

Successful Treatment of Linear IgA Bullous Dermatitis with Mycophenolate Mofetil

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Sir,

Linear IgA bullous dermatosis (LABD) is a rare, acquired, autoimmune, subepidermal blistering disorder combining the clinical features characteristic of dermatitis herpetiformis (DH) and bullous pemphigoid (BP) (1). Chronic bullous disease of childhood is believed to be a variant of LABD. The only apparent difference between the two is the younger age at presentation (2). LABD is characterized by linear deposition of IgA at the basement membrane zone (BMZ) and in some cases by circulating IgA anti-BMZ-antibodies. LABD and chronic bullous disease of childhood generally respond to a combined treatment with sulphones and glucocorticosteroids, but in some patients alternative therapeutic approaches have to be considered.

We describe a patient with LABD who responded to oral mycophenolate mofetil (MMF), a immunosuppressive drug that has also been used successfully in bullous pemphigoid (3–4).

CASE REPORT

In February 1998, a 20-year-old male subject presented himself at our clinic complaining of itching skin lesions around both elbows. Later, the lesions disseminated over the trunk and the extremities, with formation of tense bullae. Our patient had no history of other diseases and presented in a healthy state, with no gastrointestinal symptoms or systemic medication.

On the trunk and the extensor surfaces, erythematous urticarial papules and plaques were occasionally covered with vesicles containing a clear or haemorrhagic fluid that progressed to erosions with haemorrhagic crusts (Fig. 1).

All routine haematological and chemical laboratory parameters were within the normal range.

Histological examination of lesional abdominal skin showed a subepidermal bulla filled with oedema fluid, fibrin, lymphocytes, neutrophilic and numerous eosinophilic granulocytes. A mixed inflammatory infiltrate was found within the dermis.

Direct immunofluorescence examination of perilesional skin showed linear deposition of IgA, IgM and C3 along the BMZ. Indirect immunofluorescence staining with the patient's serum was positive at a titre of 1:40 on monkey oesophagus with IgA anti-basement membrane antibodies and on human split skin (1 mol/l sodium chloride) showing a linear staining pattern at the blister top. No specific IgA-reactivity against human



Fig. 1. Clinical features of the patient with linear IgA bullous dermatosis abdominal skin at the time of first presentation: a tense bulla and erosions are seen.

recombinant BP180-NC16A, ANA, anti-ENA, anti-gliadine- or endomysium antibodies could be found.

Standard systemic therapy with diamino-diphenylsulphone (DADPS) alone or in combination with glucocorticosteroids up to 0.5 mg kg^{-1} body weight was only temporarily effective. Therapy with MMF was therefore initiated, with subsequent clinical improvement. A relapse that occurred after 5 months of therapy with MMF was successfully suppressed by additional high-dose intravenous immunoglobulins (IVIG) administered 3 times at intervals of 6 weeks. The detailed treatment schedule is listed in Table I.

Since May 1999 the skin condition has been stabilized under continuing therapy with 2 g day^{-1} MMF as a single treatment. The lesions healed slowly, with residual local hyperpigmentation. Initially, a reduction of the MMF dosage resulted in exacerbation. Eventually, systemic therapy could be stopped, with no deterioration during a total follow-up period of nearly one and a half years.

DISCUSSION

The clinical, histological as well as serological features in our patient are diagnostic of LABD. The detection of circulating IgA antibodies with epidermal linear staining on human salt-split skin revealed the lamina-lucida type of the disease. However, the antigen specificity of the IgA antibodies found in LABD seems to be heterogeneous. Recent results indicate that the 97-kD-protein (97-LAD), which was initially identified within the lamina lucida of the basement membrane zone represents the extracellular domain of the 180 kD bullous pemphigoid antigen (BPag2, BP180) (5).

Despite this progress in defining the target antigens, the pathogenesis of LABD is still unclear. In rare cases the disease can be induced by drugs, characteristically after exposure to vancomycin (6). Manifestation of chronic bullous disease of childhood is often associated with preceding gastrointestinal or respiratory infections (7). In most cases, LABD follows a chronic course with relapses over years. Although a reduction of disease activity may be observed, complete healing is rare.

As established first-line treatment for LABD, systemic diamino-diphenylsulphone ($100\text{--}150\text{ mg day}^{-1}$) often proves effective. If necessary, combined treatment with glucocorticosteroids has to be considered. Different alternative approaches have been reported in patients with LABD or chronic bullous disease of childhood where the disease was refractory to the standard therapy regimens. These options include cyclosporin, colchicine or intravenous immunoglobulins (8–12).

Recently, a novel immunosuppressive drug has been introduced for prevention of organ rejection in transplantation medicine. In a non-competitive and reversible way, MMF effectively inhibits inosin-monophosphate-dehydrogenase, an enzyme responsible for the *de novo* synthesis of guanosin-nucleotides in lymphocytes. Recently, the success of MMF in the treatment of different autoimmune blistering diseases has been reported (3, 4). MMF 2 g day^{-1} is well tolerated, and only in rare cases are clinically significant signs of drug myelosuppression and hepato- or nephrotoxicity seen. Apart from T-cell inhibition, effects on B-lymphocytes seem to be important for the control of humoral immune responses. In our patient, the disease was effectively stabilized with monotherapy using 2 g day^{-1} MMF. As several attempts at tapering the MMF dose resulted in deterioration of the skin condition before the eventual long-term stabilization, it is unlikely that the additional administration of IVIG at an earlier stage would lead to the remission of the disease. To our knowledge, this is the first case in the literature of successful therapy with MMF in LABD.

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Table I. Clinical characteristics related to the treatment schedule in a patient with linear IgA bullous dermatosis

Point of time	Blisters	Systemic treatment (dosage) ^a
4/98	+++	DADPS (100 mg day^{-1})
5/98	++	DADPS (100 mg day^{-1}) + MP ($0.5\text{ mg kg}^{-1}\text{ day}^{-1}$)
6/98	(+)	DADPS (100 mg day^{-1}) + MP ($0.25\text{ mg kg}^{-1}\text{ day}^{-1}$)
7/98	–	DADPS (100 mg day^{-1}) + MP ($0.13\text{ mg kg}^{-1}\text{ day}^{-1}$)
10/98	+++	DADPS (100 mg day^{-1}) + MP ($0.1\text{ mg kg}^{-1}\text{ day}^{-1}$)
		Change of treatment
		MMF (2 g day^{-1})
11/98–1/99	+, (+)	MMF (2 g day^{-1})
3/99	++	MMF (2 g day^{-1})
		Change of treatment
		MMF (2 g day^{-1}) + 1st cycle
		IVIG (2 mg kg^{-1})
4/99–5/99	+, (+)	MMF (2 g day^{-1}) + 2nd and 3rd cycles IVIG (2 mg kg^{-1})
8/99–11/00	– ^b	Maintenance therapy
		MMF (2 g day^{-1})
11/00	–	End of systemic therapy
03/02	–	Follow-up after 17 months

^aLocal therapy consisted of antiseptic ointments (fusidic acid) and intermittent applications of betametasolone-valerate.

^bReduction of mycophenolate mofetil (MMF) dosage resulted in deterioration.

DADPS: diamino-diphenylsulphone; IVIG: intravenous immunoglobulins; MP: methylprednisolone.

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