

Treatment of Ocular Cicatricial Pemphigoid with Intravenous Gammaglobulin

Sir,

Cicatricial pemphigoid is a rare chronic vesicular bullous disease that primarily affects mucous membranes (1). Skin involvement may be seen in 20% of patients. Approximately 70% of the patients have ocular lesions, and scarring, which is rarely seen in bullous pemphigoid, is a frequent feature of the ocular lesions in cicatricial pemphigoid (2).

The initial symptom of ocular cicatricial pemphigoid (OCP) is unilateral chronic conjunctivitis with burning, irritation, and excess tearing. Within 2 years the disease is usually bilateral. OCP appears to be a slowly progressive disease that can lead to blindness. The destructive process of OCP is caused by fibrosis beneath the conjunctival epithelium. If untreated, the cornea can become completely scarred, vascularized and keratinized.

Immunofluorescence studies of patients with cicatricial pemphigoid have shown that practically all patients have *in vivo* fixed immunoglobulin, usually IgG and IgA and complement at the basement membrane zone of the lesions and in perilesional mucosa and skin (3, 4).

Systemic steroids can be of benefit in relieving symptoms and inhibiting disease progression. Treatment protocols including steroids, dapsone, azathioprine and cyclophosphamide have been reported to be effective (5). The outcome is unpredictable in the individual case, as some cases progress to blindness in spite of the above-mentioned treatment modalities. We describe a severe case of cicatricial pemphigoid where disease progression was arrested by treatment with intravenous gammaglobulin.

CASE REPORT

A 66-year-old man was referred in January 1994 with a 4-month history of a blistering dermatosis involving arms, legs and trunk. He had also suffered from conjunctival inflammation and red eyes for 6 months, starting in the left eye. He complained of discomfort on swallowing.

Examination showed a widespread bullous dermatosis on the trunk, extremities and in the face. Early bilateral symblepharon formation and trichiasis with scarring lesions in the conjunctivae. There were erosions of the oral mucosa. Full blood count, erythrocyte sedimentation rate, electrolytes, plasma immunoglobulins and antinuclear autoantibody screen were normal.

Histological examination of a skin biopsy and oesophageal mucosa showed a picture consistent with the diagnosis of pemphigoid. The diagnosis was further supported by indirect immunofluorescence staining of patient serum, which showed binding of antibodies of the IgA and IgG isotype at the epithelial site of salt-split normal human oral mucosa used as an antigen in the staining procedure.

The patient began treatment with 60 mg prednisone od and artificial tears; after 3 weeks of the therapy the disease exacerbated and prednisone was increased to 100 mg od and azathioprine 150 mg d⁻¹ was added. Gastroscopy showed erosive esophagitis and ulceration.

The ophthalmological examination at this stage showed profound bilateral conjunctival injection and oedema; on the left side, infiltrations of the cornea (Fig. 1).

At this point – 6 weeks after admission – the disease was still progressive and we added dapsone 100 mg od. One month later cyclosporine eyedrops tds were added. A subsequent reduction of prednisone was followed by increased disease activity.

Azathioprine and dapsone was discontinued and cyclophosphamide 100–150 mg od was introduced with continued administration of pred-

nison. The skin symptoms were almost controlled on this treatment, whereas ocular disease activity was only partially controlled with progressive corneal vascularization in the left eye and subsequent loss of vision. Esophageal stenosis had developed and balloon dilatation was performed. At this stage we decided to start treatment with intravenous gammaglobulin.

In July 1996 he received repeated gammaglobulin infusions (0.4 g kg⁻¹ Gammonativ[®] [Pharmacia, Uppsala, Sweden] daily over 5 days); within 1 week the skin eruption and eye redness stopped. The infusions were repeated after 8 weeks. The therapy was well tolerated. At present, 14 months after the second immunoglobulin infusion, the patient has no symptoms of active disease. He receives a minimal maintenance prednisone dose 10 mg od.

DISCUSSION

The treatment of cicatricial pemphigoid is known to be difficult (1). Our patient responded unsatisfactorily to several treatment regimens, including daily cyclophosphamide, prednisone and dapsone. The therapy resulted in some suppression of the disease activity, but did not prevent formation of new blisters or progressive ocular scarring (Fig. 1).

Intravenous immunoglobulin has proved to be effective in a number of autoimmune diseases, but intravenous immunoglobulin treatment in bullous diseases is still controversial (6, 7). Here, we present a case of severe OCP that responded to treatment with intravenous gammaglobulin.

Urcelay et al. successfully employed intravenous immunoglobulin in two patients with cicatricial pemphigoid without ocular lesions (8). In this report a higher dosage of immunoglobulin (2 g kg⁻¹) was used. But it should be stressed that the different immunoglobulin preparations from different suppliers appear to vary in efficacy.

The exact mechanism of action responsible for the therapeutic immunomodulatory effect of intravenous gammaglobulin is largely unknown, but several non-exclusive mechanisms have been suggested, e.g. neutralization of autoantibodies or superantigens, blockade of Fc-receptors, downregulation of reactive B-cell clones with selection of T-cell clones.

Treatment with intravenous gammaglobulin is expensive compared with other therapies, but it can be a valuable reserve drug for patients with cicatricial pemphigoid, where the disease proves resistant to standard immunosuppressive treatment.

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Fig. 1. (Top) At admission, bilateral conjunctival inflammation, early bilateral symblepharon formation and trichiasis with scarring lesions in the conjunctivae were noticed. (Middle) Six months later the disease was still progressive with corneal vascularization in the left eye and subsequent loss of vision. (Bottom) Ten months after completed therapy with intravenous immunoglobulin no sign of disease activity was seen.

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