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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.***

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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 pharingitis. 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/mm^3) 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, hepatitis-associated antigens and antibodies, and enteroviruses (echovirus 11, echovirus 30, coxackievirus A9) were negative. The patient expressed the HLA-phenotypes A11, A33, B52, B62, Cw4, DR2 and DR4.

A skin biopsy specimen obtained from a pustule on the thigh disclosed subcorneal pustules filled with polymorphonuclear neutrophils and spongiform pustules of Kogoj (Fig. 2). Lymphocytic perivascular infiltrate was predominantly observed in the mid- and papillary dermis. There was no evidence of vasculitis or vascular deposition of IgM and IgG.

All the drugs administered so far were stopped. The patient was treated with intravenous administration of prednisolone, and the pustular eruptions gradually subsided over 10 days, leaving large scales.

The identical syndrome of mild fever, chills, and erythematous macules with a lot of pustules appeared on her lower extremities within 12 h after oral administration of ofloxacin, 1 mg. All other drugs, such as aminophylline, bromhexine HCl and hydrocortisone, failed to induce such eruptions. The histopathological examination of a pustule induced by ofloxacin revealed the same subcorneal and spongiform pustules (Fig. 3) as seen in the original eruptions. Patch tests and lymphocyte stimulation tests with all the drugs administered were negative.

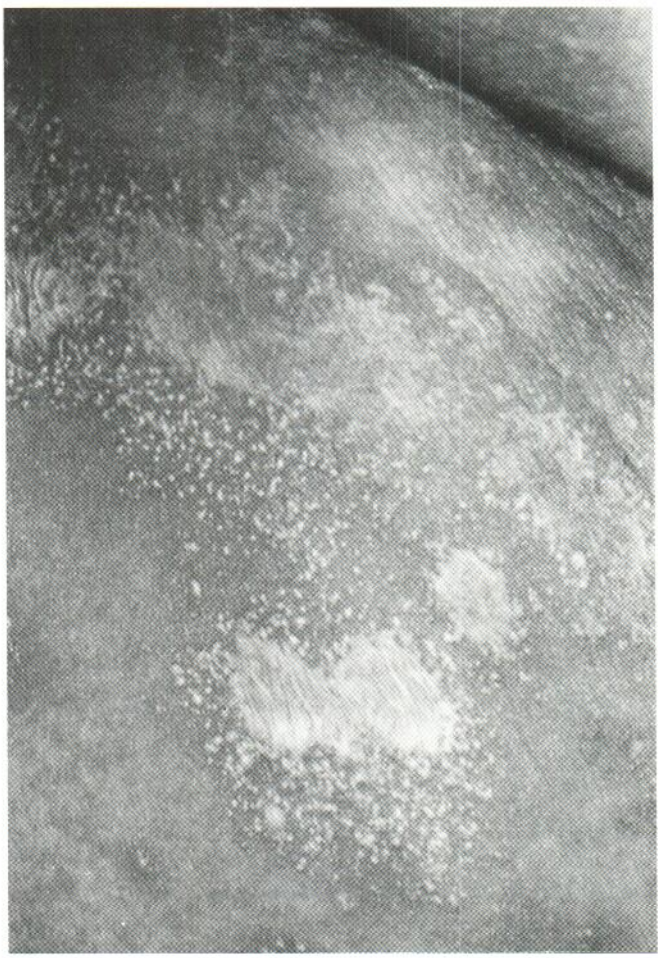

Fig. 1. Pustular eruption on the thigh.

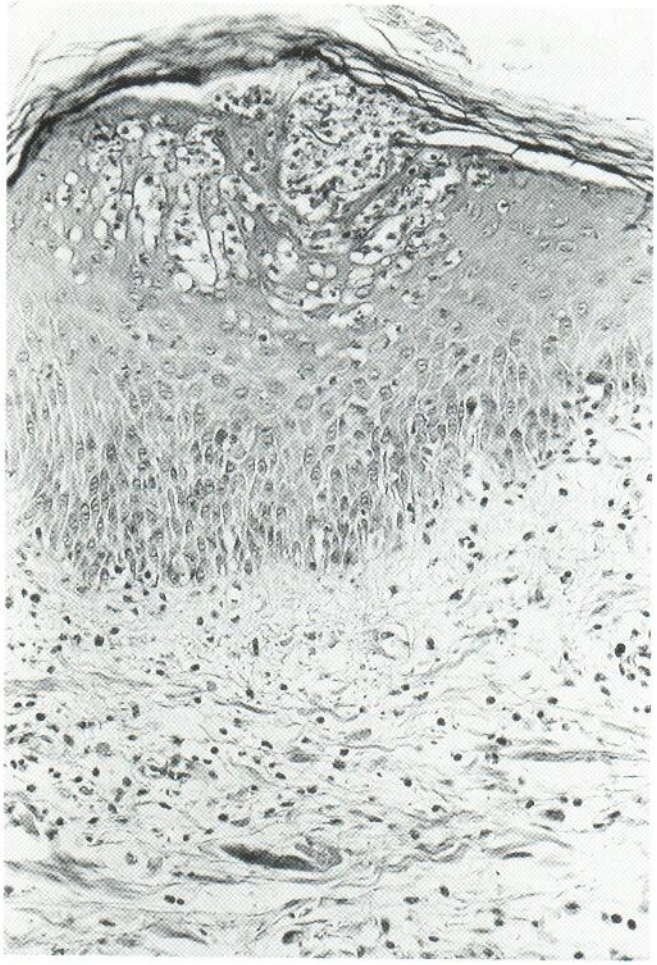

Fig. 2. Photomicrograph showing subcorneal pustule and spongiform pustules of Kogoj. A predominantly lymphocytic perivascular infiltrate was observed in the papillary dermis. (H & E ×100.)

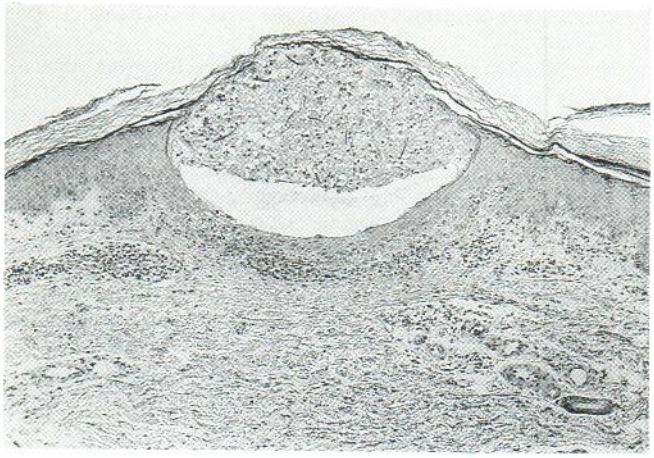

Fig. 3. Photomicrograph showing ofloxacin-induced subcorneal pustule. (H & E ×50.)

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 necrotizing angitis, 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/AEGP 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.

REFERENCES

1. Staughton RCD, Rowland Payne CME, Harper JI, McMichen H. Toxic pustuloderma – a new entity? J R Soc Med 1984; 77 (suppl 4): 6–8.
2. Roujeau J-C, Bioulac-Sage P, Bourseau C, et al. Acute generalized exanthematous pustulosis. Analysis of 63 cases. Arch Dermatol 1991; 127: 1333–1338.
3. Beylot C Bioulac P, Doutre MS. Pustulosis exanthématiques aïgues généralisées: à propose de 4 cas. Ann Dermatol Venereol 1980; 107: 37–48.
4. Rouchouse B, Bonnefoy M, Pallot B, Jacquelin L, Dimoux-Dime G, Claudy AL. Acute generalized exanthematous pustular dermatitis and viral infection. Dermatologica 1986; 173: 180–184.
5. Yamasaki R, Yamasaki M, Kawasaki Y, Nagasako R, General-

ized pustular dermatosis caused by isoniazid. Br J Dermatol 1985; 112: 504–506.
6. Kalb RE, Grossman ME. Pustular eruption following administration of cephradine. Cutis 1986; 38: 58–60.
7. MacDonald KJS, Green CM, Kenicer KJA. Pustular dermatosis induced by co-trimoxazole. Br Med J 1986; 293: 1279–1280.
8. Stough D, Guin JD, Baker GF, Haynie L. Pustular eruptions following administration of cefazolin: a possible interaction with methyldopa. J Am Acad Dermatol 1987; 16: 1051–1052.
9. Fayol J, Bernard P, Bonnetblanc JM. Pustular eruption following administration of cefazolin: a second case report. J Am Acad Dermatol 1988; 19: 571.
10. Commens CA, Fischer GO. Toxic pustuloderma following carbamazepine therapy. Arch Dermatol 1988; 124: 178–179.
11. Lambert DG, Dalac S, Beer F, Chavannet P, Portier H. Acute generalized exanthematous pustular dermatitis induced by diltiazem. Br J Dermatol 1988; 118: 308–309.
12. Shelley ED, Shelley WB. The subcorneal pustular drug eruption: an example induced by norfloxacin. Cutis 1988; 42: 24–27.
13. Jackson H, Vion B, Levy PM. Generalized eruptive pustular drug rash due to cephalexin. Dermatologica 1988; 177: 292–294.
14. Lotem M, Ingber A, Segal R, Sandbank M. Generalized pustular drug rash induced by hydroxychloroquine. Acta Derm Venereol (Stockh) 1990; 70: 250–251.
15. Rustin MHA, Robinson TWE, Dowd P. Toxic pustuloderma: a self-limiting eruption. Br J Dermatol 1990; 123: 119–124.
16. Gebauer K, Holgate C, Navaratnam A. Toxic pustuloderma. A drug induced pustulating grandular fever-like syndrome. Australas J Dermatol 1990; 31: 89–93.
17. Armster H, Schwarz T. Arzneimittelreaktion auf Amoxicillin unter dem Bild eines toxischen Pustuloderms. Hautarzt 1991; 42: 713–716.
18. Bissonnette R, Tousignant J, Allaire G. Drug-induced toxic pustuloderma. Int J Dermatol 1992; 31: 172–174.
19. Ogoshi M, Yamada Y, Tani M. Acute generalized exanthematic pustulosis induced by cafaclor and acetazolamide. Dermatology 1992; 184: 142–144.
20. Huminer D, Cohen JD, Majadla R, Dux S. Hypersensitivity vasculitis due to ofloxacin. Br Med J 1989; 299: 303.
21. Choe U, Rothschield BM, Laitman L. Ciprofloxacin-induced vasculitis. N Engl J Med 1989; 320: 257–258.
22. Baker H. Drug reactions. In: Rook A, Ebling FJG, Wilkinson DS, eds. Textbook of dermatology. 3rd edn. Boston: Blackwell Scientific Publications, 1979: 1111–1149.
23. Halevy S, Ingber A, Feuerman EJ. Subcorneal pustular dermatosis: an unusual course. Acta Derm Venereol (Stockh) 1983: 63: 441–444.
24. Yip J, Sheehan-Dare R, Cotterill J. Toxic pustuloderma due to PUVA treatment. Br J Dermatol 1991; 125: 401–402.