Palmoplantar keratoderma as a presenting sign of primary biliary cirrhosis

Kumar S. Nadhan, BS,[a] Catherine Gupta Warner, MD,[a] Mary van den Berg-Wolf, MD,[b] Jesse M. Civan, MD,[c] Shefali Ballal, MD,[a] and Christina Lee Chung, MD[a]
Philadelphia, Pennsylvania

Key words: palmoplantar keratoderma; primary biliary cirrhosis; ursodeoxycholic acid.

Primary biliary cirrhosis (PBC) is an autoimmune disease of the liver characterized by the presence of highly specific antimitochondrial antibodies with resulting immune-mediated injury of small intrahepatic bile ducts.[1] Palmoplantar keratodermas (PPKs) are characterized by hyperkeratosis of the skin on the palms and soles.[2] Multiple cases have been reported associating PPK with autoimmune thyroiditis.[3] Herein, we report a patient with acquired PPK who was diagnosed with PBC. Treatment of her PBC led to clearance of her PPK.

CASE REPORT

A 57-year-old white woman presented with a 3-month history of thickening of the skin diffusely distributed on her palms and soles with slight erythema (Fig 1). The patient exhibited no other lesions on her body and had no constitutional symptoms. Her family's dermatologic history was positive only for eczema. A biopsy specimen was obtained and revealed hyperkeratosis, rare parakeratosis, prominent hypergranulosis, and mild spongiosis of an acanthotic epidermis. PPK was on the differential, but the diagnosis was suggested to be pityriasis rubra pilaris (PRP) and treatment was initiated with acitretin 25 mg daily. Baseline liver enzyme levels were normal; however, follow-up bloodwork revealed elevated alanine transaminase (ALT) and aspartate transaminase (AST) levels at 64 U/L (normal range, 7-56 U/L) and 50 U/L (normal range, 10-40 U/L). These markers continued to increase, and 2 months into the treatment acitretin was discontinued (ALT 88 U/L, AST 187 U/L). Hepatic ultrasound revealed parenchymal changes, and a liver biopsy specimen was obtained and revealed changes consistent with early-stage PBC with the presence of "florid duct lesions," considered pathognomonic for PBC. Initial antimitochondrial antibodies were negative. Treatment for PBC was not initiated. Her presumed PRP therapy was changed to tazarotene 0.1% cream twice daily and topical psoralen plus ultraviolet A light phototherapy twice weekly with oxsoralen 1% lotion. The presumed PRP significantly improved, though did not fully resolve, over the next year. Liver enzyme levels normalized within 6 months. After 1 year of stable disease, the patient experienced a severe flare of her skin disease. A repeat biopsy specimen was obtained and showed orthokeratotic hyperkeratosis associated with hypergranulosis and moderate, regular acanthosis (Fig 2). It was read as PPK with no signs of PRP or cutaneous T-cell lymphoma. The most common causes of PPK, including malignancy and autoimmune disease, were reviewed with the patient and ruled out. The patient started topical bexarotene 1% gel twice daily and obtained a home narrowband ultraviolet B light unit.

Subsequent elevations in alkaline phosphatase (191 U/L; normal range, 44-147), ALT (61 U/L), and AST (54 U/L) 11 months later resulted in the patient's choice to discontinue bexarotene. The patient continued the home phototherapy, 3 times a week

From the Department of Dermatology,[a] Drexel University College of Medicine, and the Departments of Internal Medicine,[b] and Gastroenterology,[c] Sidney Kimmel Medical College of Thomas Jefferson University, Philadelphia.
Funding sources: None.
Conflicts of interest: None declared.
Correspondence to: Catherine Gupta Warner, MD, Drexel University College of Medicine, Department of Dermatology, 219 N Broad St, 4th fl, Philadelphia, PA 19107. E-mail: cwarnerghsu@gmail.com.

JAAD Case Reports 2018;4:41-3.
2352-5126

http://dx.doi.org/10.1016/j.jdcr.2017.07.002

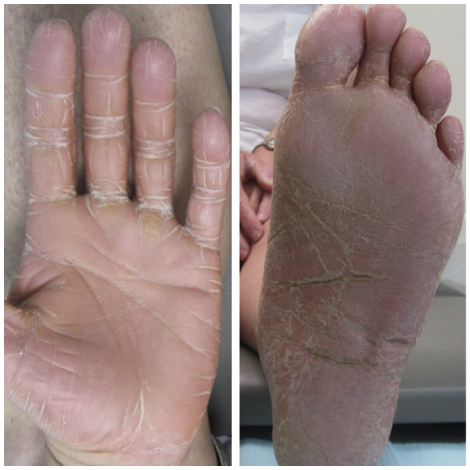

Fig 1. Palm and sole prior to treatment for primary biliary cirrhosis.

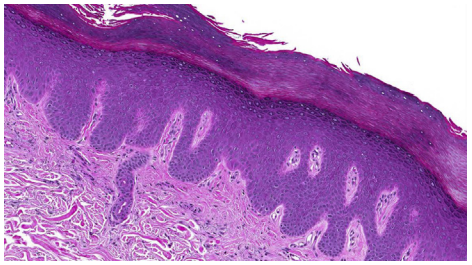

Fig 2. High-powered histologic view highlighting hyperkeratosis and acanthosis of the palm.

on her hands and feet for 5 to 8 minutes each. She also developed antimitochondrial antibodies, and therefore the diagnosis of PBC was made. On subsequent follow-up with hepatology, she was started on ursodeoxycholic acid (UDCA) for treatment of her PBC. Over the ensuing 2 months, the patient's palms and soles cleared entirely (Fig 3). She discontinued both topical treatments and phototherapy. She continues to be clear on UDCA 2 years after starting PBC treatment.

DISCUSSION

PPK may be subdivided into hereditary keratodermas and acquired forms with conditions in which PPK is an associated feature of a specific dermatosis.[1] Primary biliary cirrhosis is an autoimmune disease of the liver that affects small bile ducts.[2] Multiple cases have been reported associating acquired PPK and hypothyroidism.[3] There have also been reported associations with lupus erythematosus, myasthenia gravis, syphilis, and tuberculosis.[4-6] In these cases, the PPK cleared with treatment of the underlying ailment, suggesting a reactive pathophysiology similar to that seen in reactive arthritis and keratoderma blennorrhagicum.[1]

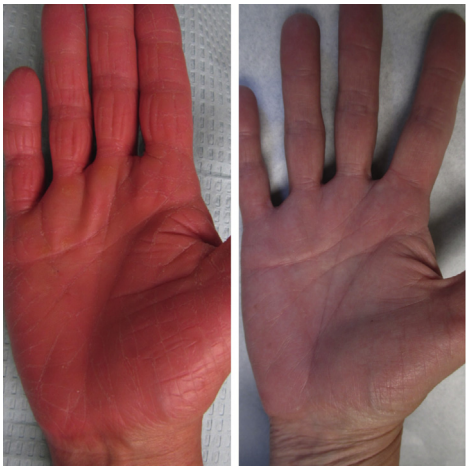

Fig 3. Partial response (left) while on treatment prior to diagnosis of primary biliary cirrhosis and resolution (right) postdiagnosis after initiation of ursodeoxycholic acid.

Genetic and environmental factors and the loss of immune tolerance all play roles in the development of PBC; however, PBC treatment is primarily aimed at stabilizing the bile ducts rather than reducing systemic inflammation. UDCA expands the bile acid pool by exerting direct choleretic, antiinflammatory, and antiapoptotic effects on hepatic epithelia.[2] Years of skin-directed therapies resulted in only moderate improvement while monotherapy with UDCA, once initiated for the underlying PBC, afforded complete and durable clearance of her PPK. In addition, UDCA decreases levels of bilirubin, AST/ALT, and alkaline phosphatase by expanding the bile acid pool and additional direct actions on bile ducts. Several similar cutaneous processes, like palmoplantar pustulosis, have been shown to arise with a background of PBC and abate with its treatment.[7-9] The presence of PBC should raise the index of suspicion for cutaneous disease processes.

In conclusion, to our knowledge, this report is the first to describe PPK developing in relation to PBC and resolving upon treatment with UDCA. Given the well-documented association of PPK with other inflammatory conditions, concern for this reactive entity should be considered in a patient with otherwise unexplained PPK.

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