

## Oral Corticosteroids did not Prevent AGEP due to Terbinafine

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Sir,

Terbinafine is the most common antimycotic agent that can result in acute generalized exanthematous pustulosis (AGEP). The clinical features, laboratory findings and histopathology of AGEP are now well described. However the optimum management of this condition has not been agreed. We read with interest the recent case described by Beltraminelli et al. (1) and would like to report a further case of terbinafine-induced AGEP, where oral corticosteroids were not useful.

### CASE REPORT

A 62-year-old woman, who had been taking 10 mg of prednisolone daily over the previous 18 months for bullous pemphigoid developed an infection of her second right toenail with *Trychophyton rubrum* and was treated with terbinafine 250 mg/day by her general practitioner. Eight days later she presented with a symmetrical papular eruption that began on her face and neck. The papules rapidly coalesced and within 2 days the rash became generalized with targetoid lesions on her arms and she developed pustules on her back. There was never any mucosal involvement. At presentation she was febrile with a leukocytosis, neutrophilia and a raised creatinine of 162 (70–140  $\mu\text{mol.l}^{-1}$ ).

The steroid dose was maintained at 10 mg prednisolone daily throughout her admission.

A skin biopsy revealed small subcorneal pustules with neutrophils. There was underlying spongiosis and upper dermal lymphocytic infiltrate. Bacterial swabs and fungal scrapings from the pustules were negative. Her eruption settled within 12 days of stopping terbinafine.

### DISCUSSION

Table I shows the scoring system devised by Sideroff et al. (2) for the diagnosis of AGEP, in which a score of more than 8 confirms the diagnosis. Our patient scored 10.

AGEP is most commonly caused by antibiotics; however terbinafine is the most common antimycotic to induce this eruption (1). The clinical features, laboratory findings and histopathology of AGEP are now well described (2), but the optimum management of this condition has not been agreed upon.

In 9 out of 13 reported cases oral corticosteroids were used for the treatment of AGEP (4–12). The phe-

Table I. Acute generalized exanthematous pustulosis (AGEP) scoring according to Sideroff et al. (2)

Characteristic	Patient's score
Development of several small pinhead-sized sterile pustules	1
Oedematous erythema	2
Commencing on the face and becoming widespread	2
Post-pustular desquamation	1
Absence of mucosal involvement	0
Acute onset within 8 days	0
Resolution by day 12	0
Fever greater than 38°C	1
Neutrophilia greater than $7 \times 10^9/l$	1
Spongiform subcorneal pustules on histopathological examination	2

nomenon of severe cutaneous adverse drug reactions developing in patients receiving corticosteroids for the treatment of chronic diseases has been described before. Two studies that examined patients who developed toxic epidermal necrolysis (TEN) while on long term glucocorticoid therapy (13, 14) showed that, not only did 5–7.5% of those on steroids develop TEN, but also glucocorticoids did not change the final evolution of the disease. Sideroff et al. (2) stated that the course of AGEP is self-limiting with the pustulosis tending to resolve within 15 days. Steroid use was associated with those cases where the drug eruption was prolonged and tended to last for longer than the stated 15 days (Table II) (4, 6–11). Given this prolonged temporal association and the fact that our patient developed AGEP despite concurrent oral corticosteroids, we question the thera-

Table II. Published case reports in chronological order showing whether short term corticosteroids were used or not for the treatment of acute generalized exanthematous pustulosis (AGEP) and its possible effect on the duration of AGEP

Year	Authors	Oral steroids used/dose (mg/kg)	Resolution (days)
1996	Dupin et al. (3)*	None	7–8
1997	Kempinaire et al. (4)	Methylprednisolone / 1	21
1998	Condon et al. (5)	Prednisolone / 1	10
1998	Papa & Miller (6)	Prednisolone / 1	30
1999	Bennett et al. (7)	Prednisolone / 1	40
2000	Hall & Tate(8)	Prednisolone / 0.5	25
2001	Rogalaski et al. (9)	Prednisolone / 0.5–2	21
2003	Taberner et al. (10)	Prednisolone / 0.5	21
2003	Lombardo et al. (11)	Methylprednisolone / 0.5	35
2005	Sinha et al. (12)	Prednisolone / dose not stated	14
2005	Beltraminelli et al. (1)	None	10
2005	This report	None	12

\*Two cases reported.

peutic value of glucocorticoids, in the management of AGEP.

However, the fact that a low dose of prednisolone does not prevent the occurrence of an AGEP is not a demonstration that steroids could not be effective as a curative treatment at higher dosages.

## REFERENCES

1. Beltraminelli HS, Lerch M, Arnold A, Bircher AJ, Haeusermann P. Acute generalised exanthematous pustulosis induced by the antifungal terbinafine: case report and review of the literature. *Br J Dermatol* 2005; 152: 780–783
2. Sideroff A, Halevy S, Bouwes Bavinck JN, Vaillant L, Roujeau J-C. Acute generalized exanthematous pustulosis (AGEP)—a clinical reaction pattern. *J Cutan Pathol* 2001; 28: 113–119.
3. Dupin N, Gorin I, Djien V, Helal H, Zylberberg L, Leibowitch M, Escande JP. Acute generalized exanthematous pustulosis induced by terbinafine [letter]. *Arch Dermatol* 1996; 132: 1253–1254.
4. Kempinaire A, De Raeve L, Merckx M, De Coninck A, Bauwens M, Roseeuw D. Terbinafine-induced acute generalized exanthematous pustulosis confirmed by a positive patch-test result. *J Am Acad Dermatol* 1997; 37: 653–655.
5. Condon CA, Downs AMR, Archer CB. Terbinafine-induced acute generalized exanthematous pustulosis [letter]. *Br J Dermatol* 1998; 138: 709–710.
6. Papa CA, Miller OF. Pustular psoriasiform eruption with leukocytosis associated with terbinafine. *J Am Acad Dermatol* 1998; 39: 115–117
7. Bennett ML, Jorizzo JL, White WL. Generalized pustular eruptions associated with oral terbinafine. *Int J Dermatol* 1999; 38: 596–600.
8. Hall AP, Tate B. Acute generalized exanthematous pustulosis associated with oral terbinafine. *Australas J Dermatol* 2000; 41: 42–45.
9. Rogalski C, Hurlimann A, Burg G, Wuthrich B, Kempf W. Arzneimittelreaktion auf terbinafin unter dem bild einer akuten generalisierten exanthematischen pustulose (AGEP). *Hautarzt* 2001; 52: 444–448.
10. Taberner R, Puig L, Gilberte M, Alomar A. Acute generalised exanthematous pustulosis induced by terbinafine. *Eur J Dermatol* 2003; 13: 313–314.
11. Lombardo M, Cerati M, Pazzaglia A. Acute generalised exanthematous pustulosis induced by terbinafine. *J Am Acad Dermatol* 2003; 49: 158–159.
12. Sinha A, Velangi S, Barrett P, Natarajan S. Bullous acute generalised exanthematous pustulosis due to oral terbinafine. *J Am Acad Dermatol* 2005; 52: 115.
13. Rzany B, Schmitt H, Schöpf E. Toxic epidermal necrolysis in patients receiving glucocorticosteroids. *Acta Derm Venereol* 1991; 71: 171–172.
14. Guibal F, Bastuji-Garin S, Chosidow O, Saiag P, Revuz J, Roujeau JC. Characteristics of toxic epidermal necrolysis in patients undergoing long-term glucocorticoid therapy. *Arch Dermatol* 1995; 131: 669–672.