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Acquired Ichthyosis in a Middle-Aged Woman

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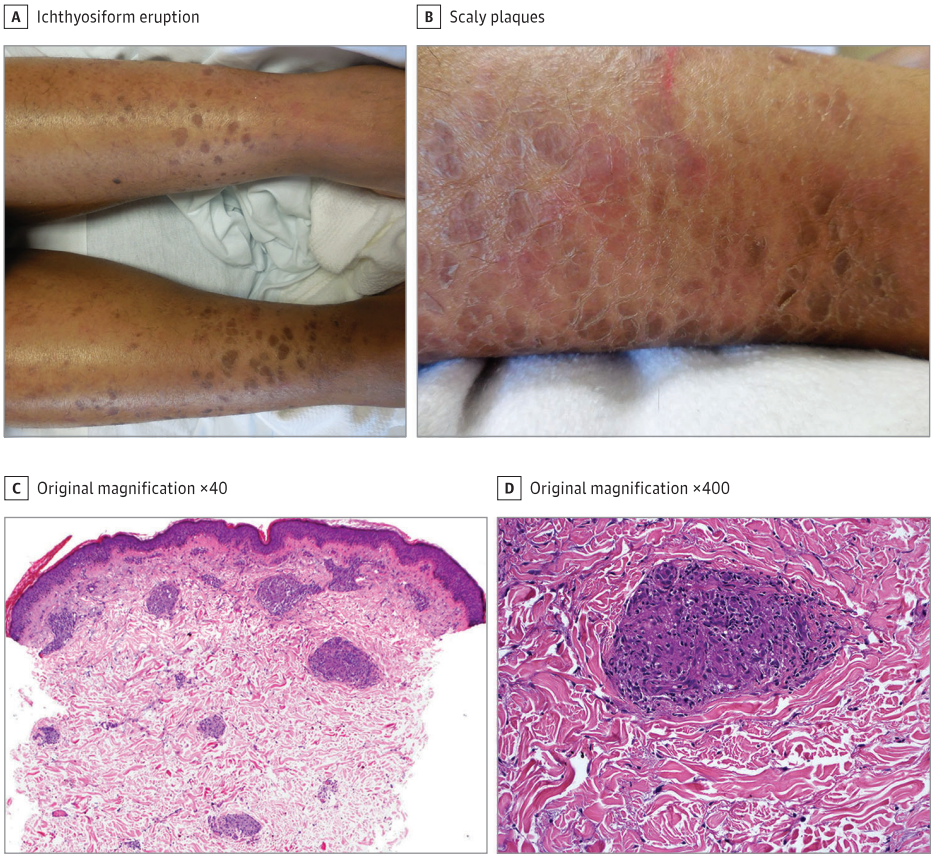

Figure. A, Dark brown, coarse, ichthyosiform scale on the bilateral lower legs. B, Firm pink plaques with overlying coarse scale. C, Granulomatous inflammation throughout the dermis with mild hyperparakeratosis around a hair follicle (hematoxylin-eosin). D, Well-formed, epithelioid granulomas (hematoxylin-eosin).

An African American woman in her 30s presented with a 6-month history of 1-cm to 2-cm erythematous and scaly plaques on her lower legs associated with 30-kg weight loss. The plaques began around her ankles and spread proximally, reaching the upper thighs by the time of presentation. She also noted new lesions on her arms and abdomen in the preceding weeks. The eruption was asymptomatic, and the plaques were preceded by lower extremity edema and weakness, resulting in difficulty ambulating and frequent falls. The patient also reported allodynia, tingling, and numbness in her lower legs. She took no medications and her medical history was significant for a first-trimester miscarriage. She was a schoolteacher and had not traveled outside of the country in the past 10 years.

Physical examination of her lower extremities revealed erythematous and indurated plaques, some with overlying coarse scale (Figure, A and B). Her neurological examination showed symmetric 4/5 strength and decreased reflexes in her lower extremities. Sensation to light touch and proprioception were diminished below the knee. Two punch biopsies were performed for histologic review (Figure, C and D).

WHAT IS YOUR DIAGNOSIS?

A. Plaque and ichthyosiform sarcoidosis

B. Lymphomatoid granulomatosis

C. Interstitial granulomatous dermatitis

D. Cutaneous tuberculosis

Diagnosis

A. Plaque and ichthyosiform sarcoidosis

Discussion

Histopathologic evaluation of the 2 different lesions showed well-formed epithelioid granulomas distributed around neurovascular bundles without evidence of vasculitis (Figure, C and D). Examination under polarized light revealed no foreign material. No microorganisms were identified with the use of special stains, including acid-fast bacilli, Fite, and periodic acid-Schiff stains. Results of in situ hybridization for Epstein-Barr virus were negative. Computed tomography of the thorax and abdomen showed bulky hilar, mediastinal, and retroperitoneal lymphadenopathy. An angiotensin-converting enzyme level was found to be 145 U/L (reference range, 8-53 U/L; to convert to nanokatals per liter, multiply by 16.667). Findings on electrocardiography, echocardiography, and urinalysis were normal. Thyroid-stimulating hormone and 25-hydroxyvitamin D levels were normal, but an increased level of 1,25 dihydroxyvitamin D was noted.

To exclude a lymphoproliferative process, fine-needle aspiration of a lymph node was performed, which revealed reactive changes. Findings of antinuclear antibody and antineutrophil cytoplasmic antibody studies were negative, and rheumatoid factor, rapid plasma reagin, and complement levels and QuantiFERON TB Gold testing values were all within normal limits. Findings from sputum acid-fast bacilli stains and *Histoplasma* antigen from a bronchial wash were also negative. A diagnosis of sarcoidosis was rendered with involvement of the cutaneous, pulmonary, and neurologic organ systems. The patient was treated with systemic corticosteroids and initially improved; however, she eventually relapsed and developed cardiac disease, necessitating implantation of a left ventricular assist device.

Sarcoidosis usually affects people younger than 50 years with a slight female preponderance. Despite investigations aimed at finding a potential etiologic trigger, including environmental agents and microorganisms, to our knowledge a causal agent is yet to be indentified and the underlying pathophysiology of sarcoidosis remains somewhat unclear. Certain human leukocyte antigen subtypes and gene variations have also been implicated. Sarcoidosis causes skin lesions in 20% to 35% of affected patients with a broad array of possible cutaneous manifestations.[1] At least 90% of patients with sarcoidosis experience pulmonary involvement during the course of the disease; however, only a small subset of these patients exhibit symptoms at the time of diagnosis.[2] Initial assessment of sarcoidosis should include electrocardiography, echocardiography, and urinalysis, as well as measurement of thyroid-stimulating hormone and 25-hydroxyvitamin D levels.[3] Elevated levels of angiotensin-converting enzyme and 1,25-hydroxyvitamin D are nonspecific but can be clues to an underlying diagnosis of sarcoidosis. Uveitis, parotitis, and neurologic involvement are other common features. Constitutional symptoms, such as fatigue, weight loss, and night sweats, are often present.[1] Patients should be evaluated for parenchymal lung disease both with radiography and with pulmonary function tests. Evaluation for ocular involvement is indicated even if the patient is asymptomatic. Systemic corticosteroids are the mainstay of therapy, but a variety of topical, intralesional, systemic, and procedural interventions have been used with varying levels of success.[4]

Red to rust-colored plaques are a relatively common manifestation of sarcoidosis, but ichthyosiform lesions are exceedingly rare and could lead to diagnostic confusion.[2] Ichthyosiform sarcoidosis occurs more commonly in patients who are not white and favors the lower extremities.[5,6] In 1 series, 95% of patients with ichthyosiform sarcoidosis eventually developed systemic sarcoidosis.[7] In extremely rare cases, ichthyosiform sarcoidosis can present as erythroderma.[8] Most cases of ichthyosiform sarcoidosis present with swelling of the affected areas, including joints.[9] Several cases have been associated with peripheral nerve involvement, such as cranial nerve palsies[5] or numbness in the affected regions.[10] Histopathologic results of ichthyosiform sarcoidosis often shows features of both ichthyosis and sarcoidosis. Hyperkeratosis with diminishment of the granular cell layer and noncaseating granulomas are often present.[7] Sarcoidosis should be considered in the differential diagnosis of acquired ichthyosis, in addition to other possible associated diseases, such as malignant tumors (eg, Hodgkin lymphoma), connective tissue disease, infection (eg, leprosy), nutritional deficiency, and endocrine derangements.[5]

This case presented a diagnostic quandary because of the relative rarity of ichthyosiform sarcoidosis, the lack of pulmonary symptoms, and the fact that lesions were not noted in the patient's tattoos. Other granulomatous diseases that can be associated with neuropathy, such as granulomatous vasculitis or leprosy, should be ruled out before a diagnosis of sarcoidosis is made.

ARTICLE INFORMATION

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