Progressive and Translucent Plaques on the Soles

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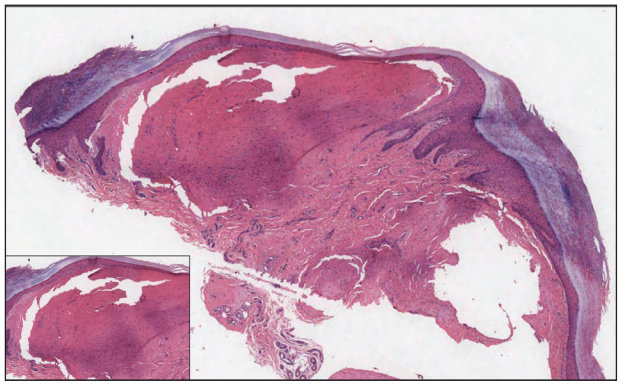

H&E, original magnification ×20 (inset, original magnification ×50).

A 64-year-old woman with a medical history of Waldenström macroglobulinemia, multiple sclerosis, and epilepsy presented with slowly growing papules on the plantar feet of 21 months' duration. She was diagnosed with Waldenström macroglobulinemia incidentally on routine blood work 3 years prior and declined treatment because she was asymptomatic. Physical examination revealed a total of 20 firm, variably sized, light pink to purple, partially translucent and telangiectatic papules and plaques bilaterally on the plantar feet. A plaque from the right sole was biopsied.

THE BEST **DIAGNOSIS IS:**

a. acral fibrokeratoma
b. cutaneous macroglobulinosis
c. erythropoietic protoporphyria
d. plantar fibromatosis
e. tophaceous gout

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The authors report no conflict of interest.
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THE **DIAGNOSIS:** Cutaneous Macroglobulinosis

Waldenström macroglobulinemia is a lymphoplasmacytic lymphoma that produces a circulating monoclonal IgM. Incidence in the United States is 1500 patients annually, most commonly men in their 70s.[1] The disease process is largely indolent, with early symptoms consisting of generalized weakness, weight loss, and fatigue. Signs of lymphadenopathy, hepatosplenomegaly, and cytopenia may emerge as the disease progresses. Diagnostic criteria include bone marrow biopsy with plasmacytoid/plasmacellular infiltrate; IgM monoclonal gammopathy; and end-organ damage, which may include cutaneous manifestations.[2]

Cutaneous findings in Waldenström macroglobulinemia are nonspecific and secondary to the disease's hematologic manifestations, presenting as livedo reticularis, purpura, and mucosal bleeding.[3] True cutaneous involvement of the disease is rare and was first described in 1978 by Tichenor.[4] Specific cutaneous lesions have 2 separate clinical presentations: (1) a primary cutaneous infiltrate of lymphoplasmacytic cells, and (2) deposition of IgM in the dermis.[5] Although the primary infiltrate of neoplastic cells appears as erythematous firm papules or plaques on the face and trunk, similar to other manifestations of leukemia cutis, deposition of IgM presents as translucent papules and plaques and is located more distally, particularly on the extensor extremities.[6] These depositional plaques are not pruritic but may be tender if located over sites of pressure, as seen with the plantar presentation in our patient.

Histologically, cutaneous macroglobulinosis demonstrates IgM deposition in perieccrine, perivascular, or intravascular tissue that is periodic acid–Schiff (PAS) positive.[7] Staining with Congo red and Alcian blue is negative. In our case, biopsy showed a nodular deposition of hypocellular globular material that stained brightly with PAS and PAS diastase. With Masson trichome stain, intensity of staining diminished, suggesting that the deposition was not composed of collagen; rather, this deposition appeared to consist of IgM storage papules on immunohistochemistry (Figure 1). Further workup revealed borderline pancytopenia and elevated globulins with a monoclonal peak on serum protein electrophoresis, confirming the diagnosis of cutaneous macroglobulinosis secondary to Waldenström macroglobulinemia.

A PubMed search of articles indexed for MEDLINE using the terms *cutaneous*, *macroglobulinosis*, *macroglobulinemia*, *Waldenström's macroglobulinemia*, *Waldenström's macroglobulinaemia*, and *macroglobulinemia cutis* revealed a total of 19 cases of cutaneous macroglobulinosis (including this case). The average age of presentation in these cases is 60 years (range, 29–83 years) with a predisposition for men (68% [13/19]). The development of cutaneous macroglobulinosis primarily has been noted following diagnosis of Waldenström macroglobulinemia (53% [10/19]), with some cases prior to diagnosis (37% [7/19]) or at the time of diagnosis (11% [2/19]). The presence of cutaneous lesions does not correlate with prognosis of the underlying malignancy.[5,8,9]

Systemic treatment of the underlying macroglobulinemia has been suggested for symptomatic cases of cutaneous macroglobulinosis.[3] Prior therapy has consisted primarily of chlorambucil; however, treatment with rituximab, occasionally in conjunction with the proteasome inhibitor bortezomib, recently has been reported.[10]

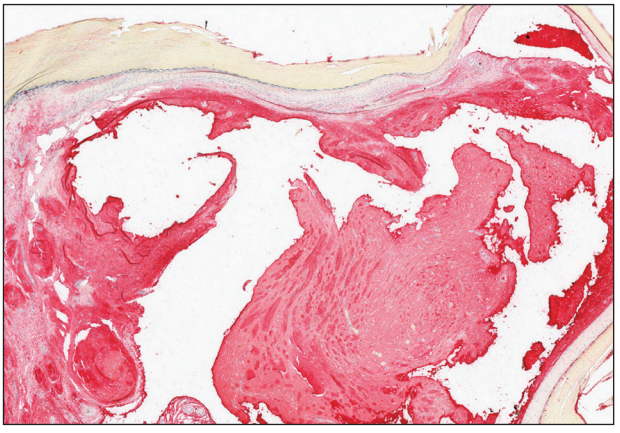

FIGURE 1. Cutaneous macroglobulinosis. Elevated levels of circulating IgM lead to nodular dermal depositions in the form of IgM storage papules on immunohistochemistry (original magnification ×40).

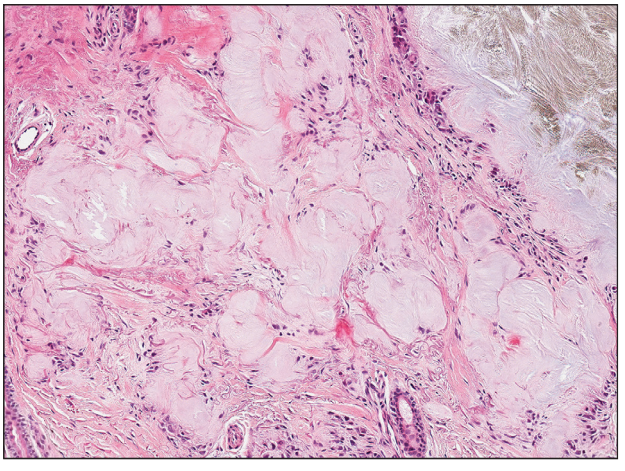

FIGURE 2. Tophaceous gout. Following formalin fixation, feathery amorphous pink areas are seen within the dermis and subcutaneous tissue surrounded by granulomatous inflammation (H&E, original magnification ×40).

Because of the symptomatic nature of our patient's lesions, she was referred to the oncology department and started on rituximab therapy. The lesions improved with therapy and have remained stable following treatment.

The differential diagnosis for tender pink papules and plaques on the arms and legs includes tophaceous gout, plantar fibromatosis, erythropoietic protoporphyria, and acral fibrokeratoma.

Gouty tophi commonly accumulate as painful, edematous, yellow to whitish nodules and tumors with erythema, often overlying joints or extensor surfaces. Histopathologic examination after formalin fixation shows needle-shaped clefts within feathery amorphous pink areas surrounded by granuloma (Figure 2).[11] Yellow, needle-shaped, negatively birefringent crystals can be viewed under polarized microscopy in alcohol-fixed samples.

Plantar fibromatosis (Ledderhose disease) is a benign proliferation of the plantar aponeurosis linked to alcohol use; liver disease; and notably epilepsy,[12] a component of our patient's medical history. Large nodules appear grossly on the plantar feet and may progress to contractures in more advanced lesions. Biopsy reveals bland hyperproliferation of fibroblasts in a background of fascial fibrous tissue (Figure 3).[12] Clinically, this diagnosis is part of the differential diagnosis of plantar nodules but appears histologically different than cutaneous macroglobulinosis because there are no hyaline deposits in plantar fibromatosis.

Erythropoietic protoporphyria is a rare disorder that primarily arises due to a congenital deficiency in the ferrochelatase enzyme involved in heme biosynthesis. Erythropoietic protoporphyria is the most common porphyria among children and typically presents in infancy or early childhood as a painful photosensitivity with ensuing cutaneous manifestations and possible hepatobiliary disease. Edema and severe burning pain can be noted within minutes of sun exposure in a dose-response relationship.[13] Histologic findings of erythropoietic protoporphyria differ based on acute or chronic skin changes. Acute lesions exhibit a predominantly neutrophilic interstitial dermal infiltrate with vacuoles and intercellular edema. Chronic changes include the accumulation of a PAS-positive, amorphous, hyalinelike substance, similar to the microscopic findings of cutaneous macroglobulinosis (Figure 4).[13]

An acral fibrokeratoma is a benign fibroepithelial tumor that clinically appears as a flesh-colored or slightly erythematous exophytic nodule that most commonly is found on the fingers or toes. Thought to arise from trauma to the affected area, it is histologically characterized by interwoven collagenous bundles with overlying epidermal hyperkeratosis, acanthosis, and deep thickened rete ridges[14] (Figure 5). Although multiple acral fibrokeratomas have been reported (similar to presentations of prurigo nodularis),[15] they more commonly appear as solitary lesions as opposed to the numerous translucent papules seen in our patient.

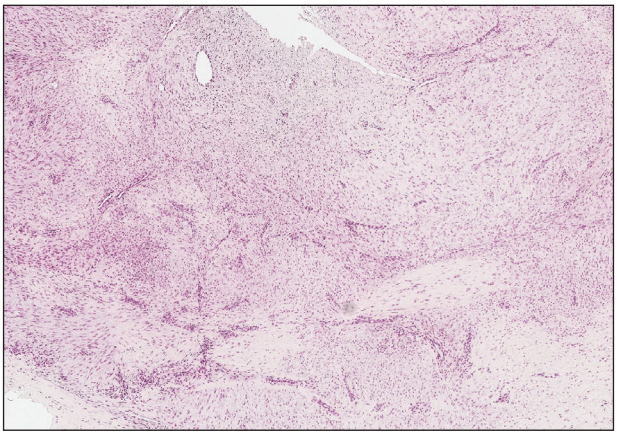

FIGURE 3. Plantar fibromatosis. A bland hyperproliferation of fibroblasts is evident within a background of fascial fibrous tissue (H&E, original magnification ×40).

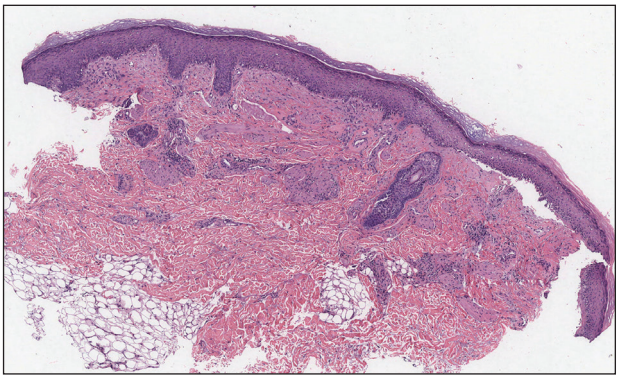

FIGURE 4. Chronic erythropoietic protoporphyria reflects cumulative skin damage and the deposition of a hyalinelike substance in the upper dermis that stains positive for periodic acid–Schiff (H&E, original magnification ×40).

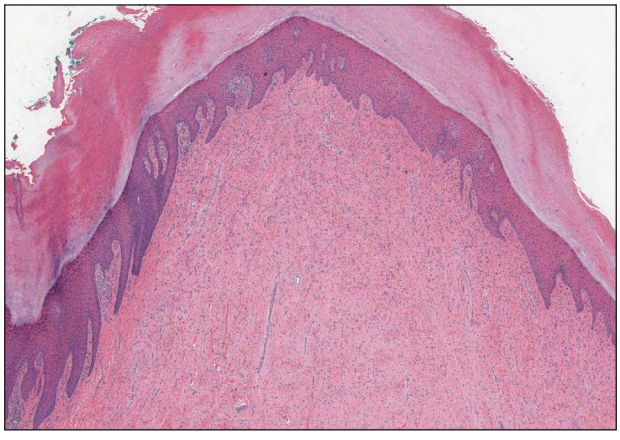

FIGURE 5. Acral fibrokeratoma. Epidermal hyperkeratosis, acanthosis, and thickened rete ridges overlie a core of collagen fiber bundles with interwoven and parallel arrangements (H&E, original magnification ×20).

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