Psoriasiform Drug Eruption Induced by Anti-tuberculosis Medication: Potential Role of Plasmacytoid Dendritic Cells

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Psoriasiform drug eruptions can be induced by several drugs (1). Psoriasis is a chronic inflammatory disease characterized by T-cell-mediated cytokine production that drives the hyperproliferation and abnormal differentiation of keratinocytes (2). Drugs can cause new lesions when there is no history or family history of psoriasis. Based on the psoriatic drug eruption probability score, β-blockers, synthetic anti-malaria drugs, non-steroidal anti-inflammatory drugs (NSAIDs), lithium, digoxin, and tetracycline antibiotics are relevant in psoriasis (1, 3–5).

Common cutaneous adverse effects of anti-tuberculosis medication include morbilliform rash, urticaria, lichenoid drug eruption, exfoliative dermatitis, hyperpigmentation, erythema multiforme-type drug eruption and Stevens-Johnson syndrome (6–8).

We report here the first case of a psoriasiform drug eruption in a man taking anti-tuberculosis medication.

CASE REPORT

In April 2009, a 76-year-old Korean man presented with pruritic erythematous papulosquamous eruption that had been present on his trunk and extremities for 1 month. His medical history included hypertension detected 5 years earlier, that had been treated with oral medication (doxazosin mesylate), which had not been changed recently. Four months earlier, in December 2008, he was diagnosed with pulmonary tuberculosis, and started anti-tuberculosis therapy with isoniazid, ethambutol, rifampicin, and pyridoxine. Three months after initiating anti-tuberculosis therapy, the pruritic scaly skin lesions developed. Prostatic carcinoma was detected one month earlier, and treated with bicalutamide and tamsulosin hydrochloride, which were started one week after the skin eruption began. The skin lesions spread from his arms to the trunk and lower extremities. On physical examination, erythematous papulosquamous lesions were found, scattered on his trunk, arms, hands, legs, and buttocks (Fig. 1). Other than an elevated eosinophil count (731/mm^3, normal range 0–483/mm^3; 10.6%, normal range 0–7%) and IgE level (361 IU/ml, normal range 0–100 IU/ml), the laboratory findings were within normal limits, including a complete blood cell count, liver and renal function tests, and urinalysis. Syphilis Venereal Disease Research Laboratory (VDRL) and *Treponema pallidum* haemaglutination (TPHA) tests were negative.

Histologically, a skin biopsy specimen showed psoriasiform epidermal hyperplasia with hyperkeratosis, confluent parakeratosis, and Munro's microabscesses in the horny layer and an absent granular layer. There was slight capillary proliferation in the tips of the dermal papillae, and a perivascular lymphocytic infiltrate with a few eosinophils in the upper dermis (Fig. 2 a, b).

After immunohistochemical staining with CD123 (Dendritics, Dardilly, France), a plasmacytoid dendritic cell (PDC) marker, laser scanning confocal microscopy (LSM510; Carl Zeiss, Jena, Germany) with LSM5 browser image software, using Alexa Fluor 488-conjugated fluorescence, visualized some scattered CD123-positive cells in the perivascular area in the upper dermis (Fig. 2c). We diagnosed a psoriasiform drug eruption, clinically and pathologically, and treated him with topical steroids and oral anti-histamines. The skin lesions progressed, so he stopped his anti-tuberculosis medication, but continued the bicalutamide and tamsulosin. The skin eruptions began to improve within a few days after discontinuing the anti-tuberculosis medication, and cleared with post-inflammatory hyperpigmentation. There has been no relapse in the 6 months since withdrawing the tuberculosis medication.

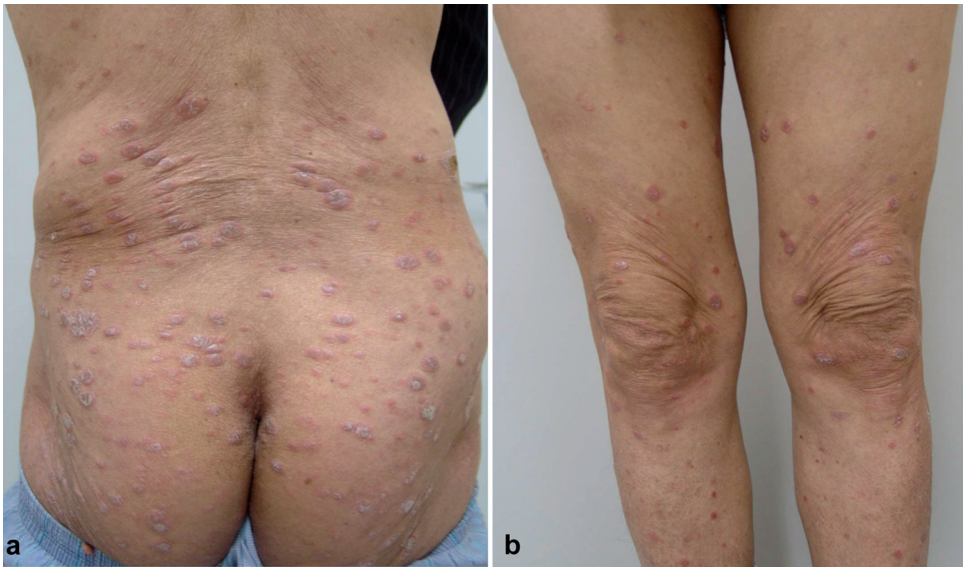

Fig. 1. Widespread erythematous papulosquamous lesions on (a) the trunk and buttocks, and (b) both legs.

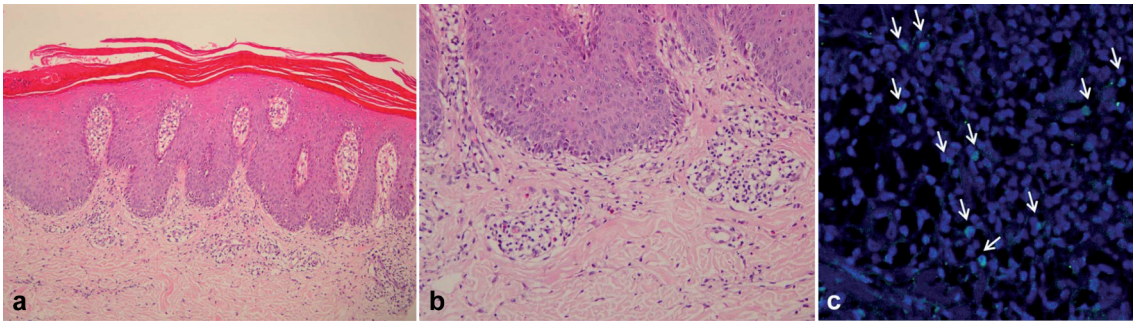

Fig. 2. (a) Histologically, the skin biopsy specimen shows psoriasiform epidermal hyperplasia with hyperkeratosis, confluent parakeratosis, Munro's microabscesses in the horny layer, and an absent granular layer (haematoxylin and eosin (H&E) ×100). (b) There are some capillary proliferations at the tips of the dermal papillae, and a perivascular lymphocytic infiltrate with a few eosinophils in the upper dermis (H&E ×200). (c) Laser scanning confocal microscopy using Alexa Fluor 488-conjugated fluorescence visualized some scattered CD123-stained cells (*white arrows*) in the perivascular area in the upper dermis against DAPI nuclear staining, blue; a merge of (DAPI) and (CD-123 stained pictures), (×400).

DISCUSSION

The histopathological features of a psoriasiform drug eruption are very similar to those of psoriasis; however, perivascular or interstitial eosinophils in the upper dermis are more frequent in psoriasiform drug eruption than in psoriasis (1). A lichenoid drug eruption, commonly associated with anti-tuberculosis medication, needs to be differentiated from the psoriasiform eruption. Our patient lacked the characteristic histological signs of lichenoid reaction patterns, such as necrotic keratinocytes and vacuolar alteration in the basal cell layer, with band-like, perivascular infiltration of eosinophils and lymphocytes in the papillary dermis (1, 9). Additionally, scattered papulosquamous lesions with thick, large, dry silvery scales were located on the trunk and extremities, similar to psoriasis vulgaris, rather than the lichenified diffuse violaceous patches on the trunk and flexural areas that are characteristic of a lichenoid drug eruption (1).

The underlying pathomechanism of drug-induced psoriasiform eruptions remains uncertain, although several immunological interactions have been hypothesized (2–4, 10). After injecting recombinant interferon (IFN)-α, psoriasis worsens, and the application of imiquimod cream can aggravate psoriasis (11). PDCs with increased IFN-α expression infiltrate the dermis of psoriatic skin. Therefore, PDC-derived INF-α expression is a probable cause of psoriasiform drug eruption. In our patient, immunohistochemical staining with CD123, a PDC marker, showed positive cells in the perivascular infiltrate in the upper dermis. Additionally, the pathomechanism of lichenoid tissue reaction is related to activated PDC-induced INF-α, which mediates the activation of INF-γ and CXCR3 ligands (12). This process leads to the accumulation of cytotoxic TH1 cells and PDCs in the lesion, and the lichenoid tissue reaction is positive for CD123 stain (13). Therefore, psoriasiform and lichenoid drug eruptions might share a common inflammatory pathway, such as the actions of PDC-derived IFN-α. From these relationships, we suggest that anti-tuberculosis medication can induce not only lichenoid drug eruption, but also psoriasiform drug eruption, via PDCs.

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