Exophytic plaque on the plantar foot

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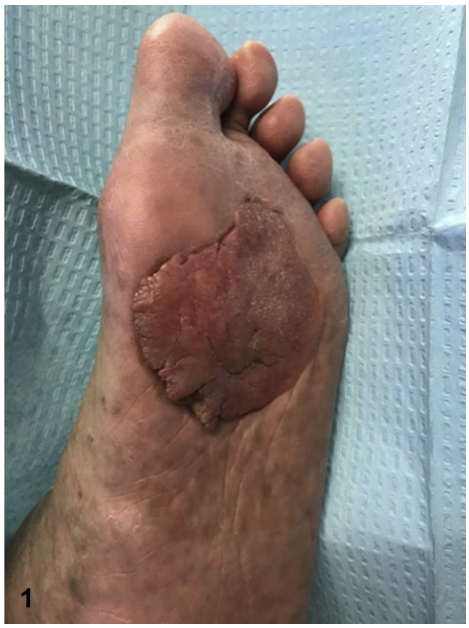

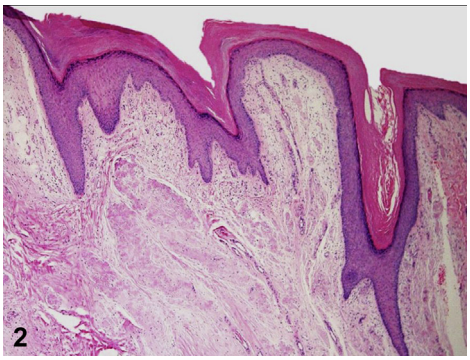

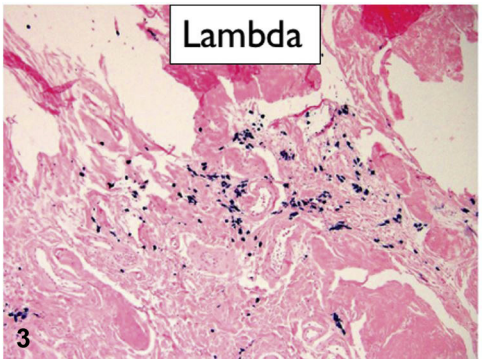

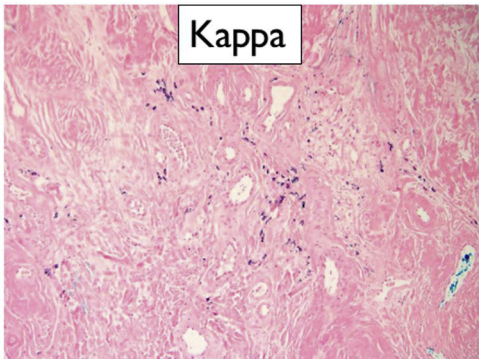

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An 82-year-old man presented with a 10-year history of an enlarging, asymptomatic plaque on his left foot. Physical examination found a 7.5- × 6.5-cm, firm, exophytic plantar mass (Fig 1). Incisional biopsy found verrucous epithelium with eosinophilic, hyaline material throughout the dermis with admixed plasma cells (Fig 2). Dermal deposits stained with Congo red exhibited apple-green birefringence under polarized light. In situ hybridization found a 5:1 ratio of λ:κ immunoglobulin light chain (Fig 3). Complete blood count, comprehensive metabolic panel, serum/urine protein electrophoresis, serum immunoglobulin light chains, electrocardiogram, and abdominal fat pad biopsy were unremarkable.

Question 1. What is the most likely diagnosis?

A. Verrucous carcinoma

B. Lichen amyloidosis

C. Cutaneous marginal zone lymphoma

D. Nodular cutaneous amyloidosis

E. Tyloma

Answers:

A. Verrucous carcinoma — Incorrect. Verrucous carcinoma shows a markedly expanded epidermis, whereas our patient's biopsy found deposits in the dermis. Furthermore, positive Congo red staining and apple-green birefringence under polarized light confirmed the presence of amyloid.

B. Lichenoid cutaneous amyloidosis — Incorrect. Amyloid deposits in lichenoid cutaneous amyloidosis are derived from cytokeratin, whereas those in nodular cutaneous amyloidosis are derived from immunoglobulin light chains produced by locally infiltrating plasma cells.[1] Furthermore, the lichenoid variant is often associated with pruritis.[1]

C. Cutaneous marginal zone lymphoma — Incorrect. Although clonal proliferation of plasma cells can be a feature of cutaneous marginal zone lymphoma, our patient's biopsy did not find lymphoid aggregates, as would be expected in this diagnosis. Furthermore, positive Congo red staining and apple-green birefringence under polarized light are indicative of amyloid.

D. Nodular cutaneous amyloidosis — Correct. Nodular cutaneous amyloidosis is characterized by amyloid deposits derived from immunoglobulin light chains produced by locally infiltrating plasma cells, whereas amyloid deposits in the macular and lichenoid variants of cutaneous amyloidosis are derived from cytokeratin.[1] The λ light chain restriction with localized plasma cell proliferation suggests immunoglobulin-derived amyloid in our patient.

E. Tyloma — Incorrect. A tyloma, or callus, may clinically mimic nodular amyloidosis. However, it is histopathologically marked by hyperkeratosis without the presence of dermal amyloid deposits.

Question 2. Which of these studies would not be indicated following our patient's clinical and histopathologic findings?

A. Complete blood count with differential

B. Anti-Ro and anti-La antibodies

C. Bone marrow biopsy

D. Glomerular filtration rate and creatinine

E. Thyroid-stimulating hormone

Answers:

A. Complete blood count with differential — Incorrect. The nodular variant of cutaneous amyloidosis is the only variant associated with a 7% to 50% risk of systemic plasma cell dyscrasia, including systemic amyloidosis.[2,3] Therefore, a complete blood count with differential is recommended to rule out a plasma cell dyscrasia.

B. Anti-Ro and anti-La antibodies — Incorrect. Nodular cutaneous amyloidosis has been strongly associated with Sjögren disease[4]; therefore, a Sjögren panel is highly recommended even in the absence of symptoms.[4] Our patient's Sjögren panel was negative.

C. Bone marrow biopsy — Incorrect. A bone marrow biopsy may be useful to rule out systemic plasma cell dyscrasia, however, an abdominal fat pad biopsy may be performed as a confirmatory test instead.[2,3]

D. Glomerular filtration rate and creatinine — Incorrect. An underlying systemic plasma cell dyscrasia may affect the kidneys[2,3]; therefore, examination of renal function is recommended. A comprehensive metabolic panel was unremarkable in our patient, ruling out involvement of both the kidneys and liver, the latter of which can also be affected in systemic amyloidosis.

E. Thyroid-stimulating hormone — Correct. Although an underlying systemic amyloidosis may affect the thyroid, it is relatively uncommon and would be warranted if the patient presents with signs of thyroid dysfunction, such as heat or cold intolerance, unexplained weight gain or loss, heart palpitations, and/or pretibial myxedema. Although no standard guidelines have been established for

workup or follow-up frequency and duration in nodular primary cutaneous amyloidosis, the following are commonly performed with regular follow-up examinations to rule out systemic disease: complete blood count, comprehensive metabolic panel, serum/urine protein electrophoresis, serum immunoglobulin light chain ratio, electrocardiogram, and either abdominal fat pad biopsy or bone marrow biopsy.[2,3]

Question 3. Which of the following would be the treatment of choice for this patient's condition?

A. Intralesional methotrexate

B. Intralesional corticosteroid

C. Surgical excision

D. Systemic retinoid

E. Cryotherapy

Answers:

A. Intralesional methotrexate — Incorrect. Although a recently published case involving nodular amyloidosis found improvement following intralesional methotrexate attributable to its antimitotic properties, data are limited to 1 case report and are lacking in recurrence rates.[5] Furthermore, our patient preferred noninvasive management.

B. Intralesional corticosteroid — Incorrect. Although corticosteroids have immunosuppressive effects, intralesional corticosteroid injections have been ineffective in improving nodular cutaneous amyloidosis.[5]

C. Surgical excision — Correct. Surgical excision has been associated with complete clearance of nodular amyloid lesions with a low likelihood of recurrence in a recently published systematic review of the literature.[1] However, the surgical results reported in the systematic review are limited to case reports. Although offered surgical excision, our patient opted for conservative management with an offloading shoe, and at 12-month follow-up, the lesion remained unchanged. Repeat laboratory values were unremarkable.

D. Systemic retinoid — Incorrect. Oral retinoids have shown improvement in the lichenoid variant of cutaneous amyloidosis, likely because of their beneficial effects on keratinization in the context of keratin-derived amyloid.[1] However, retinoids have not been found to be effective in nodular cutaneous amyloidosis.

E. Cryotherapy — Incorrect. Cryotherapy has been reported to be unsuccessful in treating nodular cutaneous amyloidosis and has been complicated by minor hemorrhage.[1]

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