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Title page

Personalized treatment of severe atopic dermatitis in a child: a ten-year follow-up.

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To the Editor,

A 4-year-old-boy with a history of persistent rhinitis and milk and/or egg induced anaphylaxis was first referred to our Allergy Unit in 2008 because of severe atopic dermatitis (AD) since the age of one month. The physical examination was remarkable due to lichenified plaques, scaly and excoriated patchy papules (Figure 1). Moreover he complained of persistent generalized itchiness, with sleeping difficulties which greatly affected his quality of life.

Unfortunately, the severity of the eczema (SCORAD 35) at the first clinical examination did not allow for performing a skin-prick test with common inhalants and food allergens. Laboratory tests showed positive serum specific IgE to house dust mites (HDM)>100 KU/l (Dermatophagoides pteronissinus and farinae), milk 12 KU/l, and egg white to a lesser extent 2 KU/l. He had already been avoiding dairy and egg products since the age of 7 months because at that time he suffered from anaphylaxis immediately after eating a cookie containing egg and milk. Conventional treatments of atopic dermatitis with regular topical application of moisturizing products,

oral antihistamines, topical and systemic corticosteroids showed only a partial recovery from birth to 4 years of age. In particular, from 3 to 6 years he was treated with frequent cycles (at least 1 cycle/month) of oral corticosteroids. For that reason, at the beginning of our childcare management we started on topical tacrolimus, but after 3 months it was discontinued due to lack of response. When he was 6 years old, he was started on cyclosporine (CsA) at a dose of 5 mg/kg/die for 9 months. Every 15 days for the first month and successively, once a month, the CsA blood level, transaminases, creatinine, electrolytes and blood glucose levels were checked. Blood pressure was also monitored in order to promptly detect possible side effects of CsA treatment. Oral CsA was effective in improving the AD severity (SCORAD from 35 to 20) and reducing the use of systemic corticosteroids. However, the patient showed a higher rate of infections (especially of the upper airways, about 14 a year) and had complicated chickenpox. Moreover, it was not possible to maintain blood CsA levels within a normal range even with therapeutic dose adjustment. After CsA suspension due to the above-mentioned side effects, a flare-up of AD occurred again from systemic corticosteroid abuse.

Suspecting a possible role of HDM allergy as a co-factor of AD severity in our patient, we discussed with his family the opportunity of starting HDM-sublingual immunotherapy (SLIT)¹.

Despite the high level of specific IgE to HDM, after 6 months of HDM-SLIT, there was no further improvement in the AD, although his rhinitis improved. For this reason, we decided to complete a 3 years cycle of HDM SLIT.

At 8 years of age, an attempt was made to reintroduce hen's eggs in his diet. We decided to start with the reintroduction of egg instead of milk because of the lower egg s-IgE level. The egg intake did not provoke IgE-mediated reactions as in the past, instead there was a progressive worsening of his AD. After 4 months he was put on an egg-free diet again.

From 8 to 12 years, he was treated with standard therapy without any long-term or satisfactory relief from the symptoms.

At 12 years of age, the patient had a further worsening of his AD. Laboratory tests were repeated showing IgE levels of 750 UI/l with HDM specific levels >100 kU/l and milk 5 KU/l.

An anti-IgE treatment was proposed to his parents and as it is an off label therapy, their written informed consent was obtained, after which he started treatment with 300 mg omalizumab (Xolair) subcutaneously every 4 weeks, in addition to sustained treatment with antihistamines and topic corticosteroids (beclomethasone dipropionate).

In order to evaluate the clinical efficacy of omalizumab therapy, the AD score (SCORAD) was monitored at each visit (Figure 2).

Omalizumab treatment lasted from October 2014 to January 2015 (fig.2).

After three injections of omalizumab, the patient showed an excellent clinical response, as demonstrated by the 50% SCORAD reduction (SCORAD from 60 to 30) with improvement in his quality of life. He did not suffer from any adverse effects related to omalizumab.

Two years after stopping anti IgE treatment he is now on antihistamines and topic corticosteroids and still has a good quality of life (restful sleep).

AD is a chronic inflammatory pruritic skin disease⁴ with a negative impact on the quality of life. The pathophysiology of AD is the product of a complex interaction between genes, environments, infectious agents, defects in skin barrier function, and immunologic responses. Activation of T lymphocytes, dendritic cells, macrophages, keratinocytes, mast cells, and eosinophils are all characteristic of AD skin inflammatory responses⁵.

According to the current guidelines³, AD is treated with topical agents, including bland emollients, topical steroids, tacrolimus and pimecrolimus, and oral agents such as systemic corticosteroids, antihistamines and cyclosporine in proportion to the clinical severity of AD. However, severe or recalcitrant AD does not often respond to various conventional therapies. Even though omalizumab has recently been used as a potential new systemic treatment for recalcitrant severe AD², it is still considered an off-label treatment.

AD pathogenesis is very complex, as mentioned above, and the response to therapy may be influenced by individual immunological responses, possibly making personalized strategies mandatory.

We have described a common case of severe AD, which in our opinion is interesting because it is a long-term example of management of such a disease through choosing a personalized therapy because of lack of response to more conventional treatments.

This case underlies the chronic evolution of such a disease, in fact our patient was evaluated with periodical follow-up visits for ten years. Over this time he was administered topical treatments with emollients and steroids, oral steroids, topical tacrolimus, oral cyclosporine and oral immunotherapy with HDM without any improvement (Fig. 3). Finally, he

showed a rapid response with anti IgE right from the very start of the treatment. We cannot demonstrate that the AD improvement was due to omalizumab alone instead of being a natural evolution of the disease, however our aim is to describe our long-term management of the disease.

Omalizumab appears to be a safe and well-tolerated treatment with clinical benefits in this patient with severe AD refractory to other systemic treatments; nevertheless, recommendation for its use in clinical practice requires evidence from randomized controlled trials².

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