Cutaneous Alternariosis Occurring in a Patient Treated with Local Intrarectal Corticosteroids

Sir,

Alternaria is widely distributed in the environment and a pathogenic role in human pathology is rare, though all the cases may not be published. In a review of world literature Badillet collected 55 cases of cutaneous alternariosis (1). Thirteen other cases have since been described (2). We report a new case of dermal alternariosis occurring in a man treated for 2 years with intrarectal steroids (betamethasone phosphate 5 mg daily, Betnesol®, Glaxo) for post-radiation rectitis.

CASE REPORT

A 69-year-old patient had had an erythematous, slightly infiltrated and crusted plaque on the back of the right forearm for 2 months. He was an elderly farmer and continued to have outdoor activities. Cutaneous biopsy had shown hyphae and round inclusions stained with PAS within giant cells within a dermal granulomatous reaction. Topical amphotericin-B given by his physician had been mildly effective, with partial regression of the plaque for 1 month.

On the patient's admission in April 1994, the plaque measured 2 × 3 cm in size (Fig. 1). The skin was thin, wrinkled and atrophic on the back of the hands and extensor surface of the arms, with ecchymotic purpura. There were numerous telangiectasiae on his moon-shaped face.

Medical history revealed prostatic adenocarcinoma in 1990, treated surgically and with radiotherapy, responsible for development of post-radiation rectitis in June 1992. He had been treated with intrarectal betamethasone enema 5 mg daily from this date. He had also been treated with nicardipin 20 mg/day for hypertension, and local application of timolol maleate and aceclidine chlorhydrate for intra-ocular hypertension and cataract.

On physical examination, general status was good. Biological tests revealed lymphopenia (0.43 10^9/l) and increased neutrophil polymorphonuclear cells (8.8 10^9/l). Basal cortisolemia at 8.00 h was twice decreased (25 and 26 nmol/l, normal 305–750 nmol/l) and corticotropin was undetectable (<5 ng/ml, normal range 5–30 ng/l). Humoral immunity was decreased with global hypogammaglobulinemia (5.8 g/l, normal range 14.5–20). Intradermal injections of various antigens revealed an absence of reactivity to tuberculin, tetanus, *Streptococcus*, *Proteus*, *Trichophyton* and *Candida*. There was only a reaction (6 mm) for diphtheria. HIV1 and HIV2 serology was negative.

A second cutaneous biopsy was taken for histological examination and mycological culture. Histological examination revealed a hyperplastic epidermis. The upper dermis showed a mixed inflammatory infiltrate with neutrophils, histiocytes and giant cells. Round intracytoplasmic inclusions staining faintly with PAS were seen in giant cells. Pseudospores and long intercellular filaments were present within the infiltrate (Fig. 2). Direct examination showed hyphae and spores. Culture in Sabouraud's gel showed dark colonies and PCA medium grew *Alternaria* sp.

The patient was treated with topical bifonazole for 1 month without success. He was then treated with surgical excision with no recurrence 6 months later. Because of the side-effects of betamethasone phosphate, unsuccessful attempts have been made with other less diffusible corticosteroid enemas. Therefore dosage of betamethasone was administered every second day.

DISCUSSION

Diagnosis of cutaneous alternariosis was possible because of the coexistence of two criteria: 1) presence on histological examination of hyphae and round inclusions (10–15 mm in diameter) within a dermal granuloma, and 2) isolation of Alternaria sp. from culture. These two criteria were necessary since Alternaria is widely distributed in the environment; moreover, it can be isolated on normal human skin and is thus usually considered to be a saprophyte (1).

In nearly all cases the infection has occurred after percutaneous inoculation. Thus, mainly farmers and people living in the country are affected. Cutaneous fragility induced by corticosteroid therapy and/or by skin disease (2) increases the possibility of percutaneous inoculation from the environment. In 38 patients, immunosuppressive agents or systemic corticosteroids favorized the infection, and in 7 other cases Cushing's syndrome was present (1, 2). In 2 cases, local corticotherapy was suspected of being a facilitating factor (3, 4).

This is the first case of cutaneous alternariosis caused by local intrarectal therapy. The treatment was given for post-radiation rectitis and was responsible for both clinical and biological signs of iatrogenic hypercorticism. Moreover humoral and cellular immunity was depressed, with lymphopenia, hyporeactivity to intradermal antigens, and decreased immunoglobulin levels. Betamethasone sodium phosphate is a hydrosoluble molecule with a molecular weight of 516.4. Its anti-inflammatory effect is 6-fold greater than those of prednisolone. Systemic diffusion of intrarectal betamethasone across intact mucosa is considered to be low, but sufficient data are lacking. In contrast, prolonged topical treatment of distal ulcerative colitis with corticosteroids containing enema produces suppression of the hypothalamic-pituitary-adrenal axis (5), and this was demonstrated clearly with betamethasone phosphate (6). The usual dosage in chronic treatment is 5 to 6 enemas monthly. In our case, the patient felt the necessity of a daily enema. This led to systemic corticotherapy with signs of hypercorticism and opportunistic infection with *Alternaria*.

Treatment of cutaneous alternariosis requires: 1) surgical removal of lesions when possible, i.e. small and non-numerous lesions, 2) if possible, suppression or reduction of immunosuppressive therapy, which can be sufficient to treat the lesions, and 3) antifungal therapy when the first 2 solutions are not

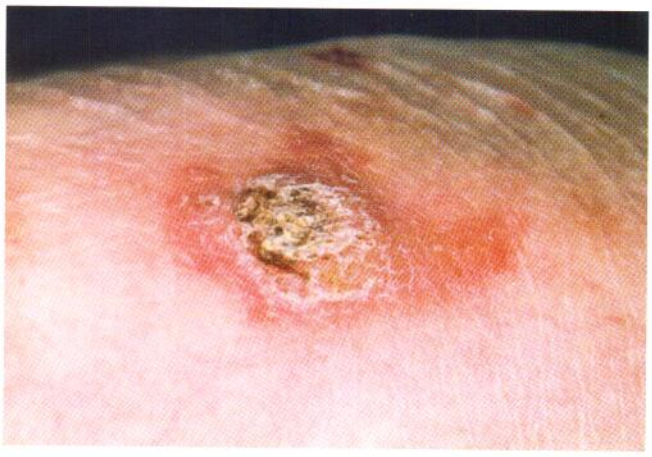

Fig. 1. Reddish squamous plaque on right arm. Note the wrinkled atrophic skin.

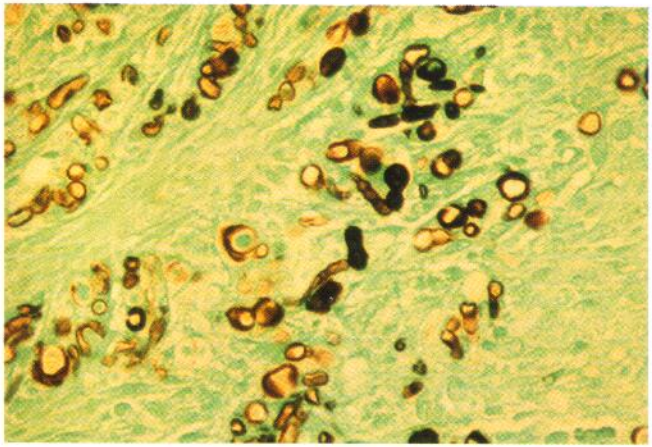

Fig. 2. Grocott G X 400. Numerous pseudospores and some septate hyphae can be seen within the dermal infiltrate.

appropriate (1). Isolated cases of successful treatment have been reported: local injection of amphotericin B (3), miconazole (7), oral ketoconazole (8, 9), oral itraconazole (2) and oral fluconazole (2). Because of the small number of cases, no controlled trial has been conducted. Itraconazole and ketoconazole seem to give the best results (1, 2, 9).

ACKNOWLEDGMENTS

We wish to thank Dr. Philippe Khouri and Dr. Hervé Lautraite for their help, and Mrs Doreen Raine for reviewing the language.

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Accepted February 6, 1995.

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