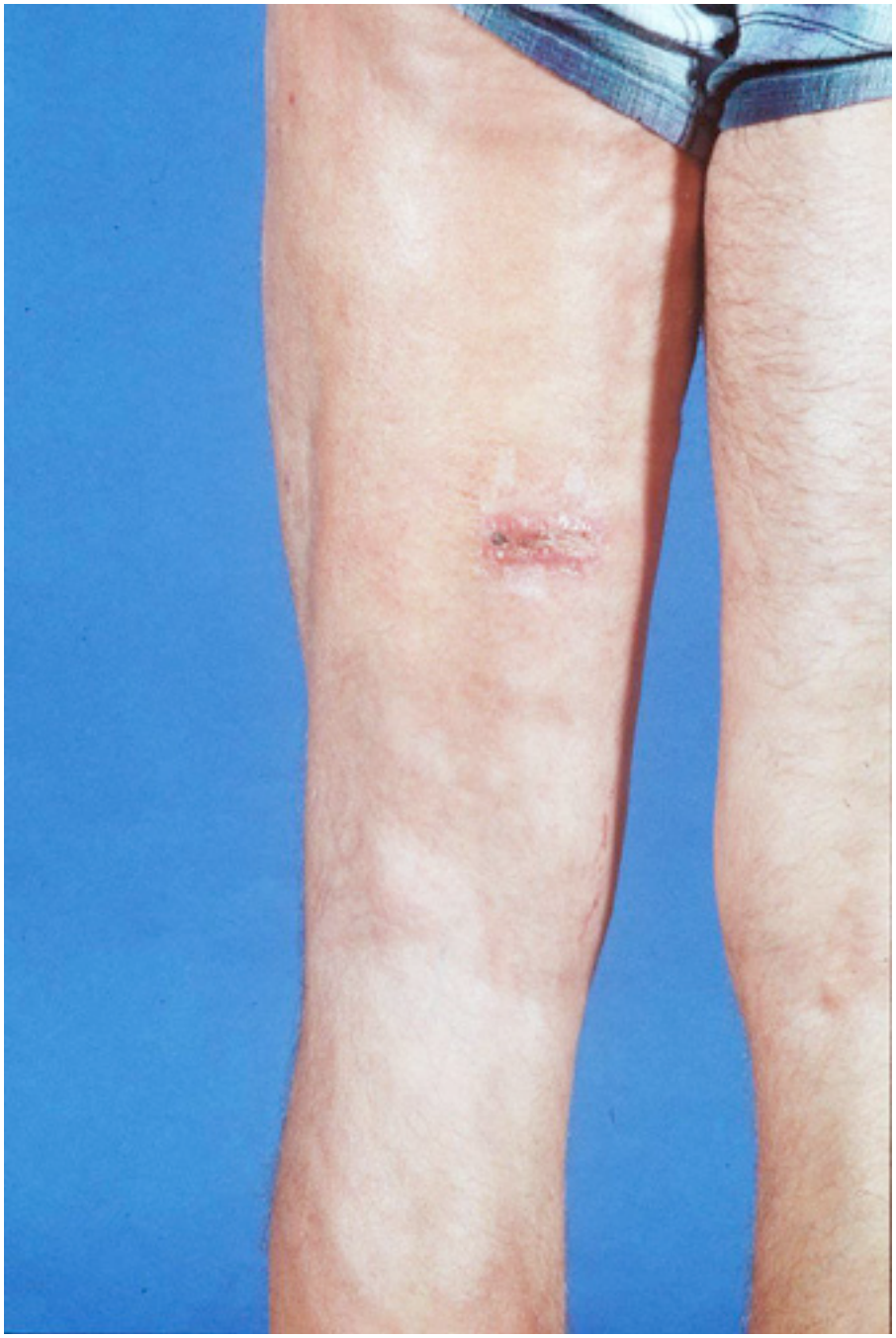
- Eosinophilic fasciitis patients present with the sudden onset of painful, tender, edematous, and erythematous extremities.
    - The disorder progresses rapidly; within weeks to months, patients develop stiffness and sclerodermatous induration, resulting in characteristic flexion contractures and impaired mobility.
    - The forearms, the upper arms, the lower legs, the thighs, and the trunk are involved (in order of decreasing frequency).
- As many as 50% of patients report an episode of strenuous physical exercise or activity immediately preceding the onset of the illness.
- Malaise, weakness, and fever are frequently present. A study in 2008 addressing the physical burden noted that fatigue was the most common symptom. Pain and itch were also frequent complaints. Of all patients, 62% noted fatigue, pain, and itch.[8]
- Overt arthritis occurs in as many as 40% of patients.
- Symptoms of carpal tunnel syndrome have been reported.
- Visceral involvement and Raynaud phenomenon are rare.

Physical

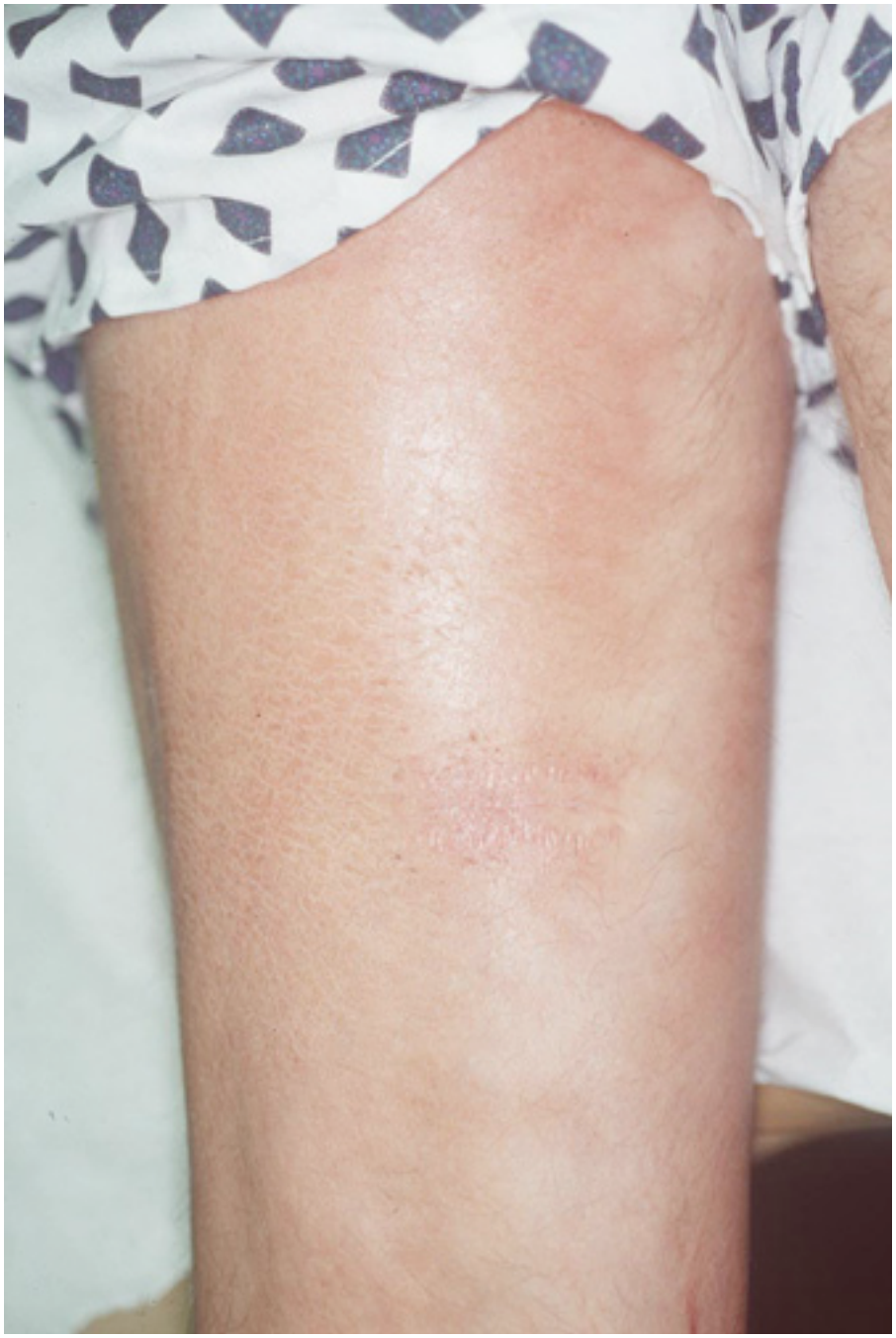
The clinical presentation of eosinophilic fasciitis evolves through 3 stages; the various stages present simultaneously in different areas of the body. The first stage presents with symmetric, diffuse, erythematous tenderness of the extremities, followed by an edematous phase that produces a coarsely dimpled appearance (cobblestoning) or a finely dimpled appearance (peau d'orange). The last phase involves rippling of the skin with areas of hypopigmentation, induration, and skin tightness.



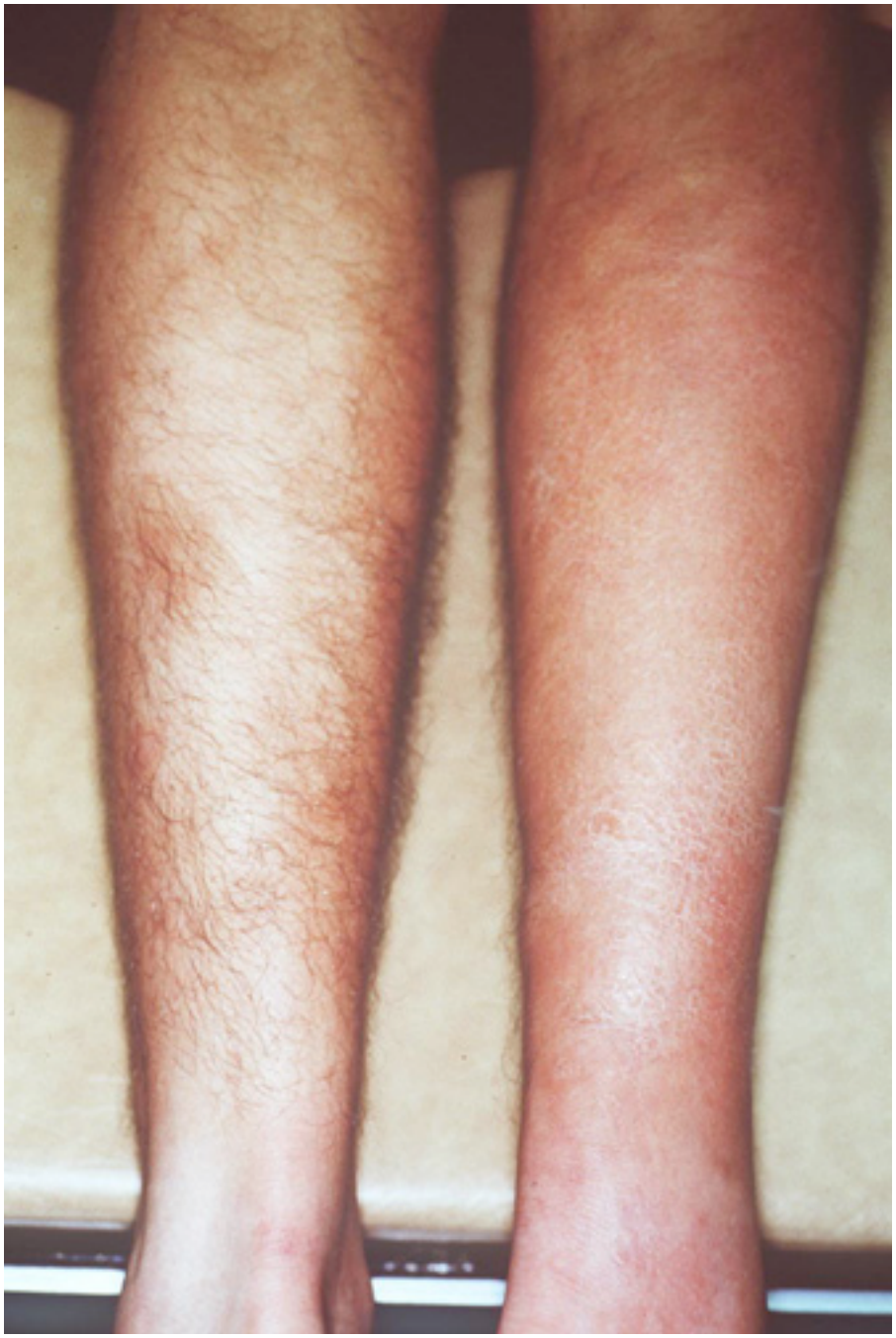
Lower back part of the legs shows hypopigmentation, induration, biopsy site, and asymmetric involvement (same patient as in Media Files 2-3).



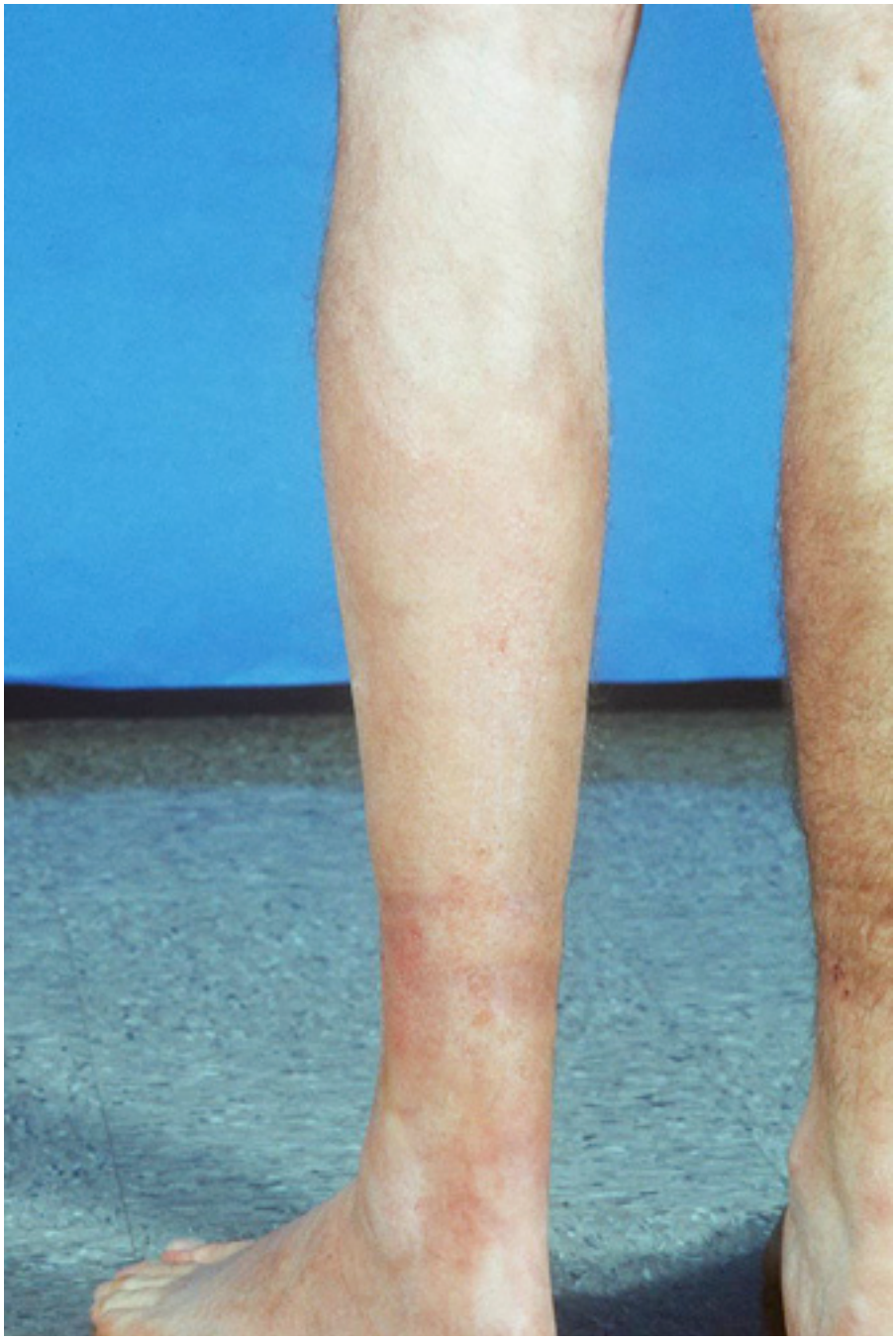
Posterior thigh shows woody induration, sclerosis, and hypopigmentation (same patient as in Media Files 1 and 3).



Close-up view of left posterior thigh 2 weeks later shows erythema, scaling, alopecia, and rippled induration (same patient as in Media Files 1-2).



Posterior part of the calf in the first week of illness shows erythema, edema, alopecia, scaling, and early induration. The right calf is relatively uninvolved with patchy erythema only (same patient as in Media File 5).



Photograph of the posterior part of the calf at 3 weeks shows complete sclerosis and induration with patchy erythema (same patient as in Media File 4).

In severely affected areas, both the skin and the subcutaneous tissues are bound-down and inseparable from the underlying muscle, and they have a woody-type appearance. With elevation of the involved extremities, furrows along the course of the superficial veins may be present; this finding is referred to as the groove sign. Although the extremities are preferentially involved (88%), the trunk may be involved. The hands, the feet, and the face are spared.

- Joint contractures of the elbows, wrists, ankles, knees, and shoulders may be found in 55-75% of patients. Unilateral involvement has been reported.[9]

- Carpal tunnel syndrome is present in 20% of patients.
- Inflammatory arthritis is present in as many as 40% of patients.
- Subclinical myositis is present in a minority of patients.
- A concurrent localized lesion of morphea may be seen in 25% of patients.
- In contrast to scleroderma, Raynaud phenomenon, abnormal nail fold capillaries, and sclerodactyly are not present. Visceral involvement is rare, with few reports of involvement of the lungs, the esophagus, and the myocardium.
- Primary presentation as angioedema was also reported in a patient.[10]

Causes

See Pathophysiology.

Differential Diagnoses

Eosinophilia-Myalgia Syndrome

Morphea

Other Problems to Be Considered

Eosinophilic-myalgia (L-tryptophan) syndrome[11,12]

Scleroderma

Toxic oil syndrome

Workup

Laboratory Studies

- CBC count shows eosinophilia (10-40%) in as many as 80-90% of patients. In addition, pancytopenia, anemia, or thrombocytopenia may be encountered in eosinophilic fasciitis.
- The erythrocyte sedimentation rate is elevated in as many as 60-80% of eosinophilic fasciitis patients.
- Immunoglobulin levels show hypergammaglobulinemia, usually polyclonal immunoglobulin G.
- Muscle enzyme levels are sometimes elevated, especially aldolase.
- The antinuclear antibody result is occasionally positive.
- The rheumatoid factor result is occasionally positive.

Imaging Studies

- If clinically indicated, MRI of the involved areas shows a high-intensity signal in the fascia. A 2005 study demonstrated that MRI shows characteristic findings of fascial thickening, abnormal signal intensity, and contrast enhancement. According to the authors, these findings are useful to make the diagnosis, to guide the location for biopsy, and to monitor the response to therapy.[13]

Other Tests

- If clinically indicated, electromyograms may show slow motor unit potentials with reduced duration and amplitude consistent with a myositis.
- Pulmonary function test results may show a restrictive pattern with severe truncal involvement.

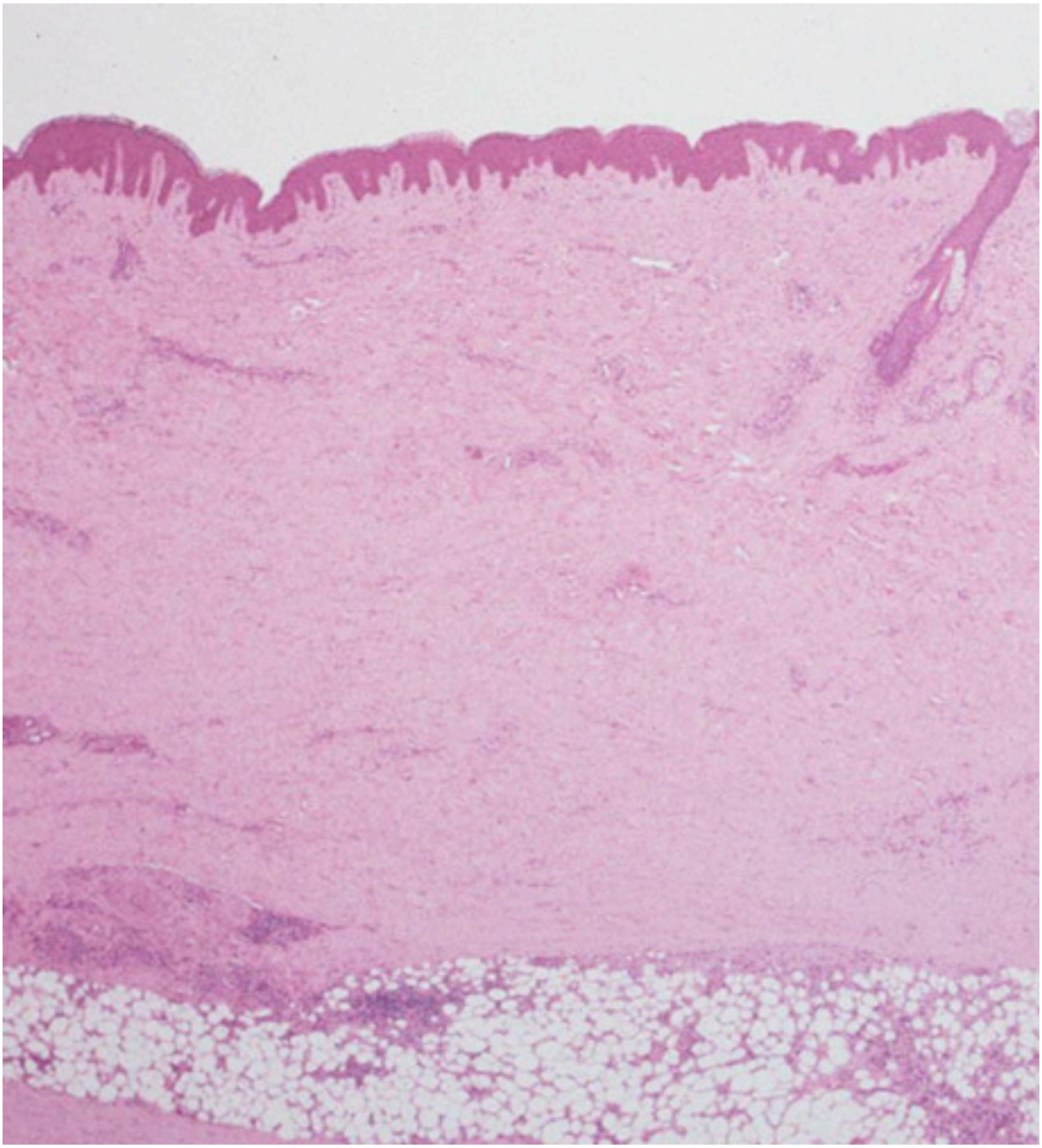
Procedures

- If abnormal values other than eosinophilia are found on the CBC count, a bone marrow examination may be necessary.
- A full-thickness incisional biopsy that includes the dermis, the subcutaneous fat, and the fascia is necessary to confirm a diagnosis of eosinophilic fasciitis.

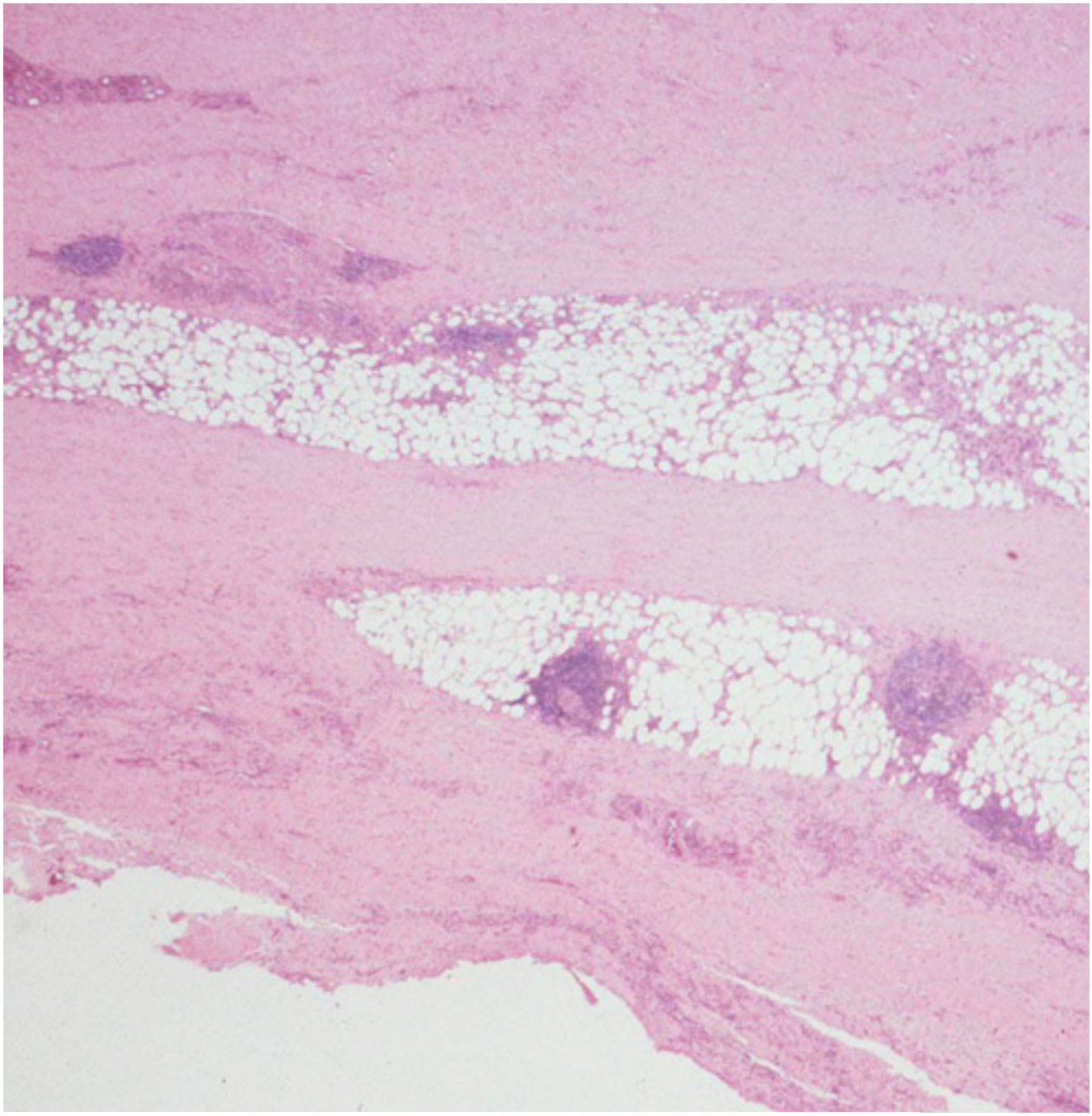
Histologic Findings

The most profound changes associated with eosinophilic fasciitis occur in the superficial fascia, which is markedly thickened, fibrosed, and sclerotic. In the early stages, fibrinoid necrosis or myxoid degeneration may be seen. The fibrosis extends into the septae of the subcutaneous fat, which entrap the fat within intersecting bands of fibrosis. The fibrotic process also extends into the lower dermis and the underlying musculature. The muscle may show focal necrosis, degeneration, and regeneration.

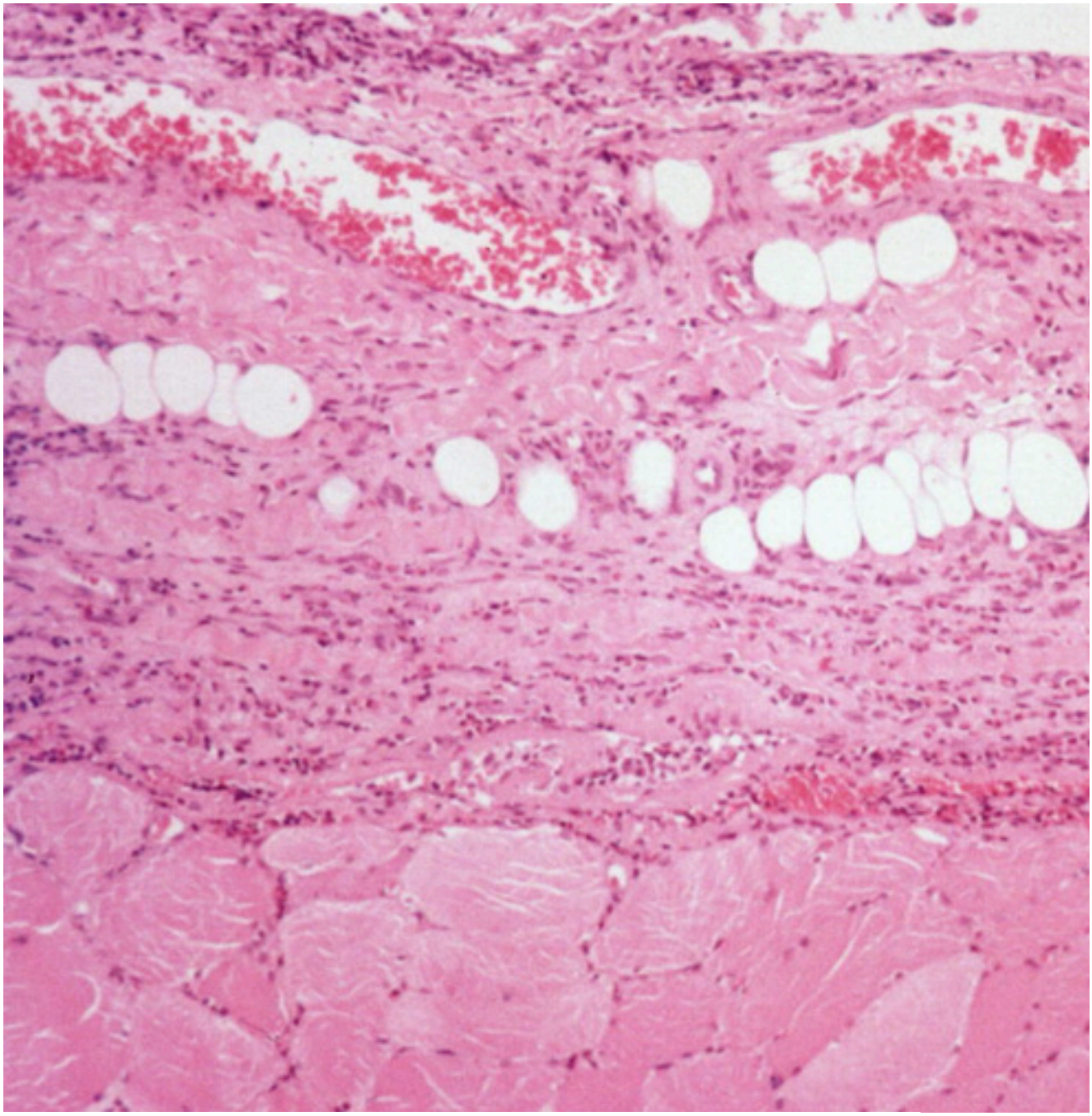
The inflammatory infiltrate is usually mild to moderate and consists of lymphocytes, histiocytes, plasma cells, and variable numbers of eosinophils. Eosinophils are not required to make the diagnosis; the term eosinophilic fasciitis refers to peripheral eosinophilia not tissue eosinophilia. The inflammatory infiltrate, including lymphoid follicles, involves the lower dermis, the septae, the fascia, and the muscle. The epidermis, the papillary dermis, and the adnexa are usually spared. On direct immunofluorescence, immunoglobulin M is found at the dermal-epidermal junction, and immunoglobulin G and C3 are found around blood vessels in the lower dermis, the fascia, and the skeletal muscle.



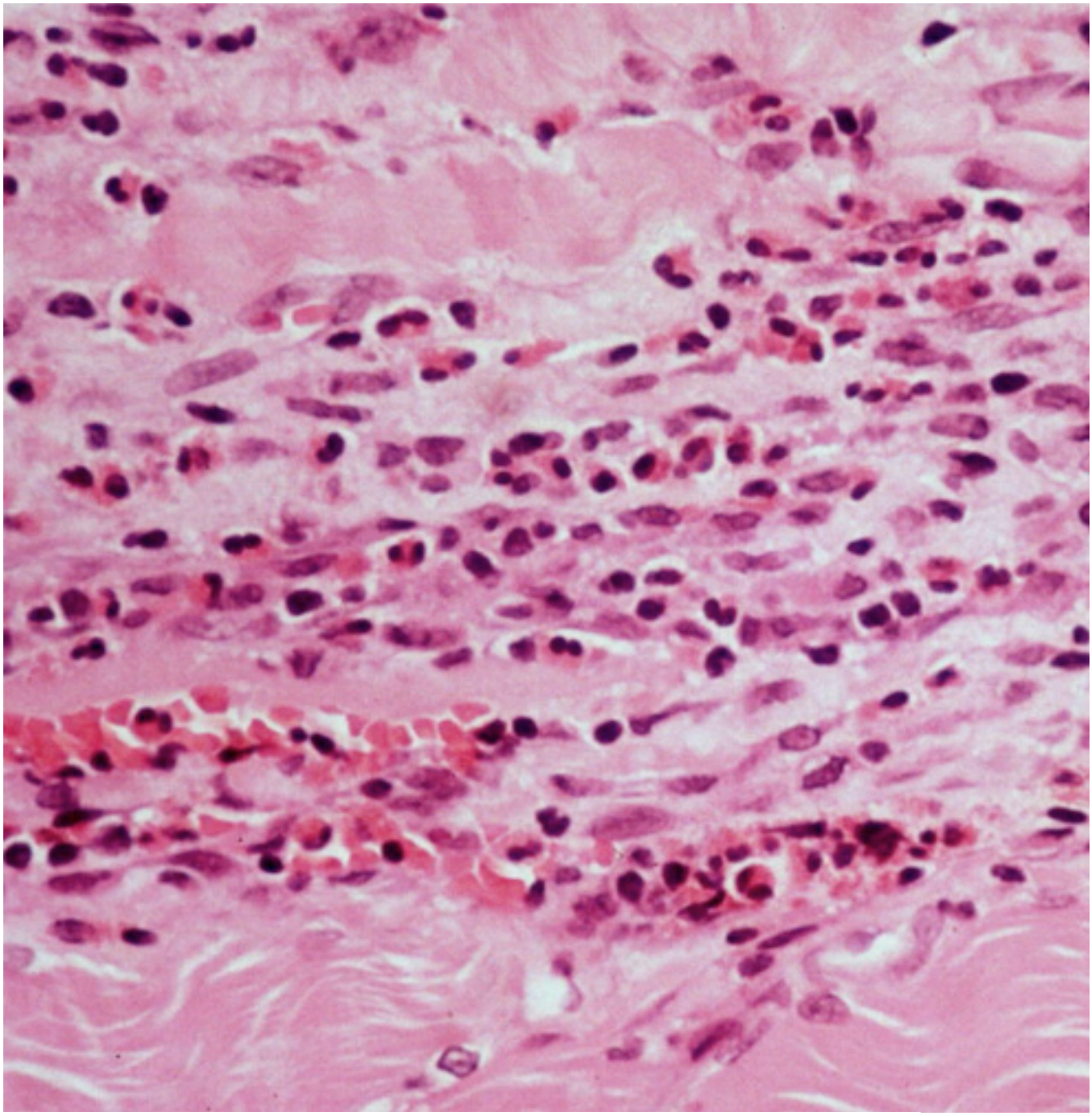
Note the marked thickening and replacement of the entire dermis with sclerotic collagen on this incisional biopsy sample from the left posterior part of the thigh.



Photomicrograph of subcutaneous fat-fascia junction shows entrapment of subcutaneous fat by intersecting thick bands of fibrosis. Thickening and fibrosis of fascia and lymphoid aggregates are seen.



Photomicrograph of fascia-skeletal muscle junction shows markedly thickened fascia with heavy inflammatory infiltration.



High-power photomicrograph of fascia shows heavy inflammatory infiltration with numerous eosinophils, lymphocytes, and occasional plasma cells.

Treatment

Medical Care

- Many eosinophilic fasciitis cases respond to corticosteroids (88%, with 25% obtaining complete recovery), although spontaneous resolution is possible. Complete recovery may take up to 1-3 years. No consensus on the treatment of eosinophilic fasciitis exists, but most studies indicate that the best response is with moderate-to-high doses of corticosteroids, especially if started early in the disease course. No set dosing schedule is available, but most studies advocate doses of 0.5-1 mg/kg/d until response, with rapid tapering to alternate day therapy.
- Several eosinophilic fasciitis cases exist in the literature of recalcitrant disease to corticosteroids in which adjunctive therapy may be required.
- Adjunctive medications for eosinophilic fasciitis include hydroxychloroquine, colchicine, cimetidine, cyclosporin,[14] azathioprine, and methotrexate. A more recent study looked at extracorporal photochemotherapy in the treatment of corticosteroid-resistant cases. After 1 year of therapy, 2 of 3 patients showed considerable improvement when combined with low-dose corticosteroids.[15]
- Newer therapies that have been used as corticosteroid adjuncts or as monotherapy for eosinophilic fasciitis include infliximab,[16] cyclophosphamide,[17] dapsone,[18] retinoid-UVA1,[19] and oral psoralen plus UVA (PUVA).[20]
- A clinical trial that may be of interest is Treatment With High Dose Methotrexate in Patients With Eosinophilic Fasciitis.

Surgical Care

Surgical decompression of carpal tunnel syndrome may be required for eosinophilic fasciitis.

Consultations

A physical therapist may be consulted. Active and passive range of motion therapy of the involved extremities and joints is crucial along with medical therapy to prevent and to treat joint contractures.

Medication

The mainstay of therapy for eosinophilic fasciitis is anti-inflammatory agents.

Corticosteroids

These agents halt active inflammatory process, ensuing fibrosis, and restriction of mobility.

Prednisone (Deltasone, Orasone)

Synthetic adrenocortical steroid drug with predominantly glucocorticoid properties. Anti-inflammatory effects include depressed production of eosinophils and lymphocytes. Anti-inflammatory processes (eg, edema, fibrin deposition, capillary dilatation, migration of leukocytes, phagocytosis) and the later stages of wound healing (eg, capillary proliferation, deposition of collagen, cicatrization) are inhibited.

Dosing

Adult

0.5-1 mg/kg/d PO/IV/IM; taper as condition improves to qod; single morning dose is safer for long-term use, but divided doses have more anti-inflammatory effect

Pediatric

Administer as in adults

Interactions

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

Contraindications

Documented hypersensitivity; viral, fungal, connective tissue, or tubercular skin infections; peptic ulcer disease; hepatic dysfunction; GI disease

Precautions

Pregnancy

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

Precautions

In patients on corticosteroid therapy subjected to unusual stress, increase dose of rapidly acting corticosteroids before, during, and after stressful situation is indicated; may mask signs of infection, and new infections may appear during use; resistance and inability to localize infection may decrease when used; prolonged use may produce posterior subcapsular cataracts, glaucoma, hypertension, salt and water retention, and increased excretion of potassium; all corticosteroids increase calcium excretion, leading to osteoporosis; regardless of dosing schedule, avascular necrosis of long bones (femoral head) may occur; while taking corticosteroids, patients should not undergo immunization procedures

Psychic derangements may appear when corticosteroids are used, ranging from euphoria, insomnia, mood swings, personality changes, severe depression, or frank psychotic manifestations; existing emotional instability or psychotic tendencies may be aggravated

Caution in nonspecific ulcerative colitis if probability of impending perforation or fresh intestinal anastomoses; active or latent peptic ulcer; renal insufficiency; hypertension; osteoporosis; myasthenia gravis; growth and development of infants and children on prolonged corticosteroid therapy should be carefully observed of impending perforation or fresh intestinal anastomoses; active or latent peptic ulcer; renal insufficiency; hypertension; osteoporosis; myasthenia gravis; growth and development of infants and children on prolonged corticosteroid therapy should be carefully observed

Follow-up

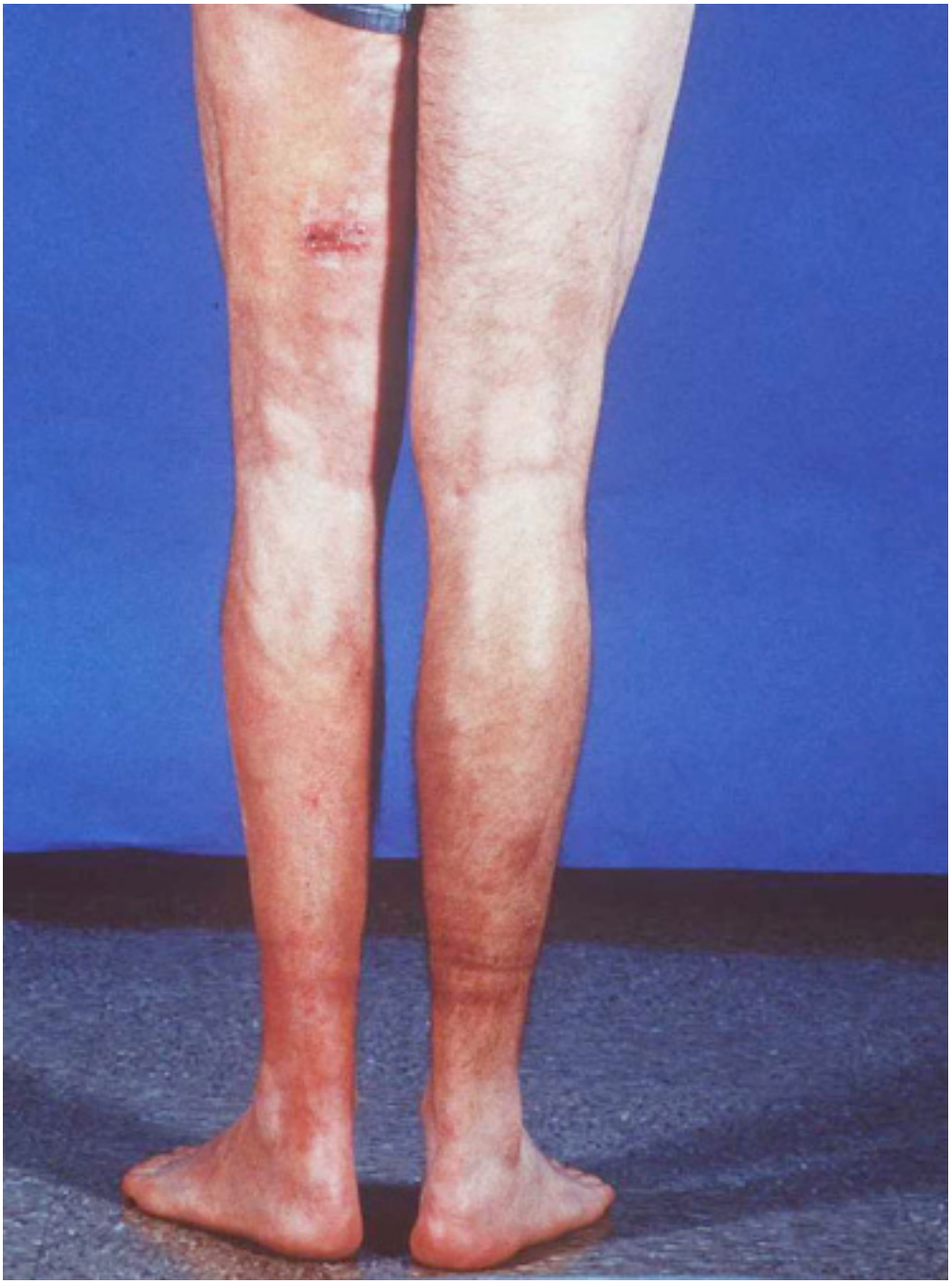
Complications

- Aplastic anemia and other forms of myelodysplasia may complicate eosinophilic fasciitis in as many as 10% of patients. Some authors advocate a bone marrow examination in all eosinophilic fasciitis patients. More recent case reports have shown associations of eosinophilic fasciitis with multiple myeloma, polycythemia vera, peripheral T-cell lymphoma, immunoglobulin A nephropathy, and idiopathic hypercalcemia.
- Associations have also been noted with systemic lupus erythematosus,[21] hyperthyroidism with thyroid adenoma,[22] and primary biliary cirrhosis.[23]

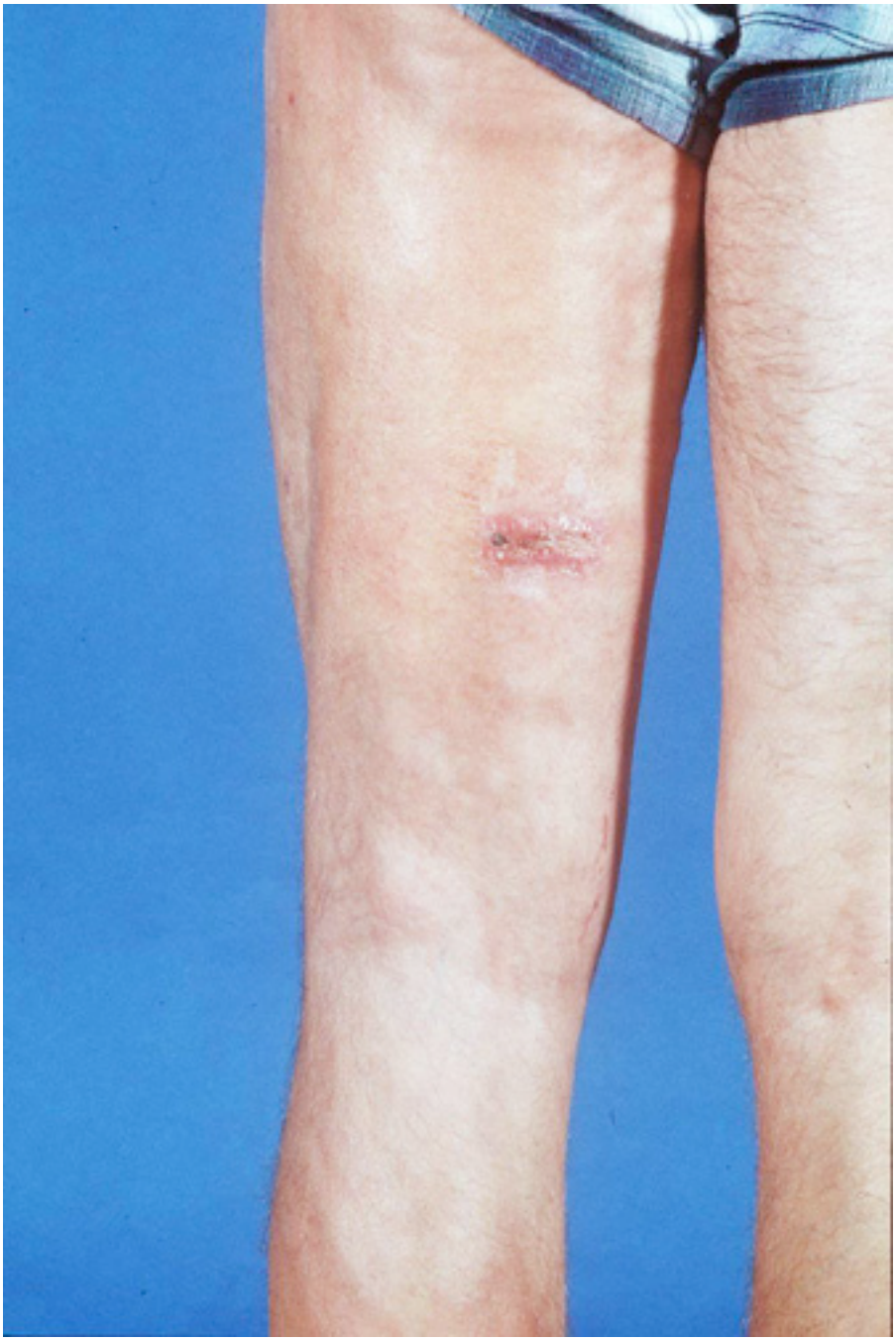
Prognosis

- The prognosis for eosinophilic fasciitis is good. Most patients experience partial or complete recovery.

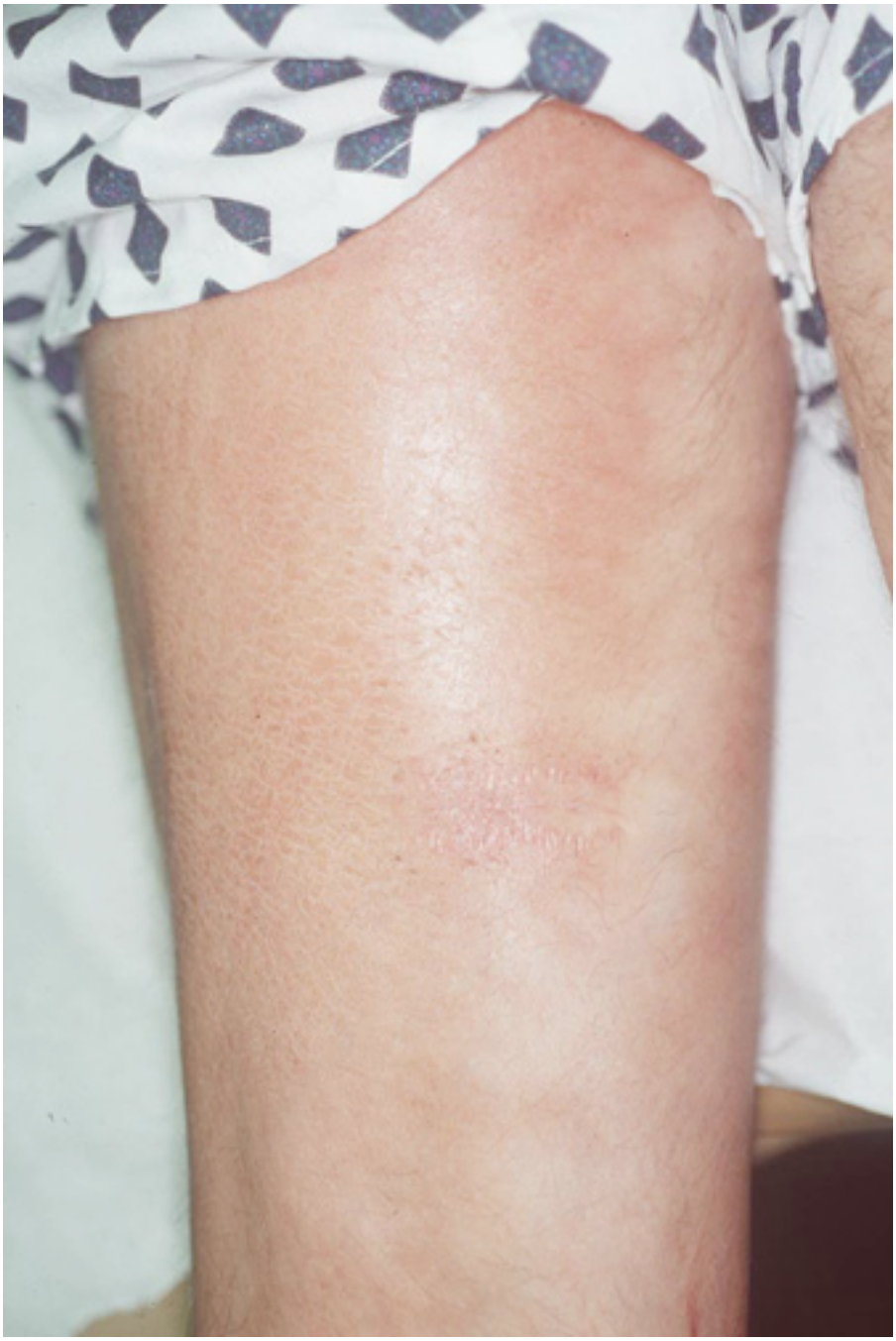
Multimedia



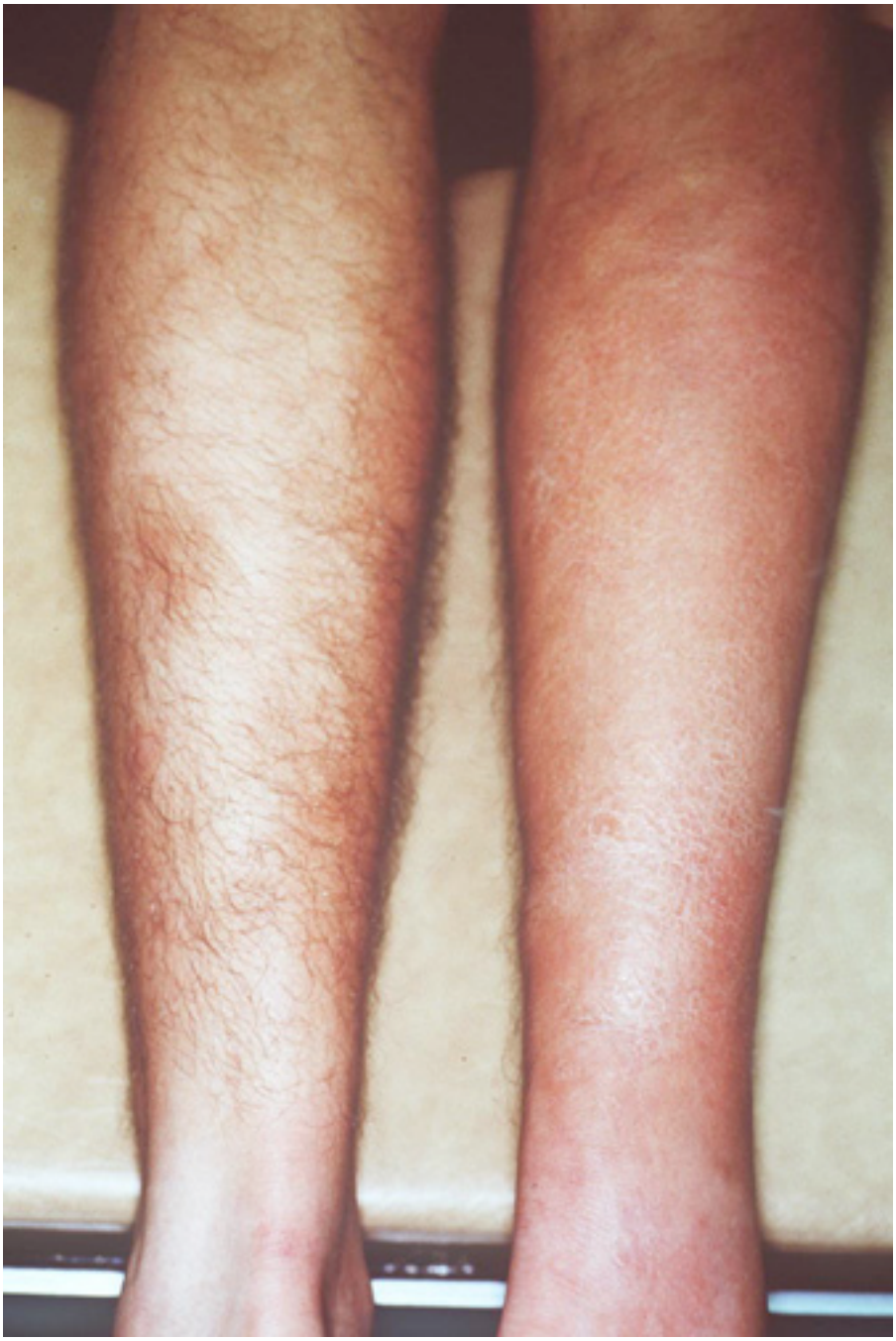
Media file 1: Lower back part of the legs shows hypopigmentation, induration, biopsy site, and asymmetric involvement (same patient as in Media Files 2-3).



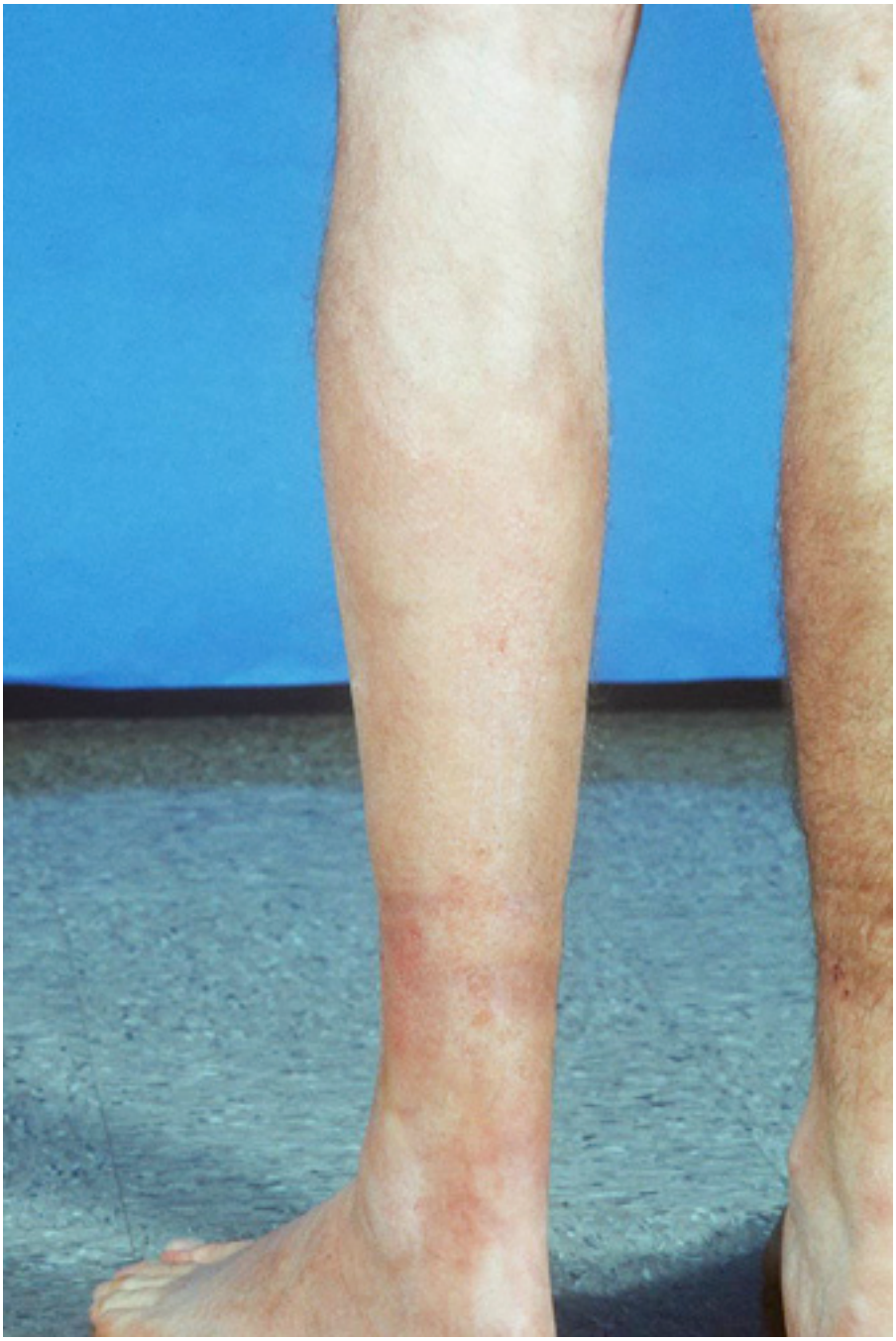
Media file 2: Posterior thigh shows woody induration, sclerosis, and hypopigmentation (same patient as in Media Files 1 and 3).



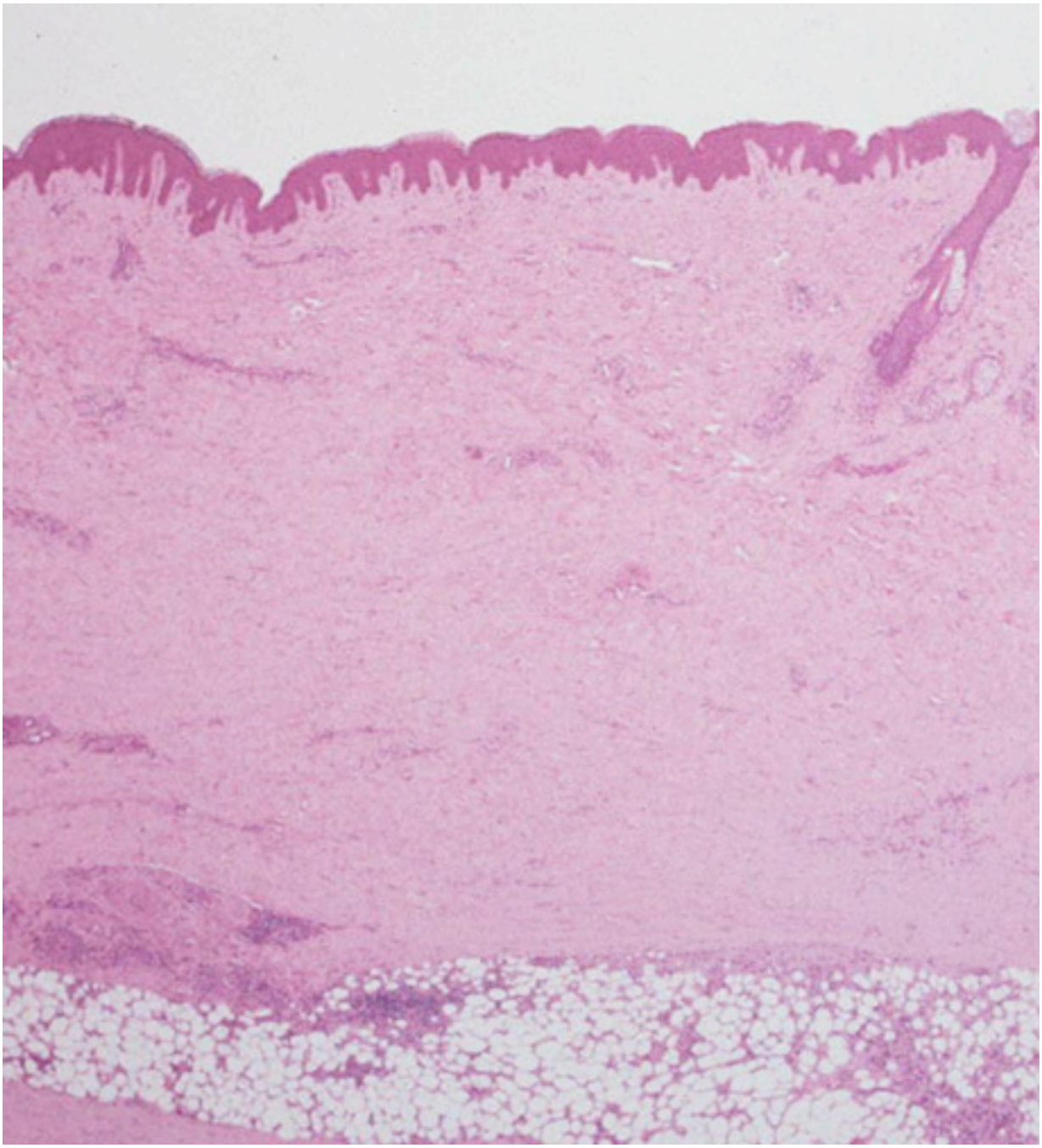
Media file 3: Close-up view of left posterior thigh 2 weeks later shows erythema, scaling, alopecia, and rippled induration (same patient as in Media Files 1-2).



Media file 4: Posterior part of the calf in the first week of illness shows erythema, edema, alopecia, scaling, and early induration. The right calf is relatively uninvolved with patchy erythema only (same patient as in Media File 5).



Media file 5: Photograph of the posterior part of the calf at 3 weeks shows complete sclerosis and induration with patchy erythema (same patient as in Media File 4).



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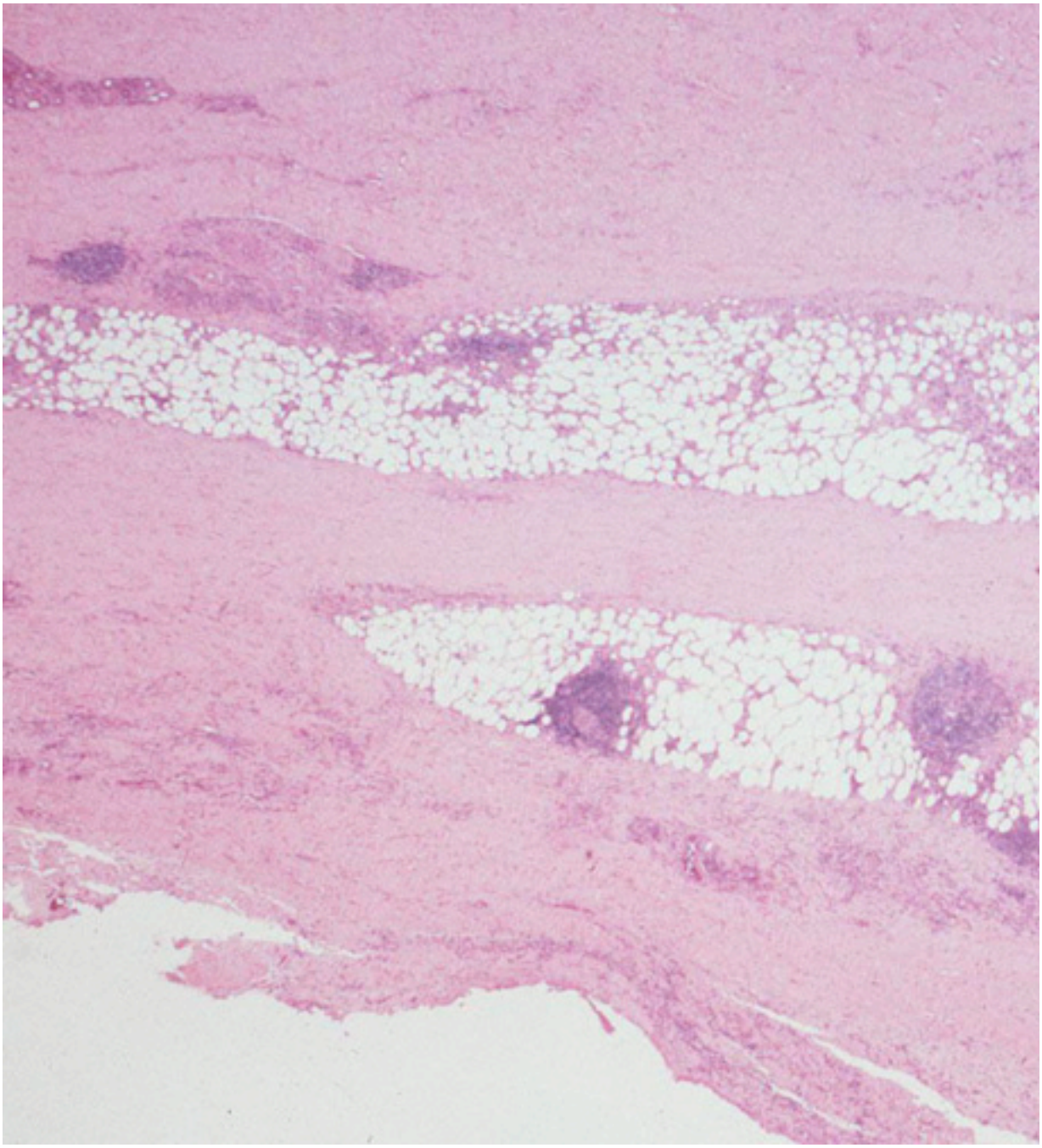
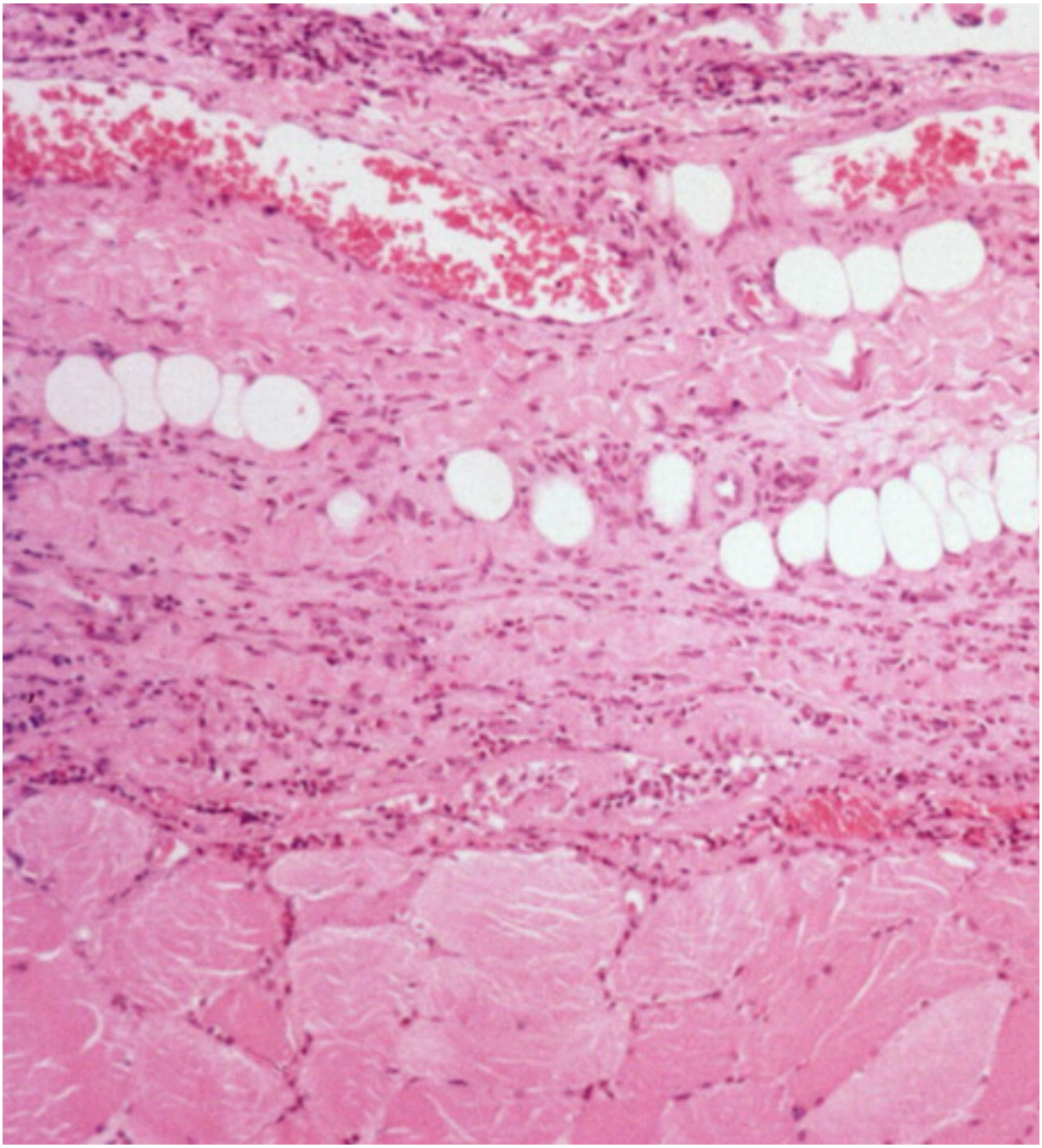
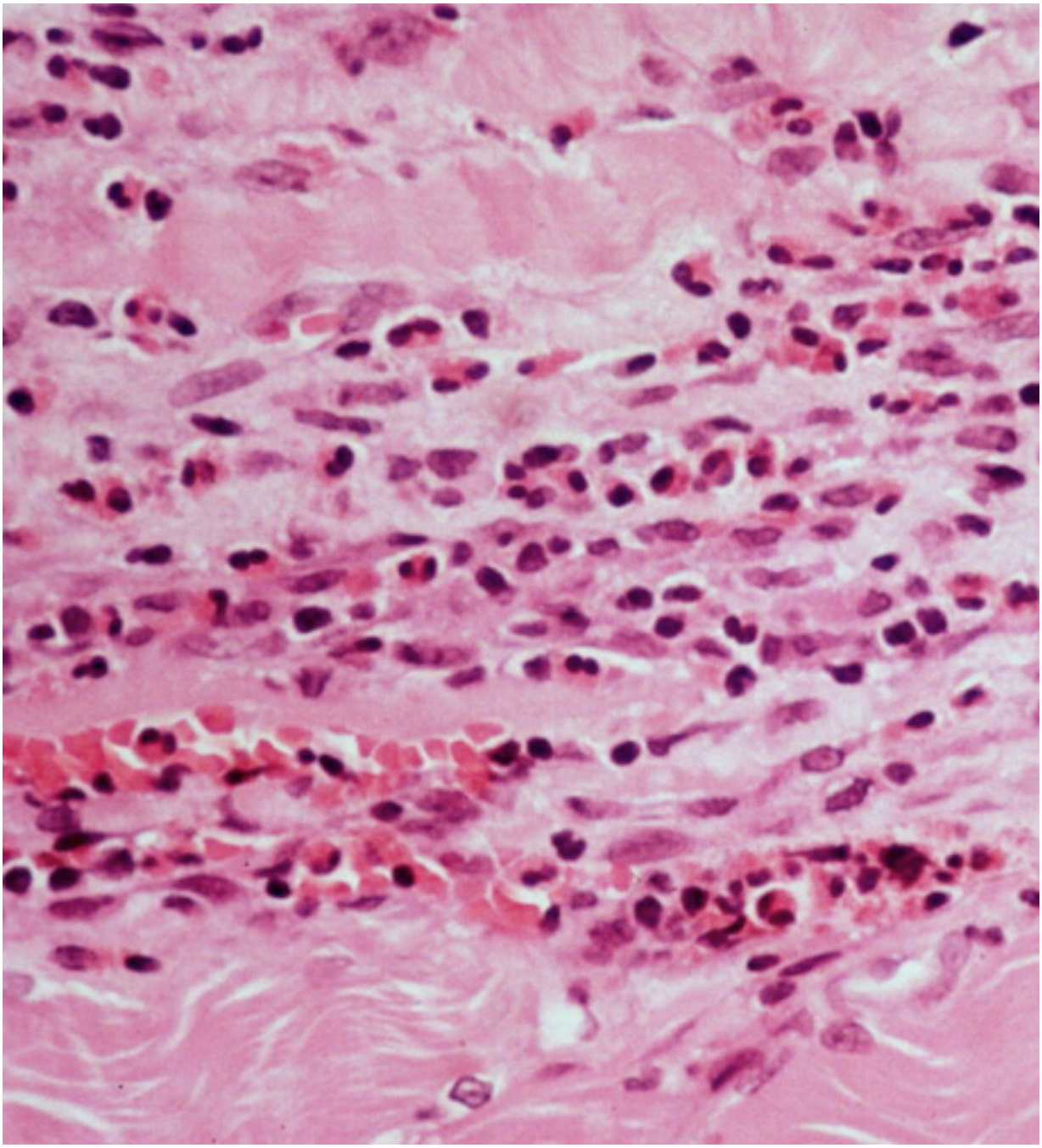


Media file 7: Photomicrograph of subcutaneous fat-fascia junction shows entrapment of subcutaneous fat by intersecting thick bands of fibrosis. Thickening and fibrosis of fascia and lymphoid aggregates are seen.



Media file 8: Photomicrograph of fascia-skeletal muscle junction shows markedly thickened fascia with heavy inflammatory infiltration.



Media file 9: High-power photomicrograph of fascia shows heavy inflammatory infiltration with numerous eosinophils, lymphocytes, and occasional plasma cells.

References

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