Eosinophilic fasciitis (EF), also known as Shulman disease and diffuse fasciitis with eosinophilia, is an uncommon condition that often is confused with scleroderma because they have similar features.

ABSTRACT: Eosinophilic fasciitis (EF) often is confused with scleroderma. A 50-year-old woman presented with progressive tightening of the skin of the arms and legs. She complained of diffuse joint pain that was prominent in the hands and wrists. Her past medical history was significant for hypothyroidism. A skin biopsy revealed superficial and deep infiltrates of inflammatory cells with eosinophils. Physical examination findings were significant for skin hypopigmentation and hyperpigmentation over her forearms and legs. EF may be difficult to differentiate from localized scleroderma, limited and diffuse cutaneous systemic sclerosis, and several scleroderma-like disorders. (J Musculoskel Med. 2012;29:45-47, 55)

Eosinophilic fasciitis (EF), also known as Shulman disease and diffuse fasciitis with eosinophilia, is an uncommon condition that often is confused with scleroderma because they have similar features. Shulman first described EF in 1974 when he saw patients with scleroderma-like skin changes but histopathological features on deep biopsy showed evidence of diffuse fasciitis. In this article, we describe an unusual case of a patient who presented to our academic clinic for consultation with either scleroderma or severe, advanced morphea.

CASE PRESENTATION
A 50-year-old white woman presented to our clinic with progressive tightening of the skin of the arms and legs that had started 8 months earlier when she was packing with her family to move to Florida. She stated that the packing took too many long hours and was very strenuous. She had noticed a hardened patch of skin on her left lower leg above the ankle, but she did not recall experiencing any injury to that area while she was packing. Progressive hardening of her arms and legs with hypopigmented and hyperpigmented skin developed gradually over a few months but spared her hands and feet. She complained of joint pain that was diffuse but was prominent in the hands and wrists, which appeared swollen and puffy. She denied any history of Raynaud phenomenon (RP), shortness of breath, chest pain, fatigue, or dysphasia. The patient started to receive 10 mg/d of prednisone a few months later, and her joint pain, swelling, and arthritis resolved completely. However, the skin tightness continued to progress to involve the whole arms and legs while sparing the trunk, face, hands, and feet. Some areas of the skin on her upper arms and thighs appeared “to have hardened wrinkles or to be cellulite-like in the thigh area,” as the patient described it.

Past Medical History
The patient’s past medical history was significant for hypothyroidism. That diagnosis had been made 7 years earlier, when she was working as a respiratory therapist at a hospital in Virginia and was complaining of progressive fatigue. She denied having had any similar skin lesions in the past. However, 7 years earlier she had had one area of erythema and slightly hardened skin over her right ankle. It was itchy but resolved in a few months without complications or scarring. Her treating physician told her at the time that she had morphea. The patient is married and has 6 children. She denied any history of drug, alcohol, or tobacco use, and her family history was negative for any autoimmune connective-tissue disease. Otherwise, findings from a review of systems were completely unremarkable. She was taking only the prednisone at 10 mg/d, her thyroid replacement medication, a multivitamin, and fexofenadine as needed for chronic seasonal allergies. A skin biopsy specimen was obtained from the patient’s right forearm at the time when her joint symptoms had resolved. It revealed superficial and deep infiltrates of inflammatory cells with eosinophils. Blood work done a month earlier showed a negative antinuclear antibodies (ANAs) test result and normal thyroid-stimulating hormone and creatine phosphokinase levels. Tests for
extractable nuclear antigen, anticentromere, Scl-70, Jo-1, and thyroid peroxidase antibodies were performed before her visit, and the results were negative. Also, her erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) and aldolase levels were within normal limits.

**Physical Examination**

Findings from the patient’s physical examination were significant for hypopigmentation and hyperpigmentation of her skin over her forearms and legs. The skin was tight; her hands and feet were spared. Multiple “orange peel,” or “peau d’orange,” signs (normal skin color with the dimpled appearance of an orange peel) and “groove” signs (dimpling of the medial upper arm with elevation, leaving an indentation on the overlying skin) were elicited. Findings from the rest of the physical examination were unremarkable.

The consulting physician requested a differential between a possibly advanced morphea and an atypical presentation of scleroderma. After examining the patient and reviewing her history, we concluded that she probably had EF.

Deep tissue biopsy had been planned by the patient’s dermatologist, but her insurance did not cover it and it was not obtained. However, this is a classic case with the sparing of the hands and feet and the physical examination findings. The initial skin biopsy, not a deep tissue biopsy, specimen showed increased eosinophils. In early, evolving, or atypical cases, a deep tissue biopsy might be needed to confirm the diagnosis; this did not apply to our patient, who presented with an established, advanced, and classic case.

**DISCUSSION**

EF is a rare fibrosing disorder that presents as skin edema and thickening followed by indurations. Histopathological findings early in the disease course show involvement of the deep fascia and lower subcutaneous tissue. Infiltration of lymphocytes, plasma cells, histiocytes, and eosinophils is observed on biopsy. In addition to involvement of deep fascia and subcutaneous tissue, the dermis becomes thickened and sclerotic and inflammatory cell infiltrates disappear.

A history of strenuous exercise preceding the development of symptoms may be reported in up to 50% of patients with EF.

**Stages of Clinical Manifestations**

The clinical manifestations of EF usually occur in 3 stages. The first stage involves pitting and edema of the affected skin; a peau d’orange appearance and indurations and the groove sign are seen in the second stage. The arms and legs are the most frequently affected sites. The hands and feet usually are spared in EF, in contrast to scleroderma, in which the hands are involved in nearly all cases.

In the third stage, there may be periarticular involvement and atrophy of muscles that may result in flexion contractures and functional disability. Peripheral nerves also may be involved, leading to nerve compression and carpal tunnel syndrome.

RP is present in nearly all patients who have systemic sclerosis (SSc) but is typically absent in EF, as in our patient. True sclerodactyly and nailfold capillary abnormalities do not occur in EF. Peripheral eosinophilia has been documented in up to 80% of patients in the early disease stages, but this and polyclonal hypergammaglobulinemia could disappear in the later stages. The ESR and CRP level also may be elevated in EF. Hematological malignancies and, in some case series, autoimmune thyroid disease have been associated with EF. The absence of RP and lack of sclerodactyly should alert the physician to consider a scleroderma-like disorder.

MRI has emerged as an important tool for evaluation of EF. On MRI, characteristic signs may be observed, such as facial thickening, hyperintense signal within the fascia on fluid-sensitive sequences, and facial enhancement after contrast. MRI also helps identify the area for deep skin biopsy. Deep skin biopsy usually is required to differentiate among erythema nodosum, bite reaction, parasitic reaction, and Well syndrome, in which eosinophilia is limited to the superficial layers.

**Treatment Is Limited**

Treatment for patients with EF is limited. Corticosteroids are first-line agents and usually are given in moderate to high doses. No controlled trials have determined the efficacy of different dosing, but the current consensus is to use up to 1 mg/kg of prednisone, with tapering tailored to the response. The duration of the therapy varies with the resolution of the symptoms.

In patients who do not respond to corticosteroids, immunosuppressive therapy (eg, methotrexate [MTX], cyclosporine, hydroxychloroquine, and psoralen and UV-A light therapy [photochemotherapy]) have been used. However, the results have not been consistent, as they are with corticosteroids. The mortality rate for patients with EF remains low. Recurrence has been documented in the literature, but data on the percentage of patients who experience relapse are lacking.

**DIFFERENTIAL DIAGNOSIS**

EF may be difficult to differentiate from localized scleroderma, limited and diffuse cutaneous SSc,
Eosinophilic Fasciitis: A Difficult Diagnosis
Published on Diagnostic Imaging (http://www.diagnosticimaging.com)

and several scleroderma-like disorders. RP usually is absent in EF. An overwhelming majority of patients with both limited and diffuse cutaneous forms of SSc have RP or it develops at or near the time of the earliest skin changes. Nailfold capillaries exhibit dilated capillary loops and avascular areas by capillaroscopy in SSc, which typically are normal in EF. The fingers, feet, and face are spared in EF but usually are involved in most forms of limited and diffuse SSc. Internal organ involvement (eg, pulmonary fibrosis, pulmonary hypertension, renal crisis) is frequent in SSc but typically is absent in EF. Unlike SSc, EF is not associated with serum ANAs or SSc-specific autoantibodies.

Similar Clinical Manifestations
Nephrogenic systemic fibrosis (NSF) occurs in patients with advanced renal failure (dialysis-dependent or estimated glomerular filtration rate lower than 15 mL/min) after the administration of gadolinium and perhaps erythropoietin; the clinical manifestations of this syndrome resemble those of EF. NSF may be distinguished from EF by involvement of the hands and feet and the absence of eosinophilia and eosinophilic tissue infiltration in patients with advanced renal failure. Scleromyxedema, an idiopathic disorder, may occur alone or in association with malignancies. Skin thickening results from deposition of an amorphous mucinous material in the dermis.

Palmar fasciitis and polyarthritis syndrome is an uncommon paraneoplastic presentation that was first described in 1982. An association was found between palmar fasciitis and polyarthritis syndrome and ovarian carcinoma; this was described as a variant of reflex sympathetic dystrophy (RSD). Palmar fasciitis and polyarthritis syndrome can mimic other conditions, including scleroderma; complex regional pain syndrome (CRPS), or RSD; Dupuytren disease; and EF. In palmar fasciitis and polyarthritis syndrome, there is an absence of RP and a lack of specific autoantibodies. The condition is characterized by rapid progression of clinical features, which helps exclude scleroderma; the synovitis and indurated swelling of digits and the rapid progression of clinical features of the hand make Dupuytren disease an unlikely diagnosis. In contrast to CRPS, palmar fasciitis and polyarthritis syndrome almost always presents with bilateral inflammatory arthritis and fasciitis that is not localized to a particular limb, and it usually has a more severe presentation that typically involves both palms while sparing the dorsal surface of the hands. Patients typically are referred to rheumatology as “scleroderma,” although they need an immediate oncology evaluation and have a very poor prognosis.

Eosinophilia-Myalgia Syndrome
The pathology of skin and subcutaneous tissue in eosinophilia-myalgia syndrome (EMS) cannot be differentiated from that in EF. Some features may be valuable in distinguishing one condition from the other. Most cases of EMS have resulted from exposure to a contaminant of L-tryptophan, which principally had been used to manage insomnia.

EMS occurs in clusters, and sporadic forms are rare. Myalgias, often severe, have been seen frequently in EMS and remain a criterion for classification. Nonpitting edema that evolves into induration with a peau d’orange appearance in EMS is similar to that seen with EF. Visceral involvement is seen more often in patients with EMS than in those with EF. Adultered rapeseed oil was associated with an epidemic of EMS-like illness in Spain. In its natural form, rapeseed oil may be somewhat toxic to humans because it contains a significant amount of erucic acid. Characteristic symptoms the EMS-like illness are myalgia, arthralgia, and dyspnea. Physical findings include limb swelling, chronic scleroderma-like skin changes, livedo reticularis, neuropathy, and joint contractures. Pulmonary infiltrates and prominent eosinophilia are other features present in EMS.

TREATMENT
The patient received prednisone 10 mg/d initially; there was poor response in the skin and underlying tissue but complete resolution of arthritis. The prednisone dosage was increased to 10 mg tid for 2 months, and there was a great response and improvement of tight tissues. Then the prednisone dosage was lowered to 10 mg bid for 2 months, then 5 mg tid for 2 months, then 5 mg bid for 2 months. Treatment with MTX was started and increased to 15 mg/wk after a few weeks. The patient had been receiving MTX for 10 weeks and prednisone at 5 mg/d for the previous 2 weeks when we examined her at follow-up. We noted a dramatic and significant improvement in her skin condition. The MTX dosage was increased to 17.5 mg/wk; the patient will be weaned off the prednisone completely and gradually over 4 weeks.

CONCLUSION
This case confused many physicians, who all agreed that the patient had what appeared to be tight skin, because it is rare. Clinicians should recognize the atypical features of SSc, which should trigger the search for mimickers. The patient lacked RP, which is typical of SSc or ANA-related diseases, and
lacked dactylitis, which is another feature of ANA-related sclerosing conditions. Localized scleroderma was suggested, but the diffuse involvement, despite its possibility, was unusual, except in some rare cases in which there could be internal organ involvement and ANA positivity. The big clue is that clinically this is not scleroderma or skin tightness or thickening. The pathology is in the fascia below the skin, which typically is spared in the hands and feet. It is not a vasculopathy and, hence, the absence of RP. A closer look at the physical examination findings and targeted history clearly point away from scleroderma and should direct the examiner to other mimickers. This is critical, because the clinical course, prognosis, and treatment are completely different from those of scleroderma, which could have a much worse outcome and could require much more toxic treatments.

References:
