Our Dermatology Online

Case Letter

Diltiazem-associated, photo-distributed hyperpigmentation in a patient with Sjögren's syndrome

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Sir,

Herein, we report a case of hyperpigmented macules on ultraviolet exposed areas during the intake of diltiazem hydrochloride (DTH) in a patient with Sjögren's syndrome.

A 63-year-old Japanese female with a history of Sjögren's syndrome and vasospastic angina presented to our hospital with brown, irregular macules on the neck, face, and both hands, which she first noticed one year earlier. The patient had a history of taking DTH for vasospastic angina for the previous fifteen years. A physical examination revealed pale brown macules and plaques irregularly scattered around the corners of the mouth, lower lip, and neck (Figs. 1a and 1b). In addition, there were numerous erythematous papules on the dorsal side of both hands. The oral mucosal membrane, scalp, and nails were not involved. A biopsy specimen taken from the dorsal side of a hand revealed individual cell keratinization in the epidermis, intercellular edema, liquefaction degeneration of the basal layer, and band-like lymphocyte infiltrate with melanophages in the superficial dermis (Fig. 2a). Immunohistochemistry revealed the infiltration of CD3+, CD4+, CD8+, and HLA-DR+ lymphocytes in the superficial dermis (Figs. 2b and 2c). Routine laboratory examinations of the blood cell count, serum, and urine showed no abnormalities. Other tests showed positive antinuclear antibody (1:80, nucleolar) and anti-SS-A antibody (240 U/mL; normal: < 9.9), whereas hepatitis C virus antibody, rheumatoid factor, anti-CCP antibody, and anti-SS-B antibody were negative. DTH was switched to another medicine, and ascorbic acid, calcium pantothenate, and topical steroids were initiated. In addition, we advised the patient to avoid sun exposure. Although no improvement was observed in the rash in the first four months, it disappeared at follow-up several years later (Figs. 3a and 3b).

Diltiazem-associated, photo-distributed hyperpigmentation is an uncommon, drug-induced lichenoid eruption. The clinical feature is slate-gray, reticulated hyperpigmentation on sun-exposed areas, and the histopathologic feature is lichenoid dermatitis with prominent pigmentary incontinence [1]. There have been nineteen reported cases, including our case, of diltiazem-associated, photo-distributed hyperpigmentation in the past. The period between the initiation of the drug and the onset has ranged from 1.5 months to 12.5 years; thus, many of the cases developed cutaneous lesions after taking the drug for a long time. The distribution of the skin rash was on the face in all cases, on the neck in thirteen cases, on the forearms in five cases, on the chest in three cases, and on the hands in two cases. Among these cases, eleven were black, three were Hispanic, four were Asian, and one was white [1-3]. In addition, only four cases were Japanese, suggesting the racial differences and the rarity of Japanese cases. Oiso et al. suggested that diltiazem-associated, photo-distributed hyperpigmentation is caused by impaired melanogenesis and aberrant transfer of immature melanosomes from melanocytes to keratinocytes [2]. In the present case, the patient had been taking

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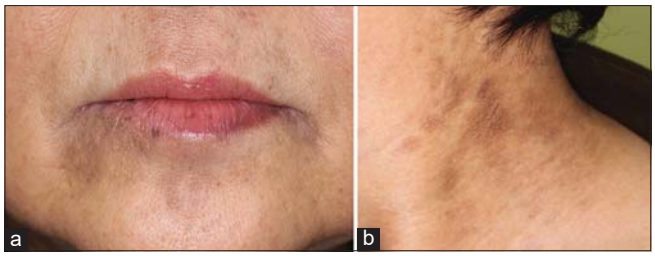

Figure 1: (a) Pale brown spots irregularly scattered on the corners of the mouth and lower lip, (b) as well as the neck.

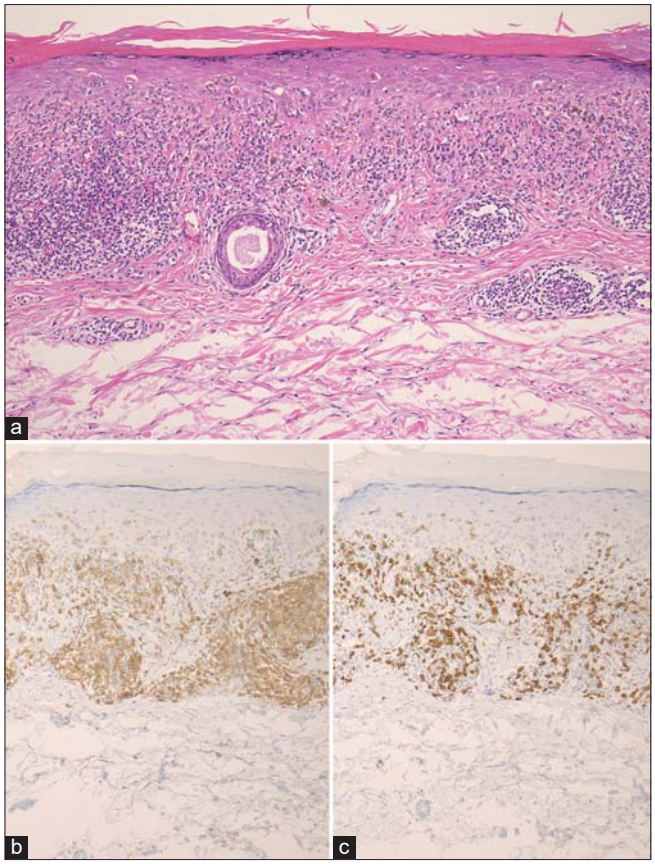

Figure 2: (a) Findings from the skin biopsy were band-like lymphocyte infiltrate with melanophages in the superficial dermis. (H&E, 100×). Immunohistochemistry revealing the infiltration of (b) CD4+ and (c) CD8+ lymphocytes in the superficial dermis.

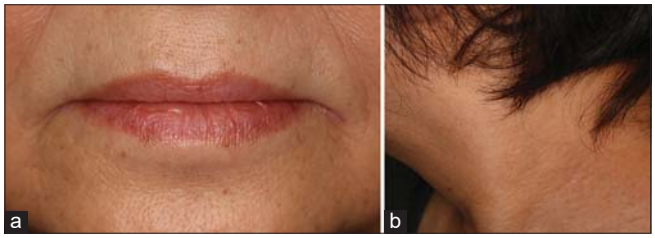

Figure 3: (a and b) The patient's eruption disappeared at follow-up.

DTH for fifteen years until the appearance of the rash, which disappeared after DTH was stopped and replaced by another medication. Unfortunately, neither patch/photopatch tests nor provocation tests were performed.

It is important to differentiate diltiazem-associated, photo-distributed hyperpigmentation from actinic lichen planus (ALP). ALP affects sun-exposed areas of the skin, and the histopathological examination reveals typical features of LP [4]. The clinical and histological findings of ALP and diltiazem-associated, photo-distributed hyperpigmentation are difficult to differentiate because of their similarities. We initially considered ALP, yet finally the diagnosis of diltiazem-associated, photo-distributed hyperpigmentation was reached due to the history of oral administration of DTH. To date, there have been no reports of Sjögren's syndrome associated with DTH-related diseases. However, Sjögren's syndrome is frequently associated with drug allergies [5], which may have contributed to the development of the skin rash in our case.

Consent

The examination of the patient was conducted according to the principles of the Declaration of Helsinki.

The authors certify that they have obtained all appropriate patient consent forms, in which the patients gave their consent for images and other clinical information to be included in the journal. The patients understand that their names and initials will not be published and due effort will be made to conceal their identity, but that anonymity cannot be guaranteed.

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