Toxic Pustuloderma Induced by Ofloxacin

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A patient with drug-induced toxic pustuloderma is presented. The patient, who was asthmatic and who was being treated with ofloxacin for bronchitis and pharyngitis, developed intense erythemas followed by subcorneal pustulation associated with fever and a neutrophil leukocytosis. The diagnosis was confirmed by oral readministration of ofloxacin, with the result that pustular eruptions were induced. This form of drug eruption had not previously been attributed to ofloxacin. Key words: Neutrophilic dermatoses; Sterile pustulosis; Subcorneal pustule; Spongiform pustule; Drug reaction.

(Accepted May 3, 1993.)


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Generalized pustulosis as a form of drug eruption is a rare entity. Toxic pustuloderma (TP) (1), first reported as a variant of severe drug-induced toxic erythema, is characterized by a generalized erythema with sterile subcorneal pustulation, fever and a peripheral blood leukocytosis. The clinical symptoms of acute generalized exanthematous pustulosis (AGEP) (2), initially reported in the French literature (3), seem to be identical with those in TP. Drugs and acute viral infections not related to psoriasis are considered possible etiologic factors in TP/AGEP (2, 4). In recent years, the reported cases of TP/AGEP following drug ingestion have been on the increase (2, 5-19).

The new fluoroquinolone antibiotic ofloxacin has gained widespread use. Although much information has accumulated about the possible adverse effects of quinolones (20, 21), pustular dermatoses are uncommon (12). In particular, no established case of subcorneal pustular eruption by ofloxacin has been reported. We here report a typical case with TP/AGEP caused by ofloxacin, which was confirmed by a readministration test.

CASE REPORT

A 64-year-old Japanese female, with no personal or family history of psoriasis, had received theophylline and ketotifen for bronchial asthma with no adverse reactions. The patient was admitted because of asthma attacks and pharyngitis. She was treated with ofloxacin 300 mg daily for a week. Simultaneously, aminophylline, 125 mg/day, bromhexine HCl, 4 mg/day, and hydrocortisone, 100 mg/day, were intravenously administered for a week. On the 5th day after administration of ofloxacin, superficial pinhead-sized pustules within areas of a widespread erythema (Fig. 1) appeared over the entire body with high fever (38.8°C). Some pustules had a tendency to coalesce.

Laboratory examination showed marked leukocytosis (18500 WBC/mm³) with 86% of neutrophils. Although a mild serum hypoalbuminemia was present, serum calcium values were within normal limits. Additional routine examinations, including liver and kidney functions, were normal. Staphylococcus epidermidis was cultured from the contents of pustules. Serologic tests for streptococcal antibodies, hepati-

![Fig. 1. Pustular eruption on the thigh.](image-url)
DISCUSSION

A generalized sterile pustular reaction can be observed in association with a variety of dermatoses, such as generalized pustular psoriasis (including acrodermatitis continua and impetigo herpetiformis), subcorneal pustular dermatosis, pustular bacterid, pustular necroizing angiitis, Sweet's syndrome, erythema multiforme, and halogen exposure (15). Pustular psoriasis and subcorneal pustular dermatosis have both been reported to be triggered by drugs (22, 23). In the present case, there was no personal or family history of psoriasis; nor were there any clinical features supportive of pustular psoriasis or subcorneal pustular dermatosis. Among these pustular dermatoses, we concluded that our patient’s eruption was TP/AGEP. The difficulty in diagnosing the patient’s condition was also rapidly solved once she was challenged by ofloxacin.

TP/AGEP has been described as a clinical entity and is characterized by the sudden onset of intense erythemas followed by sterile pustulation (2, 15). According to the clinical analysis in the 12 cases with previous drug reaction, the time between the beginning of drug administration and the occurrence of skin symptoms varied from a few hours to 10 days (2). Skin biopsy shows subcorneal and spongiform pustules containing predominantly neutrophils, and sometimes associates with a leukocytoclastic vasculitis with perivascular deposits of C3 and immunoglobulins in upper dermis. The lesions often resolve after several weeks without any systemic treatment. The etiology of TP/AGEP remains unknown. Enteroviruses, such as echovirus 11, 30 and coxsackievirus A9, are known as the triggering agents of pustular dermatoses (2, 4). Food poisoning (15), hypersensitivity to mercury (2), and PUVA-therapy (24) are also believed to play a role in initiating the disease. Most frequently TP/AGEP is induced by drugs, in particular β-lactam antibiotics, macrolides, other antibiotics and other drugs (2). The new quinolone antibiotic norfloxacin has caused a subcorneal pustular eruption (12). Pustular reactions have not been documented to ofloxacin, although hypersensitivity leukocytoclastic vasculitis has been reported (20, 21).

We conclude that our patient presents an adverse drug reaction to ofloxacin in the form of a generalized pustular eruption. The entity of this clinical picture is recognized as TP/AGEP, a severe form of toxic erythema. However, the evaluation of diagnostic criteria needs to be tested further, mainly in terms of specificity for differentiating TP/AGEP from pustular psoriasis (2). In addition, the precise mechanism inducing pustular eruption seems to be a matter of importance and needs further clarification.

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