Acquired Perforating Dermatosis Associated With Primary Biliary Cirrhosis and Hashimoto Thyroiditis

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GOAL

To understand acquired perforating dermatosis (APD) to better manage patients with the condition

OBJECTIVES

Upon completion of this activity, dermatologists and general practitioners should be able to:

1. Discuss conditions associated with APD.
2. Describe the histopathology of APD.
3. Identify treatment options for APD.

CME Test on page 462.

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Acquired perforating dermatosis (APD) is an uncommon skin eruption of unclear etiology that most often is associated with diabetes mellitus or chronic renal insufficiency. There are rare reports of APD in association with liver disease or thyroid disease. We report a case of APD in a patient with both primary biliary cirrhosis and Hashimoto thyroiditis in the absence of diabetes mellitus and chronic renal insufficiency. The patient had a partial response to narrowband UVB phototherapy.

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Case Report

A 47-year-old woman with a history of primary biliary cirrhosis and rheumatoid arthritis presented with a skin eruption of 4 years' duration. The patient stated that her skin felt pruritic overall, but the lesions had a painful quality. She could not identify any exacerbating or remitting factors. Her medications included

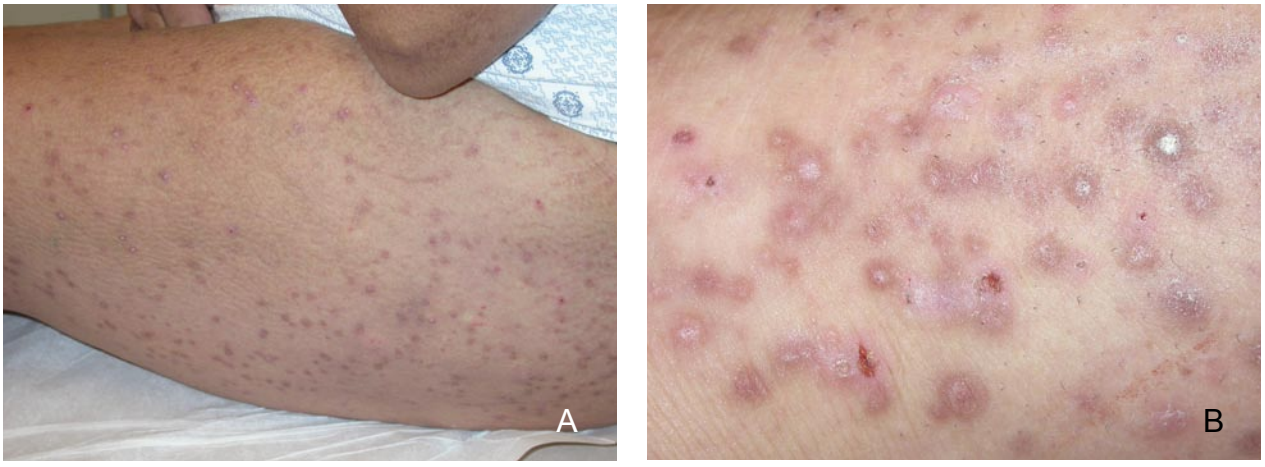

Figure 1. Crusted hyperkeratotic papules on the lateral thigh (A and B).

prednisone 5 mg daily for rheumatoid arthritis and occasional propoxyphene for pain and zolpidem tartrate for insomnia. She had no personal or family history of diabetes mellitus, renal insufficiency, or similar skin disorders.

On physical examination, the patient demonstrated mild scleral icterus. Her skin had a diffuse eruption of erythematous hyperkeratotic papules over the trunk and extremities. Several of these papules appeared excoriated and others appeared to have a central hyperkeratotic crust and hyperpigmented scarring (Figure 1).

Laboratory studies disclosed the following values: alanine aminotransferase, 122 U/L (reference range, 5−50 U/L); aspartate aminotransferase, 95 U/L (reference range, 15−50 U/L); alkaline phosphatase, 603 U/L (reference range, 35−110 U/L); total bilirubin, 6.4 mg/dL (reference range, 0.2−1.5 mg/dL); serum creatinine, 0.6 mg/dL (reference range, 0.7−1.2 mg/dL); and hemoglobin A_{1c}, 4.2% (reference range, 4.4%−5.9%). The patient had a positive antinuclear antibody titer of 1:80 (reference range, <1:40) in a homogenous staining pattern. Her viral hepatitis infection serologies and antismooth muscle antibody titers were all negative. Additionally, her antimitochondrial antibody titers were positive, 1:160 (reference range, <1:20); thyrotropin levels were increased, 10.3 mIU/L (reference range, 0.3−4.7 mIU/L); and thyroid peroxidase antibodies were elevated, 14.8 IU/mL (reference range, <2.0 IU/mL).

Results of a liver biopsy demonstrated biliary injury and loss, with bridging fibrosis, consistent with stage III primary biliary cirrhosis. Results of a skin punch biopsy were remarkable for hyperkeratosis, epidermal acanthosis, and a channel filled with neutrophils and both eosinophilic and basophilic staining debris traversing the epidermis (Figure 2). A chronic infiltrate of lymphocytes, histiocytes, and neutrophils was present at the base of the transepidermal channel. Results of a Masson trichrome stain did not demonstrate substantial amounts of collagen; results of an acid orcein stain showed some elastin fibers at the base of the transepidermal channel (Figures 3 and 4). This combination of clinical and histopathologic findings was consistent with acquired perforating dermatosis (APD).

In addition to starting thyroid hormone replacement therapy for Hashimoto thyroiditis, the patient began narrowband UVB treatments 3 times weekly for her skin condition. After several months of thyroid hormone replacement therapy and 60 narrowband UVB treatments that led to normalization of her thyrotropin levels, the patient noted no new lesions, though the resolution of her old lesions was not substantial.

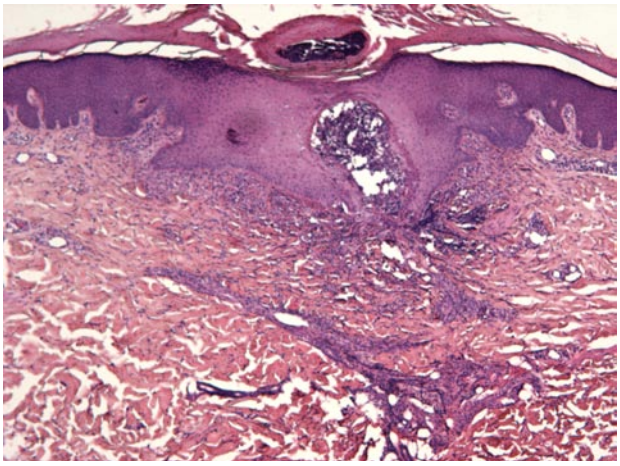

Figure 2. Epidermal acanthosis and transepidermal channel with basophilic staining debris (H&E, original magnification ×40).

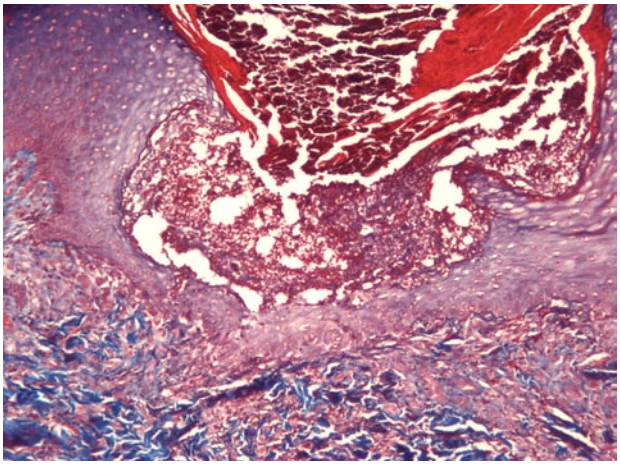

Figure 3. Collagen in thigh lesion is not substantial (Masson trichrome, original magnification ×100).

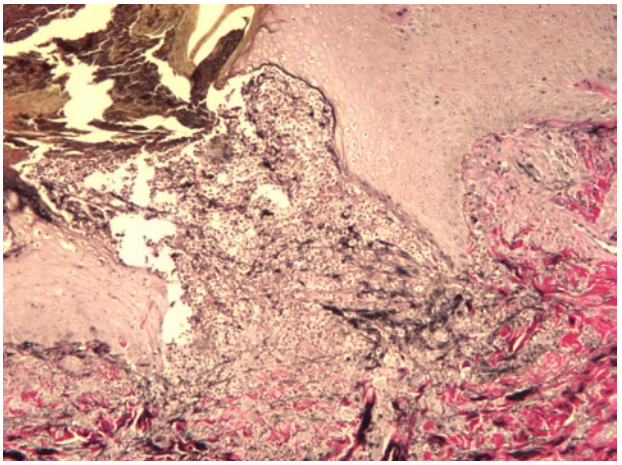

Figure 4. Transepidermal channel with numerous neutrophils and some dark staining elastin fibers (acid orcein, original magnification ×100).

Comment

APD, often thought to be synonymous with acquired reactive perforating collagenosis, is a skin condition that is usually associated with pruritus and characterized by umbilicated papules and nodules with a central adherent plug. These nodules are manifestations of transepidermal elimination of ill-defined material containing cellular debris, elastin, and collagen. The nosology of perforating dermatoses has been complicated by considerable overlap among the different entities. It generally is accepted that APD is differentiated from other primary perforating dermatoses by the presence of an underlying systemic disease. In contradistinction to the primary perforating disorders Kyrle disease, reactive perforating collagenosis, elastosis perforans serpiginosa, and perforating folliculitis, APD characteristically is associated with diabetes mellitus, chronic renal insufficiency, or both, and does not display a familial inheritance pattern.[1] Up to 11% (8/72) of patients who received hemodialysis have been reported to have APD.[2] There also have been case reports of APD in association with atopic dermatitis,[3] scabies infestation,[4,5] herpes zoster,[6-8] human immunodeficiency virus,[9] pulmonary fibrosis,[10] thyroid disease,[11] and liver disease.[12-17]

In contrast to associations between APD and diabetes mellitus or renal disease, associations between APD and liver disease are reported less frequently. Kahana et al[12] reported 2 cases of perforating folliculitis associated with primary sclerosing cholangitis. Salomon et al[13] reported a case of a 46-year-old man with alcoholic liver disease who subsequently developed a perforating dermatosis. Lee et al[14] reported a case of a 69-year-old man with hepatitis B and hepatocellular carcinoma who developed APD. Tang et al[15] reported a case of a 33-year-old man with diabetes mellitus and hepatitis B who developed APD. Faver et al[11] reported a case of a 71-year-old man with "liver dysfunction" and nephropathy and a case of a 54-year-old woman with diabetes mellitus and "chronic active hepatitis," both with APD. Skiba et al[16] reported a case of a 33-year-old woman with diabetes mellitus and sclerosing cholangitis who also developed APD. Fujimoto et al[17] reported 2 cases of APD with liver disease—one patient was a 50-year-old man with unspecified hepatitis, and the other patient was a 75-year-old man with diabetes mellitus and a hepatoma.

Reports of associations between APD and thyroid disease are even more infrequent than reports of APD and liver disease. Faver et al[11] reported 3 cases of APD associated with hypothyroidism; 2 of these patients had concomitant diabetes mellitus. Although reports of associations between APD and thyroid disease are rare, it is unclear if this is because of a true rarity of coincidence or because the thyroid status of these patients typically is not checked or reported.

The pathogenesis of APD is unknown. The prominent association of APD with the symptom of pruritus has led many authors to speculate on a connection between scratching, trauma, and APD.[3,18] Some studies have demonstrated increased expression of the 67-kD elastin receptor in lesions of perforating dermatoses; however, this expression is not uniformly elevated and the significance of this expression is not known.[17] Other studies have found elevated levels of the extracellular matrix protein fibronectin in lesions of APD, but similar to the elastin receptor findings, the significance of this observation is unknown.[19,20]

Histopathologically, lesions of APD are characterized by acanthosis and focal vacuolar alteration in the basal epidermis, with an associated underlying mixed infiltrate of lymphocytes, macrophages, neutrophils, and occasional mast cells. A transepidermal canal can be identified that often contains parakeratotic keratin, degenerated inflammatory cells, elastin, and collagen. The elastin and collagen in these lesions appear normal ultrastructurally, and results of direct immunofluorescence studies are negative.[21,22] In one study of APD associated with diabetes mellitus and renal insufficiency, needle-like crystals with some degree of calcification were identified. They were postulated to be uric acid or calcium hydroxyapatite crystals.[23]

Treatment of APD has proven to be challenging. Some clinicians report improvement of APD with topical retinoids[19,24,25]; topical, intralesional, or systemic corticosteroids[26]; oral doxycycline[27]; oral thalidomide[9]; oral allopurinol[28]; psoralen plus UVA phototherapy[29]; and broadband UVB phototherapy.[11,30] Reports of narrowband UVB phototherapy in the treatment of APD appear promising.[31,32] Ohe et al[33] reported a case series of 5 patients with APD; all patients responded to narrowband UVB phototherapy.

Conclusion

In summary, we report a case of APD associated with primary biliary cirrhosis and Hashimoto thyroiditis in the absence of diabetes mellitus or chronic renal insufficiency. To our knowledge, this is the first reported case of APD with primary biliary cirrhosis and Hashimoto thyroiditis in the English language literature.

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