

LETTER TO THE EDITOR

Combined therapy with low-dose omalizumab and intravenous immunoglobulin for severe atopic dermatitis. Report of four cases

Editor

Atopic dermatitis (AD) is a multifactorial disease. Among the various immunological alterations detected in atopic patients, two are fundamental to explain this disorder of the immune regulation: an increase in serum immunoglobulin E (IgE) levels and expansion of the Th₂ lymphocyte subpopulation with secretion of cytokines.¹

Most patients are satisfactorily managed with steroid-based strategies, but patients with extensive, severe, persistent disease often require systemic agents for adequate disease control.² Although a wide variety of systemic treatments is available, some patients with severe AD remain unresponsive to any of them.

Herein, we describe a case series of combined therapy with low-dose omalizumab and intravenous immunoglobulins (IVIG) for severe treatment-resistant adult AD (Fig. 1a). Table 1 shows their epidemiological and clinical characteristics. A minimum disease severity score (SCORAD) of 50 was present in all patients. Baseline serum IgE level was registered before starting the treatment. All

patients had high serum IgE levels (ranging between 2,058 and 35,346 IU/mL).

Patients received a 3-h infusion of IVIG 10 g (Flemogamma®; Instituto Grifols, Barcelona, Spain) and omalizumab 150 mg subcutaneously (Xolair®; Novartis Farmaceutica, Barcelona, Spain) every 2 weeks in the hospital. After 2 months of treatment, two patients experienced worsening of their prior asthma and allergic rhinitis and their omalizumab dose was subsequently increased to 300 mg subcutaneously every 2 weeks. Clinical assessments and laboratory examinations were performed at each visit. Clinical improvement was defined as a reduction in at least 50% of the baseline SCORAD after 6 weeks of treatment. Adverse effects were recorded at each visit.

Three of the four patients experienced a significant clinical improvement and a reduction in at least 50% of their SCORAD after 6 weeks of treatment (Fig. 1b). Continuous 3-month therapy with omalizumab and IVIG reduced a 50% or more pre-treatment serum IgE levels in all patients. Treatment was well tolerated and none of the patients suffered any serious adverse event. The fourth patient did not find any improvement after 4 months and treatment was discontinued.

Omalizumab is a recombinant humanized anti-IgE monoclonal antibody recently used in mono-therapy to treat patients with refractory severe AD although its results are controversial.^{1,3-6} The recommended dose of omalizumab is related to the patient's

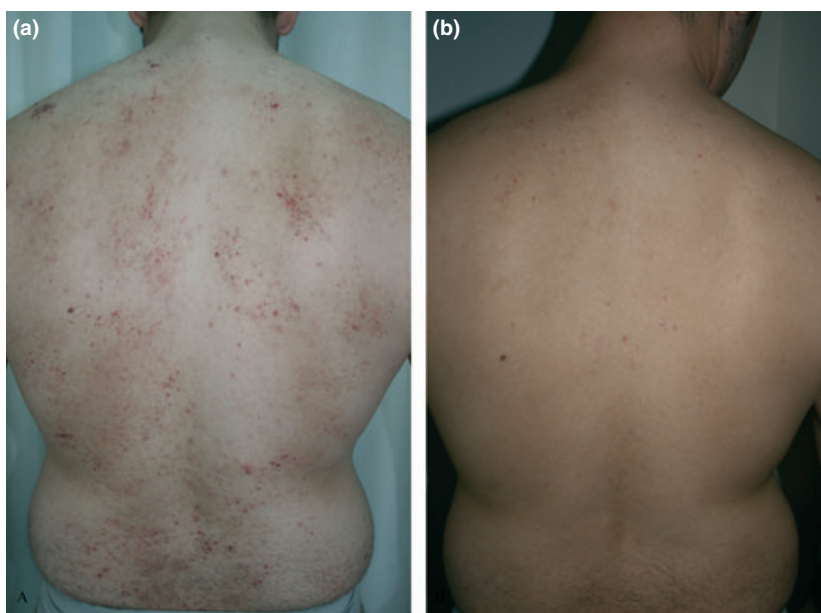


Figure 1 (a) Patient's number 2 clinical picture before starting combined therapy with low-dose omalizumab and IVIG. (b) Patient's number 2 clinical picture after 6 weeks of treatment.

Table 1 Patient's epidemiological and clinical characteristics

	Patient 1	Patient 2	Patient 3	Patient 4
Sex, age (years)	M, 35	M, 15	M, 24	F, 32
Weight	75 kg	65 kg	78 kg	69 kg
Comorbidities	Allergic asthma	Allergic asthma	Allergic asthma	Allergic asthma
History of AD	Since adolescence	Since childhood	Since childhood	Since childhood
Prior treatments	Topical and oral corticosteroids Topical CNI CyS 200 mg/day 12 months MM 2 g/day 9 months NBUVB 15 sessions Cumulative dose 11 J/cm ² Efalizumab 5 months	Topical and oral corticosteroids Topical CNI CyS 200 mg/day 6 weeks MM 2 g/day 15 months NBUVB 25 sessions Cumulative dose 18 J/cm ² Mite and pollen immunotherapy	Topical and oral corticosteroids Topical CNI CyS 200 mg/day 4 months MTX 15 mg/week 5 months MM 2 g/day 9 months AZT 1 g/day 6 months Efalizumab 6 months	Topical and oral corticosteroids Topical CNI CyS 200 mg/day 5 months MTX 15 mg/week 6 months MM 2 g/day 12 months AZT 1 g/day 9 months –
Baseline serum IgE level	35,346 IU/mL	15,632 IU/mL	2,150 IU/mL	2,058 IU/mL
Serum IgE level after 3 months of treatment	998 IU/mL	1,780 IU/mL	1,070 IU/mL	1,034 IU/mL
SCORAD index pre-treatment	67 (80% ABS)	73.5 (65% ABS)	61 (50% ABS)	71 (70% ABS)
SCORAD index after 3 months of treatment	16	35	No lesions	52
Dose omalizumab/dose IVIG and duration	150 mg/10 g, both every 2 weeks, still using	150 mg/10 g, both every 2 weeks for 2 months, then 300 mg/10 g, each 2 weeks, still using	150 mg/10 g, both every 2 weeks, still using	150 mg/10 g, both every 2 weeks for 2 months, then 300 mg/10 g every 2 weeks, withdrawal after 4 months of treatment
Adjunctive treatment	MTX 10 mg/week first 2 months Topical and oral steroids, oral antihistamines and emollients	Topical and oral steroids, oral antihistamines and emollients	Topical and oral steroids, oral antihistamines and emollients	MTX 15 mg/week Topical and oral steroids
Response and outcome	Improvement at 6 weeks, sustained after 12 months of treatment	Improvement at 4 weeks, sustained after 8 months of treatment	Improvement at 6 weeks, sustained after 7 months of treatment	No response, withdrawal after 4 months of treatment
Adverse effects	Irritation at the injection site of omalizumab	No adverse effects	Episode of hypotension after the first dose	Eczema herpeticum during the treatment

M, male; F, female; CNI, calcineurin inhibitors; CyS, cyclosporine; MTX, methotrexate; MM, mycophenolate mofetil; NBUVB, narrow band UVB; AZT, azathioprine; ABS, affected body surface area.

body weight and serum IgE levels.⁷ The lack of efficacy noted by some authors may be due, at least partly, to a non-adjusted dose of omalizumab to the patient's serum IgE levels.^{3,7} A way to avoid this lack of efficacy in patients with high serum IgE levels is to increase omalizumab dose with a parallel increase in adverse effects and treatment costs. Another alternative would be to associate an adjuvant treatment that acts via a different mechanism and may work synergistically.

The role of IVIG in severe AD has been evaluated in a few anecdotal reports with inconclusive results.^{8–10} Current data suggest that IVIG can improve skin scores in childhood AD when used as mono-therapy, although mono-therapy with IVIG does not appear

to have the same effect in adult patients.⁸ There is strong indirect evidence that IVIG should be used as an adjunctive therapy in the treatment of severe adult AD.^{8–10} The recommended treatment dose of IVIG is 0.5–2 g/kg in single or multiple doses, although one course of IVIG seems to be insufficient to modulate the course of severe AD. The main limitation to the use of IVIG is its price.⁹ Drug costs may be reduced using adjunctive low-dose IVIG.

Evidence for efficacy of either of these agents in mono-therapy is controversial, however, the use of this combined therapy may offer a useful therapeutic approach to be considered in patients with refractory AD, even in patients with high serum IgE levels.

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