

Terbinafine-induced acute generalized exanthematous pustulosis

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Abstract

Acute generalized exanthematous pustulosis (AGEP) is a diffuse pustular disorder, a member of the "neutrophilic dermatoses." Histologically, it is represented by the presence of vasculitis, linked with nonfollicular subcorneal pustules. Majority of cases is related to medication administration. In this article, we are reporting a case of AGEP caused by terbinafine, an antifungal agent.

KEY WORDS: Terbinafine, pustules, antifungal, dermatoses

Introduction

Acute generalized exanthematous pustulosis (AGEP) is a diffuse pustular disorder. It is marked by acute, extensive, small, nonfollicular, sterile pustules. It is a rapidly progressing, self-limiting disease with good prognosis.^[1] Majority of cases is related to medication administration. Discontinuation of the offending agent and symptomatic treatment are generally agreed in the treatment of AGEP.^[2] In this article, we are reporting a case of AGEP caused by terbinafine.

Case Report

A 53-year-old woman visited dermatology outpatient department with low-grade fever, generalized pruritis, and blisters all over the body since 5 days. On clinical evaluation, she exhibited numerous scattered, superficial, nonfollicular pustules of 3–4 mm size on an erythematous background, distributed all over the body sparing face and palms. On eliciting the detailed history, she revealed that she has been undergoing

treatment for *Tinea corporis* infection since 1 week with terbinafine tablets (250 mg OD). There was no history of arthralgia or psoriasis. There was no mucosal involvement or peripheral lymphadenopathy.

Hematological investigation showed hemoglobin of 10.6 g/dL and total leukocyte count of 12,700/mm³. Differential leukocyte count showed neutrophils to be 76%, lymphocytes 12%, eosinophils 10%, and monocytes 2%. Liver and renal function tests were at normal levels. Skin biopsy was taken under local anesthesia and sent for histopathological examination. Histopathological examination showed epidermis with mild acanthosis, spongiosis, focal neutrophilic exocytosis, and spongiform subcorneal pustules. Underlying papillary dermis showed edema and a perivascular infiltrate containing neutrophils, some lymphocytes, and occasional eosinophils. The features were suggestive of AGEP. The patient was advised to stop the drugs and prescribed with oral methyl prednisolone (28 mg) in tapering dose over 2 weeks. There was complete regression of pustules in following days.

Discussion

AGEP is an uncommon condition characterized by an acute episode and sudden eruption of hundreds of sterile pustules.^[3]

The causative factor of this disorder is not clear. However, often, drugs and viral infections are implicated. Recently, several reports consider that these eruptions are a new form of drug reaction.^[4]

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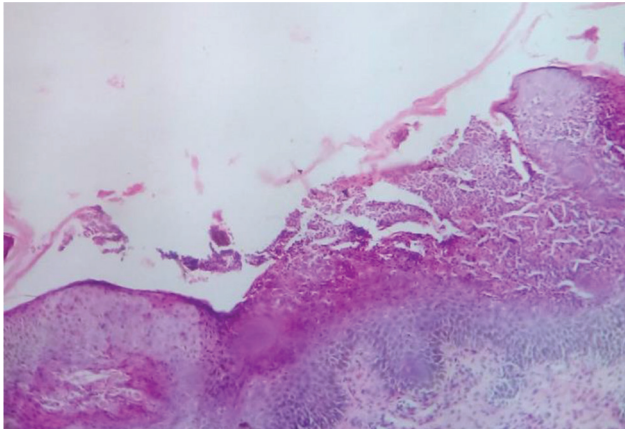


Figure 1: Histopathological section showing epidermis with mild acanthosis, spongiosis, focal neutrophilic exocytosis, and spongiform subcorneal pustules (H&E stain, lower magnification).

Macmillan, in 1973, was probably the first author to describe a case of AGEP. He called it drug-induced generalized pustular rash.^[3,5] In 1991, Roujeau *et al.*,^[6] in a retrospective study of 63 cases of AGEP, showed this illness as showing a drug causative factor and stressed upon the importance of distinguishing it from pustular psoriasis.

In 1980, in France, Beylot *et al.* set the criteria to diagnose AGEP as follows:

(i) clinical criterion—acute rash in individuals with no previous history of psoriasis, occurring after an infection or use of drugs and (ii) histological criterion—vasculitis with non-follicular subcorneal pustules.^[7,8] Thorough medical history, drug history, with clinicopathologic correlation is important in a patient presenting with acute diffuse pustular lesions to make a diagnosis of AGEP.^[2]

The mean duration of the pustules is 9.7 days (4–10 days), followed by a characteristic postpustular pinpoint desquamation for a few days. About 50% of patients exhibit other skin symptoms such as marked edema of the face, purpura lesions, and Stevens–Johnson-syndrome-like “atypical targets.” However, clinical diagnosis remains difficult if a monomorphic eruption located on hands and feet is presented. Mild mucous membrane involvement on a single site (mostly a few erosions on the mouth and tongue) may occur in about 20% of cases.^[9] The patient reported here presented with fever, generalized pruritus, and blisters all over the body without the involvement of mucus membrane. Our patient’s medical history indicated an exposure to terbinafine within 1 week before her skin eruption. This time frame was parallel to the reports of average period of AGEP to occur. The history, clinical manifestation, and laboratory investigation were suggestive of AGEP. The diagnosis was corroborated by histopathological examination. Typical histopathological findings of AGEP such as spongiform subcorneal pustules and perivascular cellular infiltrates were seen in our case (Figure 1). Two histological patterns may be seen in AGEP: (i) a toxic pustuloderma with spongiform intraepidermal pustules, papillary edema, and a mixed upper dermal perivascular inflammatory infiltrate; or

(ii) a leukocytoclastic vasculitis with neutrophil collections both below and within the epidermis.^[10,6]

It has been reported that aminopenicillins and macrolides cause more than 90% of cases of drug-induced AGEP. There are also reports of systemic antifungal agents including azoles and terbinafine causing AGEP.^[6,11] Discontinuing of the offending agent and symptomatic treatment is followed in treatment of AGEP.^[2] The overall prognosis is good in AGEP although high fever or superinfection of skin lesions can sometimes lead to life-threatening situations in patients of old age or poor general condition.^[12]

Conclusion

Terbinafine-induced AGEP is quite a rare phenomenon. Early diagnosis of AGEP and differentiation from other diseases is important to avoid unnecessary investigations and treatment.

References

- Momin SB, Del Rosso JQ, Michaels B, Mobini N. Acute generalized exanthematous pustulosis: an enigmatic drug-induced reaction. *Cutis* 2009;83(6):291–8.
- Dhillon KS, Saxena K, Garg K, Umar MS. Acute generalized exanthematous pustulosis. *J Clin Sci Res* 2012;1:192–5.
- Belda Junior W, Ferolla AC. Acute generalized exanthematous pustulosis (AGEP). Case report. *Rev Inst Med Trop Sao Paulo* 2005;47(3):171–6.
- Shelley ED, Shelley WB. The subcorneal pustular drug eruption: an example induced by norfloxacin. *Cutis* 1988;42(1):24–7.
- Macmillan AL. Generalised pustular drug rash. *Dermatologica* 1973;146(5):285–91.
- 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(9):1333–8.
- Beylot C, Doutre MS, Beylot-Barry M. Acute generalized exanthematous pustulosis. *Semin Cutan Med Surg* 1996;15:244–9.
- Haro-Gabaldon V, Sanchez-Sanchez-Vizcaino J, Ruiz-Avila P, Gutiérrez-Fernández J, Linares J, Naranjo-Sintes R. Acute generalized exanthematous pustulosis with cytomegalovirus infection. *Int J Dermatol* 1996;35(10):735–7.
- Lasić D, Ivanišević R, Uglešić B, Cvitanović MZ, Glučina D, Hlevnjak I. Acute generalized exanthematous pustulosis as a side effect of quetiapine. *Psychiatr Danub* 2013;25(1):84–5.
- Burrows NP, Russell Jones RR. Pustular drug eruptions: a histopathological spectrum. *Histopathology* 1993;22(6):569–73.
- Roujeau JC. Clinical heterogeneity of drug hypersensitivity. *Toxicology* 2005;209:123–9.
- Sidoroff A, Halevy S, Bavincq JN, Vaillant L, Roujeau JC. Acute generalized exanthematous pustulosis (AGEP)—a clinical reaction pattern. *J Cutan Pathol* 2001;28(3):113–9.

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