

PYODERMA GANGRENOSUM ASSOCIATED WITH IgA PARAPROTEINEMIA. TREATMENT WITH CYCLOSPORIN A AND PREDNISONE

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SUMMARY

A 58-year-old woman with a 20-year history of recalcitrant pyoderma gangrenosum associated with IgA paraproteinemia was treated with cyclosporin A 5 mg/kg/day combined with prednisone 30 mg/day without significant amelioration. After raising the dose of cyclosporin A to 10 mg/kg a rapid improvement was observed. Subsequently the cyclosporin A and prednisone doses were reduced progressively and a complete cure was achieved after 7 months of treatment. Three years later no relapse has occurred on a maintenance therapy consisting of 3 mg/kg/day of cyclosporin A and 6 mg/day of prednisone.

KEY WORDS

pyoderma gangrenosum, treatment, cyclosporin A, prednisone

INTRODUCTION

Pyoderma gangrenosum (PG) is a rare disease of unknown etiology and slowly progressive course. It is characterized by sterile inflammatory lesions, sometimes granulomatous and sometimes pustular or ulcerative, which show a tendency to scar at the center and to extend centrifugally. The course is chronic with alternating exacerbations and remissions, and vast ulcerations several decimeters in diameter may develop over months or years, without apparent precipitating factors. In 50 to 75% of cases PG is associated with a systemic disease, most often ulcerative colitis, Crohn's disease, polyarthritis or a gammopathy.

Immunologic mechanisms have been shown to be

involved in the pathogenesis of PG: this explains the successful use of cyclosporine A (CsA), which is characterized by a potent activity mainly on cell-mediated immunity but also on antibody-dependent immunity and chronic inflammatory reactions. CsA in the treatment of PG has been well documented (1-3).

The first case of PG treated with CsA was described by Curley et al. in 1985 (4); many other reports have followed (5-7). The literature sometimes describes therapeutic successes with low dosages of CsA (3-4 mg/kg/day (18,9)), while other authors suggest the need for a dose of 7-10 mg/kg/day (10-12), also in association with systemic steroids (4,6,9,10,13).

The following description is a case report of PG

associated with IgA paraproteinemia which was not amenable to standard therapy, but was cured with CsA at dosage of 10 mg/kg/

day in association with prednisolone 30/mg/day.

CASE REPORT

A 58-year-old woman presented manifestations of pyoderma gangrenosum (PG) at various sites since 1973, with alternate phases of remission and recrudescence, for which she was hospitalized numerous times. In February 1978 for the first time an IgA paraproteinemia with type k light chain was demonstrated to be associated with the PG. On that occasion corticosteroid therapy was instituted, which led to a remission of the cutaneous symptoms in 5 months. One year later, despite maintenance of corticosteroid



Fig. 1. Pyoderma gangrenosum: ulceration on the leg



Fig. 2. Pyoderma gangrenosum: ulceration on the lower abdomen



Fig. 3. Atrophic scar on the leg after treatment



Fig. 4. Atrophic scar on the abdomen following the treatment
therapy, the lesions reappeared, and in the same year, in addition to the monoclonal IgA anomaly, IgG and IgM levels fell and Bence Jones protein was detected in the urine. Microscopic examination of bone marrow obtained

by a needle biopsy of the sternal bone demonstrated hyperplasia of all the series, particularly the megakaryocytic one, and the presence of numerous plasma cells. Bone biopsy of the left iliac crest did not confirm the diagnostic suspicion of multiple myeloma and suggested a mild reactive medullary infiltration. A vast PG ulceration developed subsequently at the biopsy site, which proved refractory to treatment.

Until 1981 the cutaneous symptoms alternately deteriorated and partially regressed. The patient was given clofazimine, sulfones, steroids and cycles of antimetabolic therapy in successive periods. In January 1991 extensive lesions developed on the patient's left leg (photo n.1) and abdomen (photo n.2). In view of the failure of the previous treatments CsA was administered orally at the dose of 5 mg/kg/day in two divided doses combined with prednisone 30 mg/day. As the clinical picture remained unchanged, the dose of CsA was progressively increased up to 10 mg/kg/day over the subsequent 12 weeks, with a marked improvement in the symptomatology. Following the increase in cyclosporin blood levels (537 mcg/L) the drug dose was reduced to 7.5 mg/kg/day. The continuous clinical improvement allowed progressive reduction of the CsA and prednisone doses to 4 mg/kg/day and 18 mg/day, respectively. In August 1991 the patient was completely cured (Fig. 3,4) and IgA paraproteinemia had not developed into multiple myeloma. To date (February 1994) no clinical relapses have occurred with maintenance therapy of CsA 3 mg/kg/day and prednisone 6 mg/day.

COMMENT

Immunologic mechanisms have been shown to be involved in the pathogenesis of PG: this explains the successful use of CsA, which is characterized by a potent activity mainly on cell-mediated immunity but also on antibody-dependent immunity and chronic inflammatory reactions (1-3).

After the first report by Curley et al. in 1985 (4) numerous cases of relapsing PG resistant to the usual therapies have been treated successfully with CsA (6,7,10,11). Although the mechanism of action of CsA in PG is still unclear, the drug is known to act principally by inhibiting immune-mediated inflammatory events (15). It may be speculated that this inhibition affects not only specific immunologic mechanisms (helper T and cytotoxic T lymphocyte dependent activation of IL-2) but also unspecific effector cells such as histiocytes and macrophages. In addition, the expansion of suppressor T lymphocytes is enhanced.

The efficacy of CsA in PG thus represents further evidence, although indirect, of the involvement of immunologic mechanisms in the pathogenesis of this disease (9,12).

Our case of PG is similar to the one described by Penmetcha et al. (5) with regard to both the severity of the cutaneous lesions and the concomitant paraproteinemia IgA with type k light chain. In our case, unlike in those reported by other authors (8,9,13,15), doses of under 10 mg/kg/day were found insufficient to control the cutaneous symptomatology. CsA therapy did not cause adverse reactions in our patient.

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