Disseminated Reticulate Hypomelanosis Developing during Primary Biliary Cirrhosis

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Key Words
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Abstract
We report on a 50-year-old woman with disseminated reticulate hypomelanosis developing on the limbs and abdomen during primary biliary cirrhosis (PBC). Histopathological examination showed vacuolar basal cells, dyskeratosis and large multinucleated epidermal cells. Diagnosis of lichen sclerosus et atrophicus and autoimmune disease are discussed. The similarity between cutaneous changes in PBC and a graft-versus-host reaction is outlined.

Hyperkeratosis, numerous necrotic keratinocytes and bizarre large multinucleated epidermal cells were seen in the upper epidermis. Vacuolized basal cells were also present together with a subepidermal cleft. Only

Pigmentary changes are commonly observed during primary biliary cirrhosis (PBC). Hyperpigmentation, either diffuse or circumscribed, generally occurs, but depigmentation is quite uncommon [1]. We report the case of a patient with reticulate hypomelanosis during PBC.

Case Report
A 50-year-old woman was referred for a severe pruritic eruption which had started 4 weeks before.

PBC had been diagnosed 1 year earlier on the basis of elevated excretory liver enzymes (threelfold of normal), with normal cytolytic enzymes, positive antimitochondrial antibodies at a titer of 400 using the M2-ELISA technique and histological septal fibrosis with lymphocytic infiltration of periportal areas. Therapy with cholestyramine (12 g/day) and ursodeoxycholic acid (0.5 g/day) was initiated, without significant improvement of jaundice, and a progressive cutaneous hyperpigmentation developed.

On examination, diffuse erythema and leukodermic spots were also present in association with pigmentary changes. Leukome-lanoderma was prominent on the limbs and the abdomen (fig. 1). At this time, laboratory studies revealed γ-GT 592 U/l (normal < 85), ALT 122 U/l (normal < 37), SGOT 197 U/l (normal < 65), alkaline phosphatase 968 U/l (normal < 280).

Fig. 1. Achromic reticulate lesions on the forearm.
Immunoserological investigations showed antinuclear antibodies with a nucleolar pattern (titer 1:64). Other autoantibodies were undetectable. Hepatitis serology was negative, but IgM anticytomegalovirus antibody was positive with a low titer. Two successive skin biopsies were performed on nonadjacent

**Fig. 2.** Skin biopsy specimen taken from an achromic papule revealed focal epidermal alteration with large clear cells and dyskeratotic cells leading to a suprabasal cleft. Neither a dermal inflammatory infiltrate nor colloid body are found. HE. ×28.

rarely were lymphocytes present in either the dermal perivascular areas or the epidermis. Histological epidermal changes were restricted to the achromic spots. In the surrounding skin, only significant amounts of dermal free melanin or melanophages and rare necrotic keratinocytes were seen (fig. 2).

Neither cytomegalovirus DNA nor pap-illomavirus group-specific antigens were detected on biopsy specimens using monoclonal antibodies and immunoperoxidase staining. No noticeable improvement in pruritus was obtained following 2 months of phototherapy. Due to the increase in liver excretory enzymes, the specified treatment was enhanced with rifampin (0.9 g/day) and urso-deoxycholic acid (1.5 g/day). After 1 month, the patient did not complain of any pruritus; however, the pigmentary changes persisted. A new skin biopsy showed only noticeable incontinence of pigment. Simultaneous evaluation of hepatic cytolytic tests disclosed lower titers with AST 46 U/l and ALT 86 U/l, but γ-GT remained unmodified at 548 U/l.

**Discussion**

We report a case of erythematous and leukomelanodermic eruption with histological epidermal alteration without noticeable lymphoid infiltrate developing during PBC. Skin pigmentation during PBC is commonly due to the presence of excess melanin located mainly throughout the epidermis and frequently dermal pigment incontinence but without degeneration of basal keratinocytes [2]. Typical lichen planus located on both skin and mucous membranes may also occur during PBC [3], Stuccokeratosis, verruca plana, disseminated
hypopigmented kerato-sis and Darier-White disease may present clinically as disseminated, hypopigmented, slightly keratotic macules and papules. All these conditions could be fortuitously associated with PBC, but most of these hypotheses could be discarded after histological examination. An association between lichen sclerosus et atrophicus and PBC was previously suggested on the basis of a few, poorly documented cases [4, 5]. Both lichen sclerosus et atrophicus and our case shared similar histological changes with vacuolar alteration at the dermoepidermal junction leading to cleft formation and melanophages in the papillary dermis. Other histological features of lichen sclerosus et atrophicus were here lacking including thickening of the papillary dermis by either sclerosis or edema, altered elastic fibers and an underlying inflammatory infiltrate. In our case additional histopathological features included abnormal maturation of keratinocytes leading to both dyskeratotic cells and large atypical keratinocytes, some of them multinucleated. In 2 previous cases [6, 7], a similar histological pattern with marked hydropic degeneration of the basal cell layer and a rare lymphocytic infiltrate were observed during PBC. The clinical picture was quite different with annular papular eruption, and these cases have been linked to autoimmune disease. Lastly, reticulated pigmented disorder or leukomelanoderma were associated with graft-versus-host disease. The similarities between PBC and the latter have also been outlined [8]. The pathogenesis of epidermal damage occurring during both diseases remains unclear. A viral infection might explain the histological changes. An immuno-logical disturbance linked to either PBC or graft-versus-host disease may trigger an activation of a latent virus or favor an opportunistic viral infection. However, in our case, as in autologous graft-versus-host reaction [9], evidence of viral infection is lacking.

The description of a dermatosis resembling a graft-versus-host reaction developing during PBC might constitute a further clinical argument for a similarity between both diseases.

References


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