Generalized Bullous Fixed Drug Eruption after Influenza Vaccination, Simulating Bullous Pemphigoid

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Sir,
Several cases of bullous pemphigoid appearing shortly after influenza vaccination have been described (1–3). In one of them a relapse developed after further vaccination one year later (3). To our knowledge, there is no previous description of other bullous diseases appearing after influenza vaccination.

CASE REPORT

A 90-year-old woman was seen with a generalized bullous eruption. She did not remember suffering from similar lesions previously. She had hypertension treated for more than one year with hydrochlorothiazide and valsartan (Co-diovan®). Six weeks before the start of cutaneous lesions, nimodipine (Nimotop®) and ginko biloba (Tanakene®) had been added to her therapy. In October 2000 she received an influenza vaccination. She denied intake of paracetamol or any other new drug. Twelve hours after administration of the influenza vaccine, she noticed pruritus in her genital area and legs. Twenty-four hours after the vaccination, well-demarcated erythematous macules and large bullae appeared on these areas, and later on the trunk, hands and face (Figs. 1 and 2). Some lesions had a darker centre. She had oral and genital erosions. Systemic symptoms were absent. Suspecting the diagnosis of bullous pemphigoid, a cutaneous biopsy was taken, and therapy was started with 30 mg of prednisone. Histology of a skin lesion showed a prominent subepidermal bulla with scarce perivascular mixed inflammatory infiltrates, focal hydropic degeneration of the basal layer, pigmentary incontinence, dyskeratotic keratinocytes with pyknotic nuclei in the epidermis and papillary dermis, and areas of confluent epidermal necrosis. Direct and indirect immunofluorescence were negative. Ten days after its institution, prednisone and the rest of her therapy were withdrawn. Bullae disappeared in 2 weeks, and no new lesions had appeared after 10 months, but residual pigmented macules persisted. She remained normotensive on a low-sodium content diet. According to the manufacturer, influenza vaccine (Vacuna antigripal Pasteur®) is an inactivated subunit split vaccine that contains hemagglutinin, neuraminidase, and residual internal viral structural proteins, as well as thiomersal, formaldehyde, neomycin, phosphate buffered saline and octoxinol-9. 2000-01serotypes were A/Moscow/10/99 (H3N2), A/New Caledonia/20/99 (H1N1) and B/Beijing/184/93. Standard patch tests, including all the components (except for octoxinol-9), and patch test with the vaccine "as is", in previously affected skin, gave negative results.

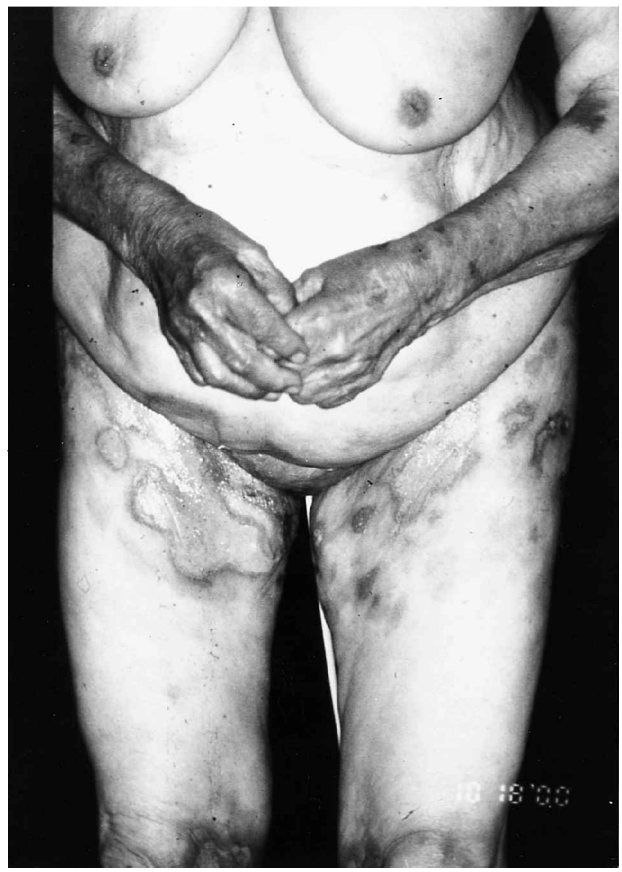

Fig. 1. Erosions after the rupture of large bullae.

DISCUSSION

We made the diagnosis of generalized bullous fixed drug eruption on the basis of the clinical picture of well-demarcated polycyclic lesions affecting the face and mucosae, the lack of systemic symptoms, the spontaneous resolution in 2 weeks without recurrence (but leaving persistent pigmented macules), and the characteristic histology and negative immunofluorescence. The lack of a history of previous localized lesions could be an argument against this diagnosis. However, in an old patient with some cognitive disturbances minor lesions could easily remain unnoticed. Moreover, the diagnosis of fixed drug eruption can be made on the first episode (4).

Generalized bullous fixed drug eruption differential diagnosis includes toxic epidermal necrolysis and bullous pemphigoid. The finding, in some cases, of C3 and IgM deposition along the basement membrane during the early phases of fixed drug eruption, can make the distinction from bullous pemphigoid more difficult (5).

Temporal criteria led us to consider influenza vaccination as the trigger of this patient eruption. The latent period after the supposed trigger for fixed drug eruption is characteristically very short (5, 6). Influenza vaccination was the only drug started shortly before the eruption. Taking into account the severity of her lesions, we considered it unethical to perform

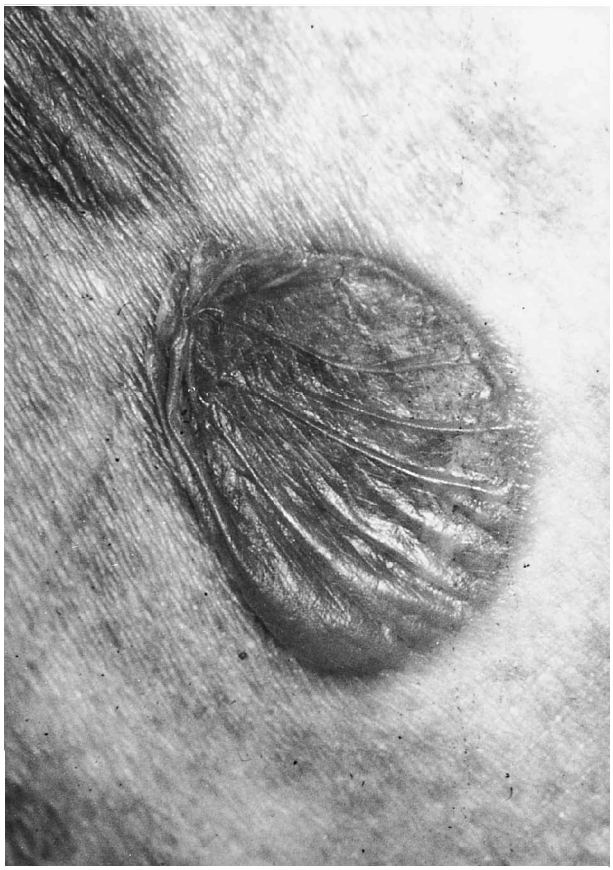

Fig. 2. Bullous lesion suggestive of bullous pemphigoid.

a provocation test. The fact that patch testing was negative is not surprising, as its sensitivity is low (7).

To our knowledge, this is the first description of generalized bullous fixed drug eruption after influenza vaccination. This difficult differential diagnosis should always be taken into account when describing bullous pemphigoid induced by vaccination, especially in relapsing cases.

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