

Widespread erythema with pustules

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After taking a cough mixture containing pholcodine, a 72-year-old man develops a widespread erythema associated with small pustules. What is the diagnosis?



Figure 1. Widespread erythema involving the trunk and limbs.

Over a six-day period, a 72-year-old man developed a widespread erythema (Figure 1) which had commenced on his legs 24 hours after he had taken a cough mixture containing pholcodine. The erythema was associated with small pustules and a blister over the right ankle. Subsequently, it became generalised and was accompanied by fever. There were no mucous membrane lesions or lymphadenopathy. Skin biopsy showed an epidermis with multiple collections of neutrophils beneath the stratum corneum (Figure 2). Investigations revealed a neutrophilia of $28.2 \times 10^9/L$, lymphopenia $0.6 \times 10^9/L$, abnormal liver function tests with a cholestatic pattern, and impaired renal function tests. The rash and laboratory findings settled in four days with topical corticosteroids and wet dressings.

Differential diagnosis

Three severe forms of drug reactions associated with generalised erythema and systemic findings can be distinguished but they may overlap in individual cases.

- **Toxic epidermal necrolysis (TEN)** is associated with a widespread tender erythematous rash and marked mucous membrane involvement, which may extend to the bronchi. TEN develops usually within two weeks of drug exposure. It appears like a widespread burn and the skin is shed to reveal a raw base. Skin biopsy shows extensive epidermal necrosis with scant lymphocytic inflammation. Peripheral blood studies may reveal neutropenia as well as lymphopenia. TEN is usually handled in intensive care, and up to a third of patients may die.
- **Hypersensitivity syndrome** has a delayed onset of two to eight weeks after drug exposure. It is associated with mononucleosis-like symptoms: facial oedema, a widespread erythematous rash and prominent lymphadenopathy. Peripheral blood studies

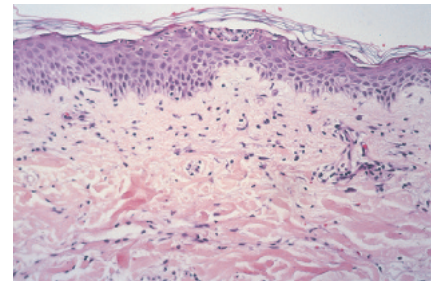


Figure 2. Skin biopsy showing neutrophils in the epidermis in collections under the stratum corneum.

initially reveal a lymphocytosis that may be atypical and progressive marked hypereosinophilia. Hepatitis is frequently seen, and interstitial pneumonitis, myocarditis, interstitial nephritis and thyroiditis may also develop. Skin biopsy shows lymphocytic inflammation with eosinophilia that may resemble a cutaneous lymphoma. Discontinuation of the causative drug is associated with slow resolution of the reaction, but corticosteroids may often be needed for treatment.

- **Toxic pustuloderma** (acute generalised exanthemic pustulosis) is the correct diagnosis in this case. It is characterised by widespread erythema studded by small pustules. The rash may be accentuated in the flexural areas. Fever, peripheral neutrophilia and organ dysfunction are often seen. Discontinuation of the offending drug usually results in rapid resolution of the rash.

Keypoint

Toxic epidermal necrolysis induced by lymphocytes, hypersensitivity syndrome associated with hypereosinophilia, and toxic pustuloderma associated with marked neutrophilia are three severe drug reactions that may present as widespread erythema with systemic involvement. Antibiotics, antiepileptic agents and allopurinol are the drugs most frequently implicated in all three reaction patterns.

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