

Acute Generalized Exanthematous Pustulosis upon Ingestion of a Progesterone Preparation

Sir,

In 1968, Baker & Ryan reported 5 patients with an exanthematic subtype of generalized pustular psoriasis (GPP) (1). The patients had developed a widespread and short-lived sterile pustular eruption either following an infection or for no apparent reason. They had no previous history of psoriasis. In 1980, Beylot et al. (2) introduced the term acute generalized exanthematous pustulosis (AGEP) for the conditions similar or probably identical to an exanthematic type of GPP. Since then, there have been many cases describing similar eruptions as pustular drug rashes or as toxic pustuloderma and considered as a new form of adverse drug reaction (3). We report a patient with AGEP without a previous psoriasis history whose condition was probably precipitated by the progesterone preparation medroxyprogesterone acetate.

CASE REPORT

A 35-year-old Japanese woman with mental retardation suffering from endometrial carcinoma underwent a simple hysterectomy in 1992. Two weeks later she was given medroxyprogesterone acetate (Provera®, 400 mg/day) orally and a mixture of tegafur and uracil (UFT®, 400 mg and 896 mg/day). No antibiotics were given. On the next day edematous erythema suddenly appeared on her palms, soles and the posterior aspect of her legs. Multiple superficial pinhead-sized pustules on an erythematous base followed, and coalesced and dried up within a few days. She became fatigued and had a temperature near 40°C. The rash had progressed over almost the entire body within 5 days. Laboratory investigations showed leukocytosis (14,400/mm³) with significant neutrophilia (14,000/mm³), hypocalcaemia (8.1 mg/dl), and liver dysfunction (glutamic pyruvic transaminase: 93 IU/l). The erythrocyte sedimentation rate and C-reactive protein (CRP) were elevated at 58 mm/h and 17.1 mg/dl, respectively. No fungi were detected from the roof of pustules using the KOH method. Cultures for bacteria in pustules were negative. The histology showed a subcorneal spongiform pustule mainly composed of neutrophils and slight acanthosis of the epidermis, oedema and a moderate perivascular lymphocytic infiltrate in the papillary dermis. She had no past history of psoriasis.

After 5 days, an intravenous drip injection of methylprednisolone sodium succinate solution (Solu-Medrol®) 1 g/day was administered for 3 days followed by oral betamethasone (3 mg/day), and all chemotherapeutic agents were stopped. The erythema and pustule decreased, and her general condition soon recovered. The pustules completely dried up after a week, and the use of betamethasone was withdrawn after 2 weeks. The course of clinical manifestations corresponded well with that of laboratory data on neutrophil count and CRP. Neither provocation nor patch test was performed because we could not obtain the patient's permission. There has been no recurrence of the lesion for at least 3 years.

DISCUSSION

The present case seems to fulfil most of the AGEP criteria. Roujeau et al. (3) concluded that AGEP is a reaction pattern and is different from GPP in two main aspects: (i) significantly shorter duration of fever and pustules in untreated patients

with AGEP; and (ii) frequent history of skin drug reaction and of recent administration of a drug which is common in AGEP but rare in GPP. However, if a patient is exposed to causative endogenous agents continuously, the condition, despite a reaction pattern, may not always take an acute course, or not always be associated with a drug history. Such cases may include GPP provoked when progesterone excretion is increased, e.g. during pregnancy (1, 4), menstruation (4, 5) or impetigo herpetiformis, which starts in the last 3 months of pregnancy and gradually heals soon after delivery. In such cases it seems next to impossible to differentiate GPP, its variant impetigo herpetiformis from AGEP, especially since AGEP occurs in patients with previous psoriatic lesions more frequently than would be expected by chance (3).

There have been several reported GPP cases in which the rash was provoked while the serum concentration of progesterone was kept high (4–6). To our knowledge, there have been no reports of pustular cutaneous reactions to tegafur/uracil. Therefore, the eruption in our case was probably precipitated by medroxyprogesterone acetate.

Major possible precipitating factors of AGEP other than drugs include viral infection and hypersensitivity to mercury (3). However, our patient did not show any suspected symptoms of viral infections and no contact with mercury before the outbreak of the rash. Therefore, it seems unlikely that the rash was caused by some infection. We consider that AGEP may be a reaction pattern affecting a patient either with or without a psoriatic background induced by different mechanisms and factors.

REFERENCES

1. Baker H, Ryan TJ. Generalized pustular psoriasis: a clinical and epidemiological study of 104 cases. *Br J Dermatol* 1968; 80: 771–793.
2. Beylot C, Bioulac P, Doutre MS. Pustuloses exanthématiques aiguës généralisées: à propos de 4 cas. *Ann Dermatol Venerol (Paris)* 1980; 107: 37–48.
3. Roujeau JC, Bioulac-Sage P, Bourseau C, Guillaume JC, Bernard P, Lok C, et al. Acute generalized exanthematous pustulosis: analysis of 63 cases. *Arch Dermatol* 1991; 127: 1333–1338.
4. Yasuda T, Ito M, Mizuno A, Kitamura N, Ohtaki N. Internal factors and pustular psoriasis. In: Farber EM, Cox AJ, Jacobs PH, Lexie Nall M, eds. *Psoriasis (Proceedings of the Second International Symposium)*. New York: York Medical Books, 1976: 140–145.
5. Shelley WB. Generalized pustular psoriasis induced by potassium iodide: a postulated role for dihydrofolic reductase. *JAMA* 1967; 201: 1009–1014.
6. Murphy FR, Stolman LP. Generalized pustular psoriasis. *Arch Dermatol* 1979; 115: 1215–1216.

Accepted February 23, 1998.

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