

LETTERS TO THE EDITOR

A Patient with an Unusual Localization of Recurrent Erythema Multiforme

Sir,

Erythema multiforme is well-known by dermatologists and is a syndrome with distinctive skin lesions with or without mucosal involvement (1). The skin lesions and diagnostic criteria have been reviewed by Huff et al. (2) and consist of symmetrically distributed, fixed, circular erythematous lesions with concentric color changes (target lesions). The lesions can show central vesicle formation. The lesions are self-limiting and disappear within 1–4 weeks. Severe forms include the presence of bullae and extensive mucocutaneous involvement. Renal involvement, pneumonia, sepsis, fluid and electrolyte imbalances can cause significant mortality (3).

The list of factors claimed to be important in the etiology of erythema multiforme is extensive and includes viral infection, other infectious agents and drugs (1–3). Recurrent erythema multiforme is a rather uncommon disorder and is reviewed by Schofield et al. (4). This form of erythema multiforme proved to be frequently precipitated by a preceding herpes simplex virus (HSV) infection.

In this case report we describe a patient with recurrent erythema multiforme, presenting with an unusual localization of the lesions.

CASE REPORT

A 43-year-old woman presented with lesions located on the dorsum of the hands and arms, the zygoma and – curiously – the ear rims (Fig. 1). They consisted of sharply demarcated erythematous plaques. The lesions at the ear rims showed clear vesicle and small bulla formation. The lesions on the hands were firm and indurated. There was no apple jelly phenomenon at diascopy. No crusts, purpura or desquamation were seen in any of the lesions. The oral and genital mucosa were not affected. The lesions were painful.

The same skin lesions had appeared 3 years earlier for the first time and emerged twice a year on the hands and arms. They disappeared each time after 5–6 days, leaving no scars. The patient never suffered from general weakness, fatigue or fever. The lesions caused itching. Epicutaneous allergy tests had been performed elsewhere. No allergies had been found. She had used no medication, except for oral antihistaminics after the lesions had emerged, or cosmetics.

She attended our out-patient department for the first time this year because the lesions appeared more frequently (six times in 10 months) and had extended to the face and ears. She now complained of severe itch and a burning pain. She had used no medication. No excess exposure to sunlight or cold could be found. No history of recurrent HSV infections could be established.

General examination revealed no fever or other systemic symptoms. Laboratory investigations showed the following results: ESR 4 mm/h, creatinine, bilirubin, alkaline phosphatase, lactate dehydrogenase and liver enzymes were within the normal range. Serum iron and iron binding capacity showed normal values. Hemoglobin, hematocrit, thrombocytes, leukocytes and differentiation were within the normal range as well. Serological examination of virus antibodies showed positive IgG titers for herpes simplex; IgM titers were negative. Screening for varicella zoster and mycoplasma pneumoniae showed no signs of an active infection process.

Histopathological examination: the epidermis showed localized acanthosis and hyperkeratosis on haematoxylin-eosin staining. Vesicles

were seen mostly just beneath the epidermis, containing eosinophilic material and polymorphonuclear leukocytes of the neutrophilic and eosinophilic type, mixed with lymphocytes. Focally intraepidermal necrosis was seen. The adjacent epidermis showed lymphocytic infiltration, hydropic degeneration and spongiosis. In the upper dermis predominantly a perivascular mixed inflammatory infiltrate was seen, with numerous eosinophils. Immunohistochemical examination showed depositions of C3 in the dermal vessels, while all other stainings were negative. The clinical and histological features led to the diagnosis of a severe dermal form of erythema multiforme. Within 4 days the lesions on the cheeks and ears had largely involuted. The lesion on the hands showed more pronounced formation of vesicles in the center of the plaques. After 10 days all lesions had disappeared without leaving scars.

DISCUSSION

Erythema multiforme was first described by Hebra in 1866 (5) and was extensively reviewed by Huff et al. in 1983 (2). They agree with Thomas et al. (6) in distinguishing two syndromes: the minor variant (classical skin lesions with limited mucosal involvement) and erythema multiforme major (a severe syndrome with extensive mucosal damage, as first described by Stevens & Johnson). Etiological factors mentioned in erythema multiforme minor are HSV infections, while erythema multiforme major is associated with mycoplasmal infections and drugs (3).

Our patient suffered from recurrent episodes of erythema multiforme minor. The localization of the lesions (sun-exposed areas) led to a differential diagnosis including polymorphic light eruption, juvenile spring eruption, contact allergy and bullous lupus erythematosus. Epicutaneous allergy testing revealed no positive reactions. Polymorphic light eruption (PLE) can indeed present with erythema and blister formation (7). Usually the lesions are not as localized as in this patient. In addition, no clear relationship with exposure to sunlight could be found, and the lesions had emerged throughout all seasons. Juvenile spring eruption of the ears, which is nowadays considered as a variant of PLE, occurs mainly in boys, in epidemics during spring (7). Chronic discoid lupus erythematosus (CDLE) or subacute cutaneous lupus erythematosus (SCLE) were considered as diagnosis. The lesions of these entities can show blistering but usually exhibit scaling as well, which was absent in this patient. No atrophy was observed, a feature commonly present in CDLE (8). Because of the results of routine histology and immunohistochemical investigations (our patient showed minimal depositions of C3 in the dermal vessels), these differential diagnosis were rejected.

Recurrent erythema multiforme is rather uncommon. It is frequently linked with HSV infections, type 1 as well as type 2 (2, 4). HSV has been demonstrated in erythema multiforme lesions, even in patients with no clinical history of HSV infections, using immunofluorescence techniques, the polymerase chain reaction and in situ hybridization (9–11). Therefore the concept is postulated that patients with idiopathic erythema multiforme may suffer from subclinical reactivation of HSV. In



Fig. 1. Erythema multiforme lesions located on ears and dorsum of the hands. Pronounced bulla formation on the ears.



recurrent erythema multiforme (Schofield et al. (4)), 71% was precipitated by a preceding HSV infection. Acyclovir supplied orally proved to be a useful treatment in 55% of patients, even when there was no clear history of HSV infections!

Brice et al. (12) compared patients with HSV infections and erythema multiforme with patients with herpes labialis only. No differences in immune mechanisms could be found (anti-HSV-IgG titers, antibody neutralization, antibody-dependent complement-mediated cytotoxicity or antibody-dependent cellular cytotoxicity).

The patient presented in this study showed erythema multiforme lesions on localizations rarely described in literature, e.g. the ear rims and zygomata. These lesions were present in combination with lesions at classical localizations, such as the dor-

sum of the hands. The presence of lesions on the ears and cheeks suggests influence of sunlight, low temperature or pressure. Indeed, the Koebner phenomenon in erythema multiforme has been described (1, 2). Furthermore, photoaccentuation of erythema multiforme has been mentioned in literature (2). However, few patients have been reported with skin lesions as distinct as in this patient. Our patient showed lesions on areas prone to sun exposition or trauma, but none of these precipitating factors could be proven anamnesticly. This suggests that possibly other factors influence the evolution of erythema multiforme lesions at these localizations.

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E.M.G.J. de Jong, R.J.J. Koopman and P.C.M. van de Kerkhof, Department of Dermatology, University Hospital Nijmegen, P.O. Box 9101, NL-6500 HB Nijmegen, The Netherlands.