CASE REPORT

Rowell's syndrome induced by terbinafine

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Accepted 9 May 2015

SUMMARY

Terbinafine, a systemic antifungal commonly prescribed for onychomycosis (fungal infection involving the nails) has been reported to cause various cutaneous adverse effects. We describe an overlap syndrome between cutaneous lupus and erythema multiforme induced by this medication with a review of other reported cases.

BACKGROUND

Drug eruptions are common. This report serves to heighten the awareness of overlap syndromes that could pose a challenge in making a diagnosis. Also, it adds another potential severe adverse effect from a common systemic antifungal, which clinicians should always consider before prescribing.

CASE PRESENTATION

A previously healthy 81-year-old woman presented with a 3-week history of generalised eruption that was mildly pruritic. She had been started on oral terbinafine for onychomycosis involving her toe nails 5 weeks prior. Examination revealed a photo-distributed eruption on her head, neck and back. Some lesions were oedematous, crusted plaques and some were targetoid (figure 1). There was no mucosal involvement. The patient was systemically well and non-feverish.

Figure 1 Multiple eroded plaques and targetoid lesions on the back.

INVESTIGATIONS

A skin biopsy from the patient's back showed vacuolar interface dermatitis with necrotic keratinocytes at the dermoepidermal junction and superficial dermal necrosis. There was extensive epidermal scale crust and atrophy (figure 2). There was no deep dermal inflammatory infiltrate or vasculitis. Direct immunofluorescence was negative.

Laboratory investigations were positive for speckled pattern antinuclear antibodies (ANA), extractable nuclear antigen (26.0; normal range <1.0), anti-RO antibody (237 U/mL; normal range <10.0) and C reactive protein (36 mg/L; normal range <7). Other results, which included double-stranded DNA antibody, antihistone antibodies, full blood count, and renal and liver function, were either normal or negative. A recent CT scan of the patient's thorax, abdomen and pelvis, did not show any evidence of malignancy.

DIFFERENTIAL DIAGNOSIS

Toxic erythema necrolysis (TEN).

TREATMENT

Terbinafine was stopped and the patient was started on clobetasone butyrate (0.05%) ointment for her facial rash, and clobetasol propionate (0.05%) ointment for the rash on her arms and back, in addition to intensive emollient therapy. Systemic corticosteroids (0.5 mg/kg/day) had been started initially by the admitting physician but were discontinued after 2 days due to mood problems.

OUTCOME AND FOLLOW-UP

The rash improved significantly after 10 days of treatment. The patient remained in remission 3 months later.

DISCUSSION

The association between lupus erythematosus (LE) and erythema multiforme (EM) was first described in 1922 by Scholtz.¹ Rowell syndrome (RS) was first described by Rowell *et al*² in which the clinical features included LE, EM-like lesions, a positive rheumatoid factor, speckled pattern of ANA and a saline extract of human tissue.

In 2010, Zeitouni *et al* proposed diagnostic criteria for RS. Three major criteria and at least one minor criterion should be present for the diagnosis of RS to be made. Major criteria include: recognition of one of the three types of LE, skin lesions characteristic for EM and speckled pattern of ANA; whereas minor criteria include: chilblains, anti-Sjögren's syndrome antigen A SS-A (Ro) or SS-B (La) antibodies and positive rheumatoid factor.³ Kacalak-Rzepka *et al*⁴ reported a patient

To cite: Murad A, Shudell E, Mulligan N. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2015-210360

Figure 2 (A) Skin histology from targetoid lesion showing interface dermatitis and mild vacuolar change. Necrotic keratinocytes are present at dermoepidermal junction (H&E; original magnification $\times 40$). (B) Skin histology from eroded plaque demonstrating epidermal scale crust, interface dermatitis, superficial dermal perivascular inflammatory infiltrate composed of lymphocytes and histiocytes with occasional neutrophils and eosinophils (H&E; original magnification $\times 40$).

with photodistributed discoid lesions associated with erythroderma-like skin changes secondary to sodium valproate. Their patient improved with 60 mg prednisolone, which was tapered over 2 weeks. Norfloxacin has also been reported, by Baroni *et al*,⁵ to cause RS in a 70-year-old who required treatment with systemic steroids and hydroxychloroquine. The case related to terbinafine reported by Champagne *et al*⁶ was more consistent with either a drug-induced subacute cutaneous LE or possibly a drug aggravated subacute cutaneous LE. Strikingly,

the eruption had a prolonged course that prompted treatment with systemic corticosteroids and hydroxychloroquine.

Our patient had a definite history of developing the eruptions 3 weeks after starting oral terbinafine, which subsequently resolved completely within a few weeks after stopping the medication and starting topical therapy. She fulfils the criteria for drug-induced RS even in the absence of a positive rheumatoid factor. Presentations of severe cutaneous adverse reaction from medication, particularly in overlap syndromes, may pose a challenge diagnostically and therapeutically, especially in the elderly, when the risk of drug toxicity could sometimes limit the choice of treatment. Although our patient could not tolerate systemic steroids, alternative systemic therapy was not required.

Learning points

- ▶ A detailed drug history should always be carried out because the most important step in the management of drug eruptions is cessation of the medication.
- ▶ It is important to be aware of overlap syndromes to avoid uncertainty in making the diagnosis, which could then lead to a delay in initiating treatment.
- ▶ Early cessation of the drug prevents progression of the eruption and avoids the need for treating patients with a potentially toxic systemic therapy.

Acknowledgements The authors would like to acknowledge Professor Conor O'Keane, Dr Yvonne McCarthy, Dr Conor McCarthy, Dr Miriam Fitzgerald and Dr Killian Nugent.

Contributors AM was involved in writing the manuscript. All authors were involved in critical review of the manuscript.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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