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is widely distributed in the environment and a pathogenic role in human pathology is rare, though all the cases may not be published.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 Badillett 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 eczematous purpura. There were numerous telangiectasies 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 chloride for intra-ocular hypertension and cataract.

On physical examination, general status was good. Biological tests revealed lymphopenia (0.43 × 10⁹/l) and increased neutrophil polymorphonuclear cells (8.8 × 10⁹/l). Basal corticolemia at 8:00 h was twice decreased (25 and 26 mmol/l, normal 30–75 mmol/l) and corticosterone 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 for 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 favored 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 that 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

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

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Fig. 2. Grocott G X 400. Numerous pseudosporles 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).

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Very Low-dose Chloroquine Treatment for Porphyria Cutanea Tarda

Sir,

A 74-year-old woman came under our observation in September 1993, with a 2-year history of recurrent vesicles and bullae occurring mainly in areas of repeated traumas and exacerbating by sunlight exposure. Her past medical history was negative for alcohol or drug intake.

Physical examination revealed some vesicle-bullous lesions on her hands and dorsum of the feet, where she also had some atrophic scars. Histopathology of a lesion showed a subepidermal bulla with a festooned base, consistent with the diagnosis of porphyria cutanea tarda (PCT). Diagnosis was confirmed by the blood tests, iron 158 mg/dl (normal values 50–160), transaminases ALT 78 U/l and AST 97 U/l (n.v. 0–40), gamma-glutamyltransferases 50 U/l (n.v. 10–50), and by the urine porphyrin content: total porphyrins 3,470 g/24 h (n.v. 50–200), uroporphyrins 1,760 g/24 h (n.v. 15–50) and coproporphyrins 1,710 g/24 h (n.v. 35–150).

In October, chloroquine treatment (0.5 g twice weekly) was started. After the first two doses, the patient had an acute reaction consisting of fever (39°C), malaise, nausea, vomiting, anorexia, abdominal pain, constipation and arthro-myalgias, persisting for 5 days. This symptom complex was associated with increased serum levels of transaminases (ALT 94 U/l, AST 126 U/l) and with a massive increase in urinary porphyrin output (total porphyrins 3,750 g/24 h, uroporphyrins 2,400 g/24 h, coproporphyrins 1,920 g/24 h).

One month later, very low doses of chloroquine (62.5 mg/ weekly) were resumed. Apparently, the patient tolerated them well and showed a rapid biochemical and clinical improvement. During the following months, daily urinary porphyrin excretion slowly declined, attaining values near normal in July 1994 (total porphyrins 121 g/24 h, uroporphyrins 96 g/24 h, coproporphyrins 25 g/24 h). The levels of serum transaminases and gamma-glutamyltranspeptidases became normal, skin lesions healed and the patient’s general condition ameliorated after only a few months’ treatment. No new lesions were observed and periodic ophthalmological examinations revealed no evidence of retinopathy.

Phlebectomy and antimalarials are considered the mainstay of therapy for PCT (1). Phlebectomy, however, may be contraindicated in patients with anemia, cardiopulmonary disease or HIV infection. In addition, antimalarials may be more effective than phlebectomy in the treatment of PCT (2). Chloroquine therapy needs caution, however, as it may cause acute reactions or

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