The patient was diagnosed with stage 2B MF and treated first with local radiation therapy and then with oral bexarotene, 75 mg, twice daily. After 4 months there was a complete response.

Discussion | The occurrence of lipodermatosclerosis mimicking MF has been poorly described in the literature, with only 1 other case reported to our knowledge. Several clinical morphological and textural features should be considered when evaluating similar lesions on the legs. Lipodermatosclerosis often presents as a localized, painful, indurated plaque with erythema and hyperpigmentation on the lower legs in a setting of venous insufficiency. The chronic form is said to resemble an “inverted champagne bottle.” The typical presentation of MF is erythematous patches, plaques, or tumors with fine scale that favor sun protected areas.

Treatments for MF are based on the stage of the disease and include topical corticosteroids, topical nitrogen mustard, total skin electron beam therapy, oral retinoids, subcutaneous interferon alfa, histone deacetylase inhibitors, alemtuzumab, psoralen plus UV-A photochemotherapy (PUVA), and extracorporeal photopheresis.

Lipodermatosclerosis is the result of chronic venous insufficiency. Both septal and lobular panniculitis as well as lipomembranous changes are seen on pathologic analysis. Mainstay treatments include compression, leg elevation, topical and/or intraleisional corticosteroids, and anabolic steroids for recalcitrant disease.

Mycosis fungoides should be included in the differential diagnosis of any cutaneous patch or plaque that does not respond to first- and second-line treatments. A low threshold for obtaining biopsy should be the rule for any patient with a chronic, recalcitrant eruption.

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Treatment of Eosinophilic Fasciitis With Sirolimus

Eosinophilic fasciitis (EF) is a disorder in which the subcutaneous tissues become indurated and then sclerotic leading to myalgia, arthralgia, and occasionally contractures and disability. High-dose systemic steroids are first-line therapy; however, steroid-sparing agents are often used owing to disease progression or to avoid the adverse effects of long-term corticosteroid use. We describe a case of EF with rapid response to sirolimus.

Report of a Case | A man in his 30s had a 6-month history of arthralgia involving his shoulders, hands, knees, ankles, and feet, which made it difficult for him to stand or walk for long periods. He complained of swelling and “skin tightness” of his arms, lower legs, and hands. On examination, he had woody induration of his distal extremities creating both peau d’orange surface change and linear depressions along the veins of his right forearm consistent with a groove sign. His fingers were held in a slight flexion contracture at the proximal interphalangeal joints (Figure, A).

Laboratory tests revealed a transient eosinophilia (total eosinophil count, 600/μL), polyclonal hypergammaglobulinemia, a mildly elevated erythrocyte sedimentation rate (22 mm/h), and negative results for antinuclear antibodies and anti-U1RNP and anti-Scl-70 antibodies. He lacked features of systemic sclerosis, including Raynaud phenomenon, sclerodactyly, or nail fold capillary changes. An incisional biopsy of his calf extending into the deep subcutaneous fat, but not including fascia, revealed thickening of the subcutaneous septae with edema and a lymphoplasmacytic infiltrate with eosinophils. The histopathologic findings was most compatible with a deep sclerosing process such as morphea profunda or EF. Given his cutaneous findings and histopathologic deep sclerosis, he was diagnosed with EF.

Figure 2. Incisional Biopsy Specimen From Right Distal Calf Lesion

Epidermotropic lymphocytes are seen occurring in collections and individually along the dermoepidermal junction. Notice the irregular nuclear contours (hematoxylin-eosin, original magnification ×600).
The patient was treated with physical therapy, low-dose prednisone, and methotrexate, 25 mg/wk, for 4 months without an improvement in induration or pain. His prednisone dose ranged between 5 and 20 mg/d for 7 months (the patient had concerns about the adverse effects of high-dose steroids). Given the progressive sclerosis, methotrexate treatment was stopped; prednisone regimen was continued at 5 mg/d; and sirolimus therapy was started at 2 mg/d. Within 6 weeks, there was a reduction of pain and skin thickening (Figure, B). Nine months into therapy, the patient remained on the regimen of sirolimus, 2 mg/d, and prednisone, 5 mg/d. He experienced occasional hand arthralgia but regained the ability to walk long distances, exercise in the gym, and make a fist. The sirolimus regimen will be tapered once his clinical symptoms have completely resolved.

Discussion | Mechanistic target of rapamycin (mTOR) is a cell-signaling serine–threonine kinase that exists as 2 distinct complexes, mTORC1 and mTORC2. Sirolimus predominately inhibits mTORC1 and is commonly used to prevent graft rejection in transplant patients. Sirolimus has been shown to decrease the development of fibrosis in transplanted donor organs in both animal models and clinical studies.1 The mTOR complexes are one of the downstream signals of transforming growth factor (TGF)-β, a key regulator of fibrosis, and inhibition of mTOR is believed to decrease fibroblast function, collagen deposition, and epithelial to mesenchymal transition, a process important in generating fibroblasts and myofibroblasts.2 Sirolimus has led to improvement in cases of nephrogenic systemic fibrosis and modest improvement in systemic sclerosis.3-4 Recently, a dual inhibitor of mTOR complexes 1 and 2 has been shown to reverse TGF-β-induced fibrosis by dermal fibroblasts.5

Eosinophilic fasciitis is a sclerosing disorder for which both high-dose corticosteroids and methotrexate treatments are frequently used, but a complete response is seen in only two-thirds of cases.6 Based on this case report, sirolimus holds potential as an alternative therapy for EF. Further research on mTOR and the development of newer mTOR inhibitors could provide future therapies for other difficult-to-treat sclerosing skin disorders.

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Topical Ruxolitinib for the Treatment of Alopecia Universalis

Alopecia areata and variants alopecia totalis and alopecia universalis are common conditions for which treatment options are limited. Oral Janus kinase (JAK) inhibitors have recently been shown to be effective for the treatment of these disorders. There are, however, risks for serious adverse effects with systemic therapy that may be avoided if topical therapy were an option.

Report of a Case | A patient in her late teens presented for evaluation and management of alopecia universalis. Treatment with prednisone, intralesional triamcinolone, sulfasalazine, topical squaric acid dibutylester, and topical anthralin had been ineffective. The patient had not had any treatment in the previous 2 years. She was otherwise healthy and took no medications. There was no family history of alopecia areata or other autoimmune disease. Findings from a complete review of systems were negative. On examination, there was complete absence of scalp and arm hair and only sparse hair growth of the right lateral eyebrow (Figure, A).

In light of the recent successful treatment of alopecia areata and variants with the JAK inhibitors tofacitinib and ruxolitinib, these were discussed as therapeutic options. Apprehensive of the potential risks of these medications, the patient and her parents decided to pursue a trial of a topical JAK inhibitor. Topical formulations of both tofacitinib and ruxolitinib have been demonstrated to be effective in reversing disease in a murine model of alopecia areata, and topical tofacitinib ointment has been demonstrated to be well tolerated and effective for the treatment of plaque psoriasis. To our knowledge, the use of topical JAK inhibitors has not yet been explored for the treatment of alopecia areata and variants in humans.

Results of baseline laboratory tests, including Quantiferon-TB Gold (Quest Diagnostics), human immunodeficiency virus, and hepatitis B and C blood tests were negative, and a complete blood cell count and comprehensive metabolic panel were within normal limits, though the white blood cell (WBC) count was borderline low, and so causality is suggestive of systemic absorption; however, the patient’s WBC count after starting topical ruxolitinib treatment is 3800/μL, which is small, stable decrease in WBC count at 3800/μL, 4100/μL, and 3800/μL, respectively. Otherwise, there were no abnormalities in complete blood cell count or renal or liver function.

Discussion | To our knowledge, this is the first report of successful treatment of alopecia universalis with a topical JAK inhibitor. While additional studies will be needed to confirm the efficacy, further explore the safety and tolerability, and determine optimal concentrations of topical ruxolitinib and other topical JAK inhibitors for alopecia areata and variants, the results in this case are promising. Although uncommon, serious adverse effects including cancer have been reported in patients taking oral JAK inhibitors. In the case of the present patient, the small decrease in WBC count after starting topical ruxolitinib treatment is suggestive of systemic absorption; however, the patient’s baseline WBC count was borderline low, and so causality is difficult to assess.

Topical JAK inhibitors represent an exciting new treatment opportunity for an often psychologically devastating condition. Given the likely more favorable safety profile associated with topical administration, their use may be considered in patients for whom the potential for serious adverse effects makes oral administration unattractive, most notably the pediatric population.

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