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Eosinophilic Pustular Folliculitis Induced by Allopurinol and Timepidium Bromide

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Sir,
We describe a woman with numerous papules and pustules on her face and upper trunk induced by allopurinol and timepidium bromide. The histopathology showed the destruction of hair follicles and the infiltration of eosinophils, which we diagnosed as eosinophilic pustular folliculitis.

CASE REPORT

A 57-year-old Japanese woman was treated with oral allopurinol and timepidium bromide for ureterolith since April 1998. One month later, she presented with an eruption on her face, followed by numerous rice-sized papules and pustules on her face and upper trunk, a fever and bilateral cervical lymphoadenopathy were also present (Fig. 1). The woman visited our hospital for examination in June 1998. Laboratory studies revealed eosinophilia (white blood cell, 7,400/mm^3; eosinophile, 25%, 1,850/mm^3), mild liver dysfunction (glutamic oxaloacetic transaminase, 36 IU/ml; glutamic pyruvic transaminase, 65 IU/ml; gamma-glutamyl-transpeptidase, 159 IU/ml; alkaline phosphatase, 436 IU/ml) and a strong inflammatory reaction (C-reactive protein, 8.3 mg/dl). No elevations were found in her serum viral titers (human herpes simplex virus, Epstein-Barr virus

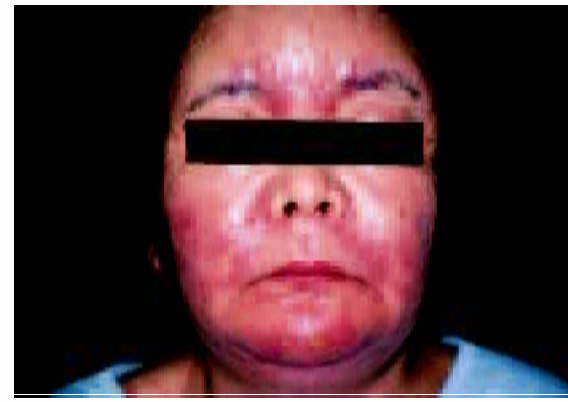

Fig. 1. Clinical findings at first examination: numerous papules and pustules on the patient's face.

and cytomegalovirus), and bacterial cultures from the pustules on her face and tonsils were negative.

Since we suspected a drug complication, allopurinol and timepidium bromide were discontinued, and oral prednisolone (30 mg) was administered for 3 days. Despite the treatment, the skin lesions disseminated, and numerous papules were seen merging on the erythema. The patient's liver function continued to worsen and it was decided to treat her using steroid semi-pulse therapy (methylprednisolone sodium succinate, 500 mg over 3 days, i.v.). After this treatment, the patient's condition improved. The pustules and erythema began to disappear from the center, causing an annular erythema with scales. Skin biopsy specimens from her face showed the dense infiltration of numerous eosinophils to the hair follicles. No mucin deposits around the hair follicles were observed, but severe infiltrations consisting of eosinophils, lymphocytes and plasma cells were seen around the capillaries in the middle dermis (Fig. 2). These histopathological findings led us to suspect that the patient was suffering from drug-induced eosinophilic pustular folliculitis. Six months later, after obtaining negative results for a patch test, scratch test and lymphocyte-stimulating test using allopurinol and timepidium bromide, we performed an oral provocation test, starting with 1/10 of the therapeutic dose of each drug and increasing to 1/5 of the dose, half the dose and a single dose, or until skin eruptions appeared. After taking half the therapeutic dose of allopurinol, numerous follicular papules appeared on her face, chest and arm. The patient also developed eosinophilia (eosinophils increased from 540/mm^3 to 1260/mm^3), but there were no other symptoms. The addition of a single therapeutic dose of timepidium bromide produced half rice-sized follicular papules on her leg in addition to eosinophilia (eosinophils increased from 540/mm^3 to 912/mm^3), but no other symptoms. We therefore diagnosed her disease as eosinophilic pustular folliculitis induced by a combination of allopurinol and timepidium bromide.

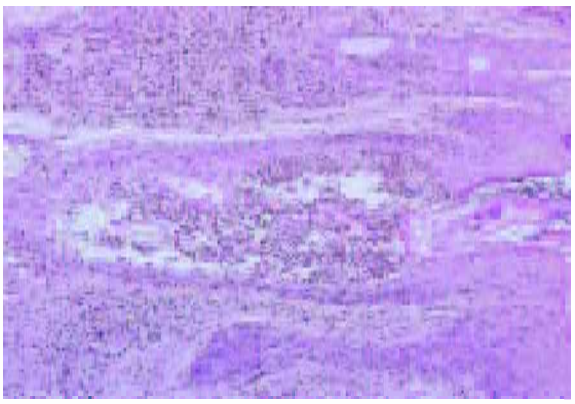

Fig. 2. Skin biopsy specimen; Hair follicles were infiltrated by numerous eosinophils.

DISCUSSION

Allopurinol has been shown to diminish serum uric acid levels by interfering with the conversion of hypoxanthine to xanthine and of xanthine to uric acid (1). Allopurinol is known to cause severe drug-induced eruptions, erythroderma and Stevens-Johnson's syndrome along with eosinophilia, liver and renal malfunctions. Allergy induced by allopurinol is known as the "allopurinol hypersensitivity syndrome" (2). Allopurinol has also been shown to interact with ampicillin and warfarin (3). Drug eruptions induced by allopurinol tend to persist for a long period and can be exacerbated even after the discontinuation of the drug (4). Oral timepidium bromide, an antispastic and lenitive drug with an anticholinergic action, is used for the treatment of gastric ulcers, cholecystitis and ureteroliths. The differential diagnoses of our case included infectious folliculitis, acute generalized pustular bacterid, miliaria crystallina with pustules, psoriasis pustulosa, eosinophilic pustular folliculitis, acneiform drug eruption and drug-induced acute generalized exanthematous pustulosis. The clinical features of our case are essentially similar to those of acute generalized exanthematous pustulosis, but the histopathological features are different. Acute generalized exanthematous pustulosis is characterized by subcorneal pustules with numerous neutrophil infiltrations (5). A case of eosinophilic pustular folliculitis induced by a patch test with indeloxazine hydrochloride has been reported (6). Mizoguchi et al. reported a case of acute generalized exanthematous pustulosis with eosinophilic pustular folliculitis induced by carbamazipine (7).

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