

Cyclosporine treatment decreases the percentage of cutaneous lymphocyte antigen (CLA)+CD4+ T cells in children with severe atopic dermatitis

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Key words: atopic dermatitis; cyclosporine; CLA+ T cell.

Skin-homing T cells expressing cutaneous lymphocyte antigen (CLA) are important in the pathogenesis of atopic dermatitis (AD) (1). Cyclosporine, which controls cytokine production by T cells and regulates their activation, is safe and effective in the treatment of severe AD (2, 3). The effect of this drug on circulating CLA+ T cells in AD, however, is not known. We therefore evaluated the effect of cyclosporine treatment on clinical outcome and CLA+ T cells in children with AD.

Ten children with severe, lichenified skin lesions [severity scoring of atopic dermatitis (SCORAD) index > 50], refractory to topical steroid therapy were treated with cyclosporine (5 mg/kg/day), while 10 children with AD were treated with thymopentin (50 mg, 3 times/week), for 6 weeks. None of these 20 patients had used any systemic steroids for at least 6 months prior to the study. They were compared with 11 healthy children as age- and sex-matched controls, with no history, symptoms or signs of AD or any other respiratory allergic disease. Clinical outcome was monitored by the SCORAD index (4). Peripheral blood T-lymphocyte subpopulations, including CLA+ T cells, were assayed by flow cytometry.

The percentages of peripheral blood CD4+CLA+ and CD3+CLA+ T cells were significantly higher in children with AD before treatment than in controls. The SCORAD index was decreased

significantly after treatment with cyclosporine or thymopentin. Cyclosporine treatment significantly reduced the percentages of CD4+CLA+ (Fig. 1) and CD3+CLA+ T cells ($P < 0.05$), but not the percentages of CD3+, CD4+, CD8+, and CD8+CLA+ T cells. In contrast, treatment with thymopentin did not affect CLA+ T cells.

In this study, we demonstrated that the percentage of CD4+CLA+ T cells was significantly higher in peripheral blood mononuclear cells (PBMCs) of children with severe, chronic AD than in those of healthy children. CLA participates in selective transendothelial migration of

memory/effector T cells by binding to E-selectin on endothelial cell layers after activation by proinflammatory cytokines (5, 6). Although CD4+ T cells have been regarded as important in the pathogenesis of AD, we found that the percentage of peripheral blood CD4+ T cells did not differ between AD children and healthy children.

We also found, in combination with markedly improved clinical symptoms, a significant decrease of CD3+CLA+ and CD4+CLA+ T cells after treatment with cyclosporine, except for CD8+CLA+ T cells, although treatment with thymopentin did not affect

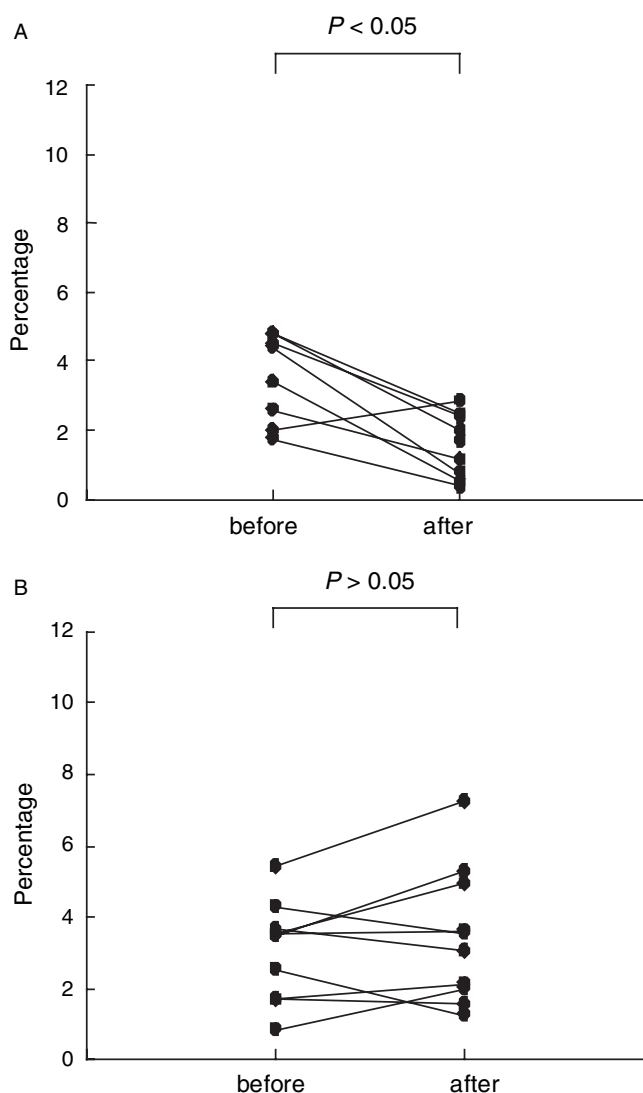


Figure 1. Changes in CD4+CLA+ T cells in children with AD after treatment with (A) cyclosporine or (B) thymopentin. The percentage of CD4+CLA+ T cells decreased significantly after 6 weeks of treatment with cyclosporine ($P < 0.05$), but not thymopentin.

those cells. These results may be the first report on decrease of CLA expression from peripheral blood CD4+ T cells after treatment with cyclosporine in children with atopic dermatitis.

In conclusion, CD4+CLA+ T cells may be important in the pathogenesis of severe AD and in the mechanism of action of cyclosporine.

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The accuracy of the diagnosis of suspected macrolide antibiotic hypersensitivity: results of a single-blinded trial

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Key words: allergy; macrolide hypersensitivity; oral drug provocation test.

Macrolide antibiotics are characterized by a chemical structure including a large lactone ring

bearing two sugar side chains.

According to the number of side chains linked to the ring, they are classified into macrolide antibiotics at 14

(erythromycin, troleandomycin, roxitromycin, dirithromycin, clarithromycin), 15 (azithromycin) and 16 (spiramycin, josamycin, midecamycin) atom lactone rings.

Allergy to macrolide antibiotics is reported to be exceptional (0.4–3% of treatments) (1), but there is little information in the literature to chalk out a diagnostic strategy. Furthermore, there are few published series (not more than 40 cases) and therefore underlying immuno-allergic mechanisms have rarely been evaluated.

The most frequently adopted attitude by the physician treating a patient with suspected allergy to a macrolide is the definitive withdrawal of the whole class of macrolide antibiotics. However, in the course of an antibiotic treatment, whatever the molecule involved, reactions mimicking allergic symptoms without any underlying allergic mechanism directed against the drug are frequent. There are real differential diagnoses and

Suspected hypersensitivity reactions to macrolide antibiotics can rarely be confirmed by an oral drug provocation test.

it is necessary to be able to bring these to mind and to demonstrate them (2).

In our study, we have analysed the clinical and allergy-testing data of all the outpatients referred to our clinic over the last 5 years for suspected hypersensitivity to macrolide antibiotics after drug intake.

Of 139 patients referred to the Drug Allergy Unit of the University Hospital of Montpellier between October 1996 and December 2001, 107 patients (83 women, 24 men, aged 3–75 years) accepted to undergo a single-blinded oral drug provocation test (DPT) with the suspected macrolide (Table 1). According to the referring physician, they had a clinical history of allergy to different macrolide antibiotics. The delay between the reaction and the carrying out of the DPT varied between 6 and 93 months. The reason for the prescription was always an upper respiratory infection, not always febrile. The clinical signs were mainly mucocutaneous manifestations (26 maculo-papular eruptions, 41 urticarias and 16 angioedemas) but there were also systemic manifestations (five anaphylaxis). Eight patients could not specify symptoms (Table 1).

Oral DPT for all patients and, for some of them, skin tests (prick tests and intradermal tests) with the available injectable macrolide antibiotics (spiramycin, erythromycin) were carried out under strict hospital surveillance. Skin tests were performed according to the EAACI guidelines (3) by prick tests at the concentration of 10 mg/ml, followed by intradermal tests at the concentration of 0.1 mg/ml, then 1 mg/ml and finally 10 mg/ml if previous tests were negative. Oral DPTs were performed according to a previously described protocol (4) with increasing doses of the suspected causal macrolide antibiotic which was administered every 30 min, starting with the dose of 1 mg, for a total of six doses, until reaching the cumulative daily therapeutic dose. They were single-blinded and carried out very progressively under strict clinical surveillance. After having ingested the last dose, patients continued to be supervised for a further 2 h. Following this period, they were then directed to their domicile with a prescription of glucocorticoids and oral antihistamines to take in case of delayed cutaneous reactions. They also received our full