

## Cyclosporin A in Metastatic Crohn's Disease

*Sir,*

Skin lesions are frequently described in Crohn's disease (CD), and their incidence ranges from 22 to 45% (1). Cutaneous manifestations of CD can precede or follow the diagnosis of the bowel disease and can sometimes appear at the same time as the gastrointestinal involvement. Among the cutaneous lesions described in the literature, some, such as perianal fissures and fistulas, vesicopustular eruptions, clubbing and cutaneous manifestations secondary to malabsorption, are related to the severity of the gastrointestinal disease. Others, including metastatic Crohn's disease (MCD), do not seem to be related to the degree of intestinal inflammation (2). We report here a case of MCD of the vulva successfully treated with cyclosporin A (CyA).

### CASE REPORT

A 20-year-old female patient was referred to our department on account of the presence of ulcerative vulvar lesions resistant to treatment. Previous treatment included both systemic and local antibiotics, topical corticosteroids, antiseptics and curettage of the lesions.

The history revealed the patient to have been suffering from CD since the age of 11. Recurrences of the disease had been treated with cycles of sulfasalazine, corticosteroids and metronidazole; and in 1989 a colectomy with ileostomy leaving a closed rectum was necessary. After the operation the patient developed a peristomal dermatitis but her general condition was good until April 1993, when the first lesions appeared on the genitalia. At first the patient noted erythema and oedema of the labia

majora and minora. In the following months the clinical picture progressively worsened and cutaneous abscesses appeared which then spontaneously turned into ulcers. There was no active inflammation of the rectum. The patient was sent to us by the surgeons who were planning to carry out a vulvectomy. When the patient came under our observation she was not undergoing any therapy. The clinical examination revealed widespread erythema and oedema on the labia majora and minora, extending to the perineal and perianal areas, as well as numerous ulcerative lesions (Fig. 1). The patient complained of acute pain. The histologic examination confirmed the diagnosis of MCD, revealing the presence of mildly acanthotic epidermis with neutrophilic exocytosis prevalently on the uppermost layers and perivascular and interstitial inflammatory cell infiltrate consisting of lymphocytes, plasma cells, histiocytes, epithelioid cells and multinucleated giant cells. Stains for fungi, acid fast bacilli and spirochetes were negative.

In December 1993 we began treatment with CyA at the dosage of 4 mg/kg/day after first checking for the absence of clinical, laboratory or anamnestic contraindications. This dosage was maintained for a month, after which the vulvar ulcers appeared to be considerably improved. The dosage was then reduced by 1 mg/kg/day each month for 2 months until the complete resolution of clinical manifestations. A further month of therapy at the dosage of 2 mg/kg/day maintained the clinical remission. CyA treatment was stopped in April 1994 and the patient was still free of relapses in October 1994.

### DISCUSSION

MCD refers to cutaneous or mucous granulomatous lesions separated from the affected gut by normal intact mucosae or skin (3). It is a rare inflammatory condition presenting different



Fig. 1. Erythema and oedema on the vulva and labia majora, with numerous ulcerative lesions.

clinical features: papular-nodular lesions of the trunk or the extremities, ulcerated plaques of the limbs, granulomatous cheilitis and erysipeloid lesions of the face (2, 4). In the genitalia, the most frequently described cutaneous changes are erosive-ulcerated lesions (1, 4).

Parks et al. (5) were the first to describe cutaneous ulcerations of the perineum, vulva and groin from CD in 1965. Involvement of the vulva by MCD is rare. In a recent review, published in 1991, it was noted that out of 431 female patients affected by bowel CD, only 8 had a vulvar involvement (6). In most cases reported in the literature, the vulvar lesions appeared several years after the first diagnosis of CD (4). In some patients, on the other hand, the vulvar lesions also appeared after the colectomy.

In our patient the CD of the vulva occurred 4 years after the colectomy, in a period of remission of the intestinal symptoms and in a treatment free period. MCD of the vulva, especially when it precedes overt involvement of the ileum and colon, can make diagnosis difficult. Differential diagnosis may include pyogenic infection of the vulva such as hidradenitis suppurativa, granulomatous diseases of the genitalia such as tuberculosis, actinomycosis and lymphogranuloma venereum and the genital erosions of Behçet's syndrome.

Treatment of cutaneous CD includes all the drugs usually utilized for the therapy of bowel involvement: steroids, sulfasa-

lazine, azathioprine, zinc sulphate, antibiotics and metronidazole (1). When genitalia involvement is severe and persists during a quiescent intestinal phase of the disease, surgical treatment can be considered. This may include vulvectomy, simple excision of the diseased tissue, myocutaneous skin grafts or simple debridement (7). In the last few years CyA has also been utilized with conflicting results for treatment of CD (8). The drug has also been successfully used in the therapy of perianal localization and fistulas of CD (9).

The histologic features of sarcoidal type granulomas in the papillary dermis, of granulomatous vasculitis in the deep dermis and in the subcutaneous tissue, as well as the absence of immune-complexes on direct immunofluorescence, suggest that metastatic lesions of CD result from a delayed hypersensitivity reaction to antigens not yet identified (3). CyA, by acting on the interaction between antigen, antigen-presenting cells and T lymphocytes, inhibits the release of lymphokines which are the cause of T-helper lymphocyte expansion and T-cytotoxic lymphocyte activation. CyA can also inhibit the recruitment and the activation of macrophages as well as the antigen-presenting cells in immune reactions (10). By reducing the intensity of the delayed hypersensitivity reaction, CyA can be used in MCD. This is the first case of vulvar MCD successfully treated with CyA, and the good results obtained justify further trials when standard therapy has failed.

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Accepted December 15, 1994.

Federico Bardazzi, Maria Silvia Guidetti, Beatrice Passarini, Elisa Spetoli. Department of Dermatology, University of Bologna, Via Massarenti 1, 40138 Bologna, Italy.