

Correspondence

Treatment of severe refractory adult atopic dermatitis with ustekinumab

Editor,

A 21-year-old Caucasian woman presented in March 2003 with a longstanding history of atopic dermatitis (AD) in addition to allergic contact dermatitis that emerged in response to paraphenylenediamine and had been diagnosed one year earlier (Fig. 1). She had undergone topical treatment with corticosteroids and calcineurin inhibitors with little improvement in her condition. Over the next six years, the patient underwent various treatments such as intermittent cycles of oral cyclosporine (4 mg/kg/day), ultraviolet B narrowband therapy (three times weekly), oral prednisone (1 mg/kg/day), and subcutaneous efalizumab (0.7 mg/kg initially followed by 1 mg/kg).

In December 2009, the patient began treatment with ustekinumab administered in a single dose of 45 mg. Two weeks later, the patient reported a substantial clinical

improvement in her condition, especially in the pruritus. This improvement was rated on a 10-point visual analog scale (VAS). The VAS value before treatment was 9. One month later, the lesions had cleared and only hyperpigmented residual lesions presented on physical examination. The VAS value of pruritus was 0. A second 45-mg dose was administered at that point, according to the recommended dosage in psoriasis (at weeks 0 and 4, followed by every 12 weeks). The patient has currently completed month 12 of treatment. Her condition remains improved and pruritus is absent (Fig. 2).

Patients with AD often require systemic immunomodulatory and immunosuppressive agents (cyclosporine, azathioprine, methotrexate, and mycophenolate mofetil), but the use of these agents is limited by their potential toxicity and inadequate patient responses. Ustekinumab is a fully human immunoglobulin G1 (IgG1) monoclonal antibody that binds with high specificity to the p40



Figure 1 Generalized atopic eczema on the arms shows signs of itching and scratching



Figure 2 The eczema and pruritus are completely controlled after 12 months of continuous treatment

subunit of interleukin-12 (IL-12) and IL-23. These immunoregulators are thought to play a role in immune-mediated inflammatory diseases. IL-12 is a heterodimer, consisting of p40 and p35 subunits. The IL-12 p40 subunit is shared by IL-23, another heterodimeric cytokine. IL-23 promotes the development and proliferation of T cells producing IL-17 (Th17). IL-12 has the capacity to regulate the differentiation of naive T cells into Th1 cells and the differentiation of CD8+ T cells into mature cytotoxic T lymphocytes.

The exact etiology of AD is not completely understood. It was originally thought to result from a pathological Th2 immune response in the acute phase, with a switch toward a Th1 phenotype during the chronic phase.¹ Classically, immunological theories have relied on the presence of two separate Th cell pathways of inflammation: Th1 (cell-mediated) and Th2 (humoral). Recent studies have provided evidence for a third effector CD4+ Th pathway, separate from Th1 to Th2. These T cells have been designated Th17. Naive T cells are polarized to Th17 cells in the presence of transforming growth factor- β 1 (TGF- β 1), IL-6, and IL-23. IL-23 is produced by antigen-presenting cells and promotes the expansion and survival of Th17.² Th17-associated cytokines, IL-17 and IL-22, have many proinflammatory effects in a wide variety of cells, including keratinocytes, macrophages, and endothelial cells. IL-17 is highly expressed in autoimmune disorders such as Crohn's disease, multiple sclerosis, AD, psoriasis, and rheumatoid arthritis. The IL-17/IL-23 pathway appears to be involved in the maintenance of these chronic inflammatory diseases.³

In 2003, Toda *et al.*⁴ found elevated levels of IL-17 in acute lesions in AD. Koga *et al.*⁵ demonstrated that the percentage of Th17 cells was increased in peripheral blood of AD patients compared with a healthy group and was associated with the severity of AD. Immunohistochemistry of skin lesions demonstrated a higher percentage of Th17 cells in acute than in chronic lesions. These data suggest the participation of Th17 cells in the development of AD.

A case of alopecia universalis with agminated lentiginosis and multiple café-au-lait macules: a synchronous coincidence?

Editor,

Alopecia universalis is characterized by the rapid and complete loss of all hair from the scalp, face, eyebrows, and eyelashes, and from other hairy areas of the body.¹ Agminated lentiginosis is a rare pigmentary disorder characterized by the presence of multiple lesions of simple lentigo localized to a particular body segment, often cor-

The presence of Th17 cells in AD and psoriasis suggests the existence of a common pathway in the development of both inflammatory disorders. The binding between ustekinumab and IL-23 prevents the upregulation of Th17 cells. Therefore, ustekinumab may represent a good therapeutic option not only in psoriasis but also in AD. Our patient with longstanding AD showed a striking improvement after one month of ustekinumab therapy. The onset of action began in the first week of treatment, and the excellent response was maintained at week 52. In summary, we report the first case of the successful management of refractory AD in an adult with a new biologic therapy, ustekinumab.

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responding to one or more dermatomes. Histologically, the lesions have the typical features of lentigo.² Café-au-lait macules (CALMs) are discrete, well-circumscribed, round or oval, uniformly pigmented patches.³ We report an 8-year-old girl with an unusual combination of alopecia universalis, multiple CALMs, and diffuse numerous lentigines on the scalp, neck, and trunk bilaterally in a peppered distribution.

An 8-year-old girl visited our dermatologic clinic with a four-year history of alopecia universalis and progressive