Erythema Annulare Centrifugum and Intestinal *Candida albicans* Infection–Coincidence or Connection?

Sir,

Erythema annulare centrifugum (EAC) was defined as a persistent erythema characterized by annular, circinate, gyrate or serpiginous lesions. It starts as a small erythematous papule, usually enlarging slowly with central clearing and peripherally spreading to form the typical annular lesion. Slight scaling on the inner aspect of the advancing, palpable border or vesiculation may occur. The plaques vary from 1 cm to 50 cm in diameter, with an active border of 2–10 mm (1).

Histologically, a superficial and a deep type of EAC can be distinguished. According to Ackerman, superficial EAC shows a moderately dense superficial perivascular infiltrate of lymphocytes, histiocytes and rarely eosinophils (2). Moreover, slight oedema of the papillary dermis and focal spongiosis can be found. The deep type shows a moderately dense lymphohistiocytic infiltrate around superficial and deep blood vessels (2).

CASE REPORTS

Case 1

A 63-year-old man was first seen in October 1994 for evaluation of a sharply limited, annular and configurated erythematous lesion at his right groin. This non-pruritic lesion had enlarged slowly since its sudden onset 1 week earlier. There was a slight scaling but no vesiculation present. The patient's medical, family and social histories were non-contributory. Except glibenclamid for therapy of a type IIb diabetes mellitus the patient had no systemic medication. Topical treatment of the skin lesion with glucocorticoid ointment (prednicarbat) for 1 week remained unsuccessful.

Physical examination at admission did not show any abnormalities except the finding of an erythematous, annular lesion with central clearing at the patient's right groin (Fig. 1). The lesion had an erythematous to bluish aspect and a palpable border.

Laboratory investigations were within normal ranges. *Borrelia burgdorferi* serology was negative and the lack of *Borrelia* skin infection was confirmed by polymerase-chain reaction (PCR) on a lesional skin sample. Indirect and direct immunofluorescence investigations remained negative.

Histologic examination of lesional skin from the right groin showed a superficial perivascular lymphohistiocytic infiltrate and several eosinophilic granulocytes scattered in dermal oedema. The epidermis was normal. The PAS staining was negative. Histopathologic features were compatible with the diagnosis of EAC.

Scrapings for fungi from the ringed lesion were repeatedly negative by microscopical examination as well as by culture. Examination of the stool was strongly positive for yeast: *Candida albicans* was found on culture ($>10^6$/ml stool).

The first attempts to treat the lesions with topical steroids (prednicarbat) for 2 weeks remained unsuccesful. With regard to the intestinal candidiasis, we then decided to treat only with amphotericin B 400 mg/d perorally for 4 weeks. With this regimen the annular erythematous skin lesion rapidly regressed within 1 week, leaving only a slight pigmentation (Fig. 2), which disappeared within a month.

Case 2

A 45-year-old woman was first seen in January 1995 with a 3-week history of an elevated, annular, palpable erythematous lesion at her neck (Fig. 3). The slightly scaly lesion was pruritic from time to time. The patient's medical, family and social histories were non-contributory, besides contact sensitization to nickel and colophony. Physical examination at our department did not show any abnormalities except a slight mamillary eczema.

Red and white cell count was within normal ranges; serologic examination for *Borrelia burgdorferi* infection was negative. Scrapings for fungi from the annular lesion were negative by both microscopical examination and culture. Again, *Candida albicans* was found on culture of the stool ($>10^6$/ml).

Histologic examination of lesional skin from the neck showed a slight acanthosis and papillomatosis, subepidermal oedema and a marked lymphohistiocytic infiltrate in the upper dermis, consistent with erythema annulare centrifugum Darier. The PAS staining was negative.

While topical treatment with steroids (prednicarbat) for 1 week remained unsuccessful, oral treatment of the intestinal candidiasis

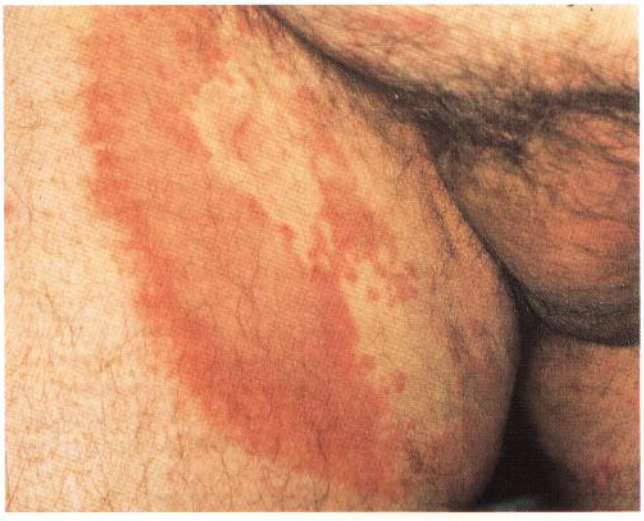

Fig. 1. Patient 1: erythematous annular lesion with slightly elevated border at the patient's right groin.

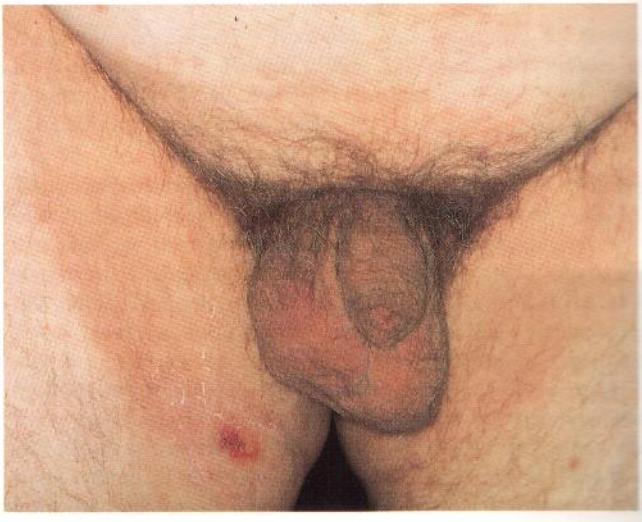

Fig. 2. Patient 1: area with residual pigmentation after 1 week of antifungal treatment.

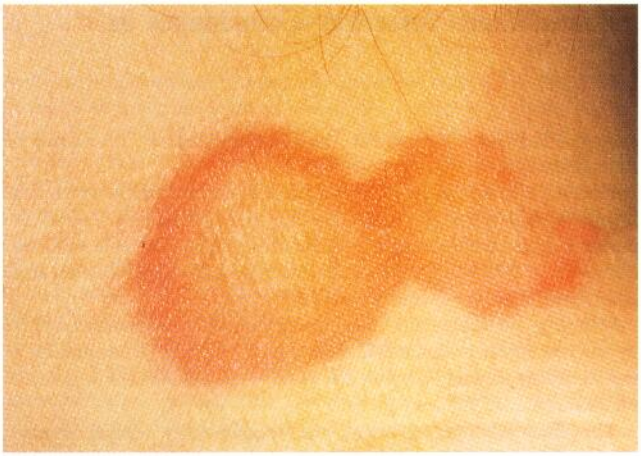

Fig. 3. Patient 2: erythematous annular lesion with slightly elevated border at the patient's neck.

with nystatin 6 × 500,000 I.E./d for 2 weeks led to a rapid and complete regression of the skin lesions.

DISCUSSION

EAC can be found as a cutaneous response to fungal or yeast infection. Several cases of EAC are reported to be dermatophytids (4). Immuno-allergologic evidence is based on the positive reaction to trichophytin injections, resulting in a replica of the EAC (4).

Shelley mentioned a patient with EAC resulting from fungal hypersensitivity to the *Penicillium* of blue cheese (5). This, however, seems to be a rare event.

There are several case reports of patients in whom this clinical symptom reflects a hypersensitivity to *Candida albicans* (6–10). In most of these patients, with *Candida albicans* growing as a commensal in their mouth and/or rectum, a strongly positive skin test reaction to the *Candida* extract was found, supporting the idea of a Candida-induced EAC. Therefore, our observations support the assumption that some forms of EAC may be the result of a hypersensitivity reaction to *Candida albicans*. The connection between the intestinal yeast infection and EAC is strongly supported by the fact that the steroid-resistant skin lesions disappeared with amphotericin B treatment within 1 week.

Similar therapy results are reported for oral and vaginal nystatin coupled with yeast-free diet (6). In some patients the skin lesions recurred during therapy-free intervals (7).

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Accepted July 15, 1996.

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