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Dupilumab improved atypical fibrotic skin plaques in atopic dermatitis

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Case Report

Atopic dermatitis (AD) is characterized by dominance of T helper type 2 (Th2) cytokines associated with infiltration of inflammatory cells.¹ Th2 cytokines, especially IL-13, also contribute to fibrotic remodeling of the skin, as shown in murine AD models.² Dupilumab is an interleukin (IL)-4 receptor- α antagonist, which blocks both IL-4 and IL-13 signaling, and is approved for the treatment of moderate to severe AD.³ Dupilumab is effective for treating AD symptoms such as eczema and pruritus; however, its efficacy for skin fibrosis remains unknown. We herein report that dupilumab successfully treated atypical AD-associated plaques with marked fibrosis on histology.

A 50-year-old female with a past history of childhood asthma presented with a 25-year history of severe AD recalcitrant to conventional therapy. Laboratory investigations revealed eosinophilia (14.7% of total white blood cell count, 1,440 eosinophils/mm³; normal, 70-450), elevated levels of serum Th2 chemokine, thymus and activation-regulated chemokine (TARC, 11,740 pg/ml; normal, <450) and total IgE (20,000 IU/ml; normal, <170). In addition to eczematous lesions typical to AD, multiple red, hard, smooth plaques on the neck were noted (Fig. 1A). A skin biopsy taken from the plaque showed irregular thickening of the epidermis, spongiosis, dense inflammatory cell infiltration including eosinophils and focal fibrosis in the dermis (Fig. 1B). Masson trichrome staining showed that collagen fibers in the papillary and reticular dermis were markedly increased (Fig.1C). Other conditions that caused skin fibrosis such as systemic sclerosis and morphea were not supported by clinical or pathological findings of this case. Therefore, the neck plaques were diagnosed as AD-associated atypical eczematous plaques with fibrosis, probably caused by habitual scratching by the patient.

The patient had been refractory to conventional therapies, such as class 2 topical corticosteroids, oral ciclosporin (2 mg/kg/body), and excimer light. Therefore, we decided to treat the patient with dupilumab (300 mg subcutaneous injection every other week). The typical AD clinical manifestations such as eruptions and pruritus of the back, elbows, and face remarkably improved. Intriguingly, the neck plaques almost completely resolved 8 weeks after the initiation of dupilumab treatment. (Fig. 1D) The TARC and total IgE levels decreased to 167 pg/ml and 3,281 IU/ml at 24 weeks after the initiation of dupilumab.

In this report, we demonstrate remarkable improvement of AD-associated chronic fibrotic skin lesions by dupilumab treatment. Fibrotic remodeling of the skin is a feature increasingly recognized in human AD, and IL-13 is considered as a major stimulator of inflammation and fibrosis in animal models. Chronic Th2 responses induce excessive deposition of extracellular matrix in fibroblasts and activate tissue-repair macrophages.⁴ IL-4 and IL-13 can activate these macrophages and may be important for the development of remodeling with epithelial alarmins like IL-33.⁴ In addition, IL-4 and IL-13 are known to be related to late fibrosis in morphea, and these cytokines upregulate collagen synthesis and inhibit collagenase activity.⁵ Dupilumab is proposed to be a candidate for treating other fibrotic diseases, such as morphea.⁶ As sustained Th2 responses trigger tissue fibrosis, our observation may be extensible to other chronic allergic diseases that accompany fibrosis such as asthma.⁷ This case provides clinical evidence that dupilumab has the potential to improve skin fibrosis in at least some patients with AD.

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Figure legend

Figure 1. Clinical appearance and histology

(A) Clinical pictures of the neck. The skin biopsy site is indicated by an arrow-head. (B) Histology of a dome-shaped red plaque on the right neck (hematoxylin and eosin stain). Scale bars, 100 μ m. (C) Immunohistochemistry with Masson trichrome stain. The papillary (black box) and reticular (yellow box) dermis. Scale bars, 100 μ m. (D) Clinical pictures of the neck 8 weeks after the initiation of dupilumab treatment.

Figure 1

