

References

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Dupilumab in a child with severe atopic dermatitis and severe asthma—a rare case with severe limbitis and exercise-induced anaphylaxis

Dear Editor,

Dupilumab is a safe and effective treatment in children from 6 to 11 years old with severe atopic dermatitis (AD), which is insufficiently controlled with topical therapy.¹ We present a child with severe AD and atopic comorbidities who showed rapid improvement of AD under dupilumab treatment. However, he developed limbitis, hypereosinophilia, and anaphylaxis. This case report shows it is essential to monitor severe atopic children who are treated with dupilumab for conjunctivitis and eosinophilia.

An 11-year-old boy with severe refractory AD started dupilumab treatment. He suffered from multiple atopic comorbidities, including food allergies with anaphylaxis to cow's milk protein and peanuts, moderate to severe allergic asthma, and allergic rhinitis, treated with beclomethasone/formoterol, ciclesonide, montelukast, antihistamines, azelastine-fluticasone, as well as prednisolone during exacerbations.

After 4 weeks of dupilumab treatment, the Eczema Area and Severity Index (EASI) score improved significantly from 28 to 0.5, and lung function showed an improvement of the Forced Expiratory Volume (FEV1) of 7% pre- and post-bronchial dilatation. After 8 weeks, the patient developed mild conjunctivitis and eosinophilia of $2.66 \times 10^9/L$ (normal: $0.05\text{--}0.50 \times 10^9/L$). Therefore, the next dupilumab administration was postponed for 2 weeks, after which the eosinophil count decreased ($2.02 \times 10^9/L$). The conjunctivitis was treated with dexamethasone eye drops. However, after the dupilumab administration, the eosinophil count increased again to a level of $2.92 \times 10^9/L$, and the patient developed oral allergies as well as urticaria to food products normally tolerated: bread, strawberries, apples, mandarins, and potatoes. Moreover, he developed severe palpebral and bulbar conjunctivitis with limbitis in both eyes, without limbal stem cell deficiency (Fig. 1). Given the severity of the limbitis, dupilumab was discontinued after 20 weeks. Notably, after discontinuation, the allergic symptoms did not resolve. Three

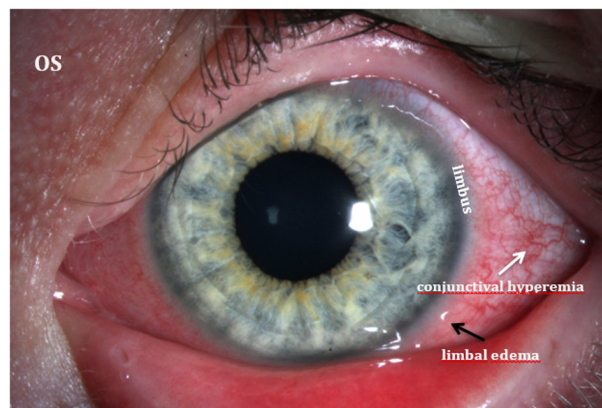


Figure 1 The eye of the patient with limbal edema visualized. This figure shows the left eye of the patient. The limbus is specified, the conjunctival hyperemia is indicated with the white arrow and limbal edema with the black arrow

weeks after the discontinuation of dupilumab, the patient had an anaphylactic reaction with generalized urticaria, angioedema, and wheezing after biking to school during the pollen season, which the patient does regularly without complaints. He was treated with intramuscular adrenaline and intravenous clemastin and hydrocortisone after which the eosinophils dropped to $1.14 \times 10^9/L$. Simultaneously, the new oral allergies resolved.

Our patient developed eosinophilia with oral allergies and urticaria to food previously tolerated under dupilumab treatment. Transient eosinophilia was seen in previous trials in AD, asthma, and chronic sinusitis patients.² A possible explanation is the blockage of IL-4 and IL-13-induced migration of eosinophils from serum to tissue, with accumulation in the serum as a result.² It has been suggested that eosinophilia is associated with elevated IgE, mast cell, and basophil levels, which play an important role in allergic reactions.³ Exercise-induced IgE-mediated anaphylaxis is well known, especially in wheat.⁴ In our patient, there was no relation with food intake but there was with exposure to pollen. Given the associations with eosinophilia and mediators that play an important role in allergic reactions, the hypereosinophilia induced by dupilumab may have caused hypersensitivity to food products and eventually caused an IgE-mediated exercise-induced anaphylaxis triggered by pollen.

Furthermore, our patient developed severe conjunctivitis with limbitis. Conjunctivitis is the most common side effect of dupilumab and is mostly mild.¹ Severe eye symptoms, like limbal involvement, are described in adults but not yet in children.¹ However, it is essential to recognize conjunctivitis with limbal involvement early, since it can lead to limbal stem cell deficiency, which can lead to permanent visual loss.⁵

In conclusion, although dupilumab is a very effective treatment for AD, it is essential to monitor severe atopic children for eosinophilia with possible associated symptoms. Furthermore,

early recognition of conjunctivitis is essential to prevent limbal involvement and to ensure intervention.

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Funding source: None.

Conflict of interest: The authors have no conflict of interest to declare.

doi: 10.1111/ijd.16259

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A case of facial linear focal elastosis with rare clinical features

Dear Editor,

A 93-year-old Asian woman presented with a 2-year history of a solitary, whitish, atrophic, and linear plaque on her right zygomatic arch area (Fig. 1a,b). The lesion was asymptomatic, and she denied any history of facial trauma or surgery. Her

underlying medical diseases included hypertension, type 2 diabetes mellitus, and dyslipidemia for which she was prescribed amlodipine, metformin, and atorvastatin, respectively. Her family history was unremarkable. No accentuation was observed through Wood's lamp examination, and laboratory tests were not performed. Histological examination revealed (i) a solar elastosis in the superficial dermis; (ii) an increase in and aggregation of basophilic, degenerated elastic fibers with a wavy pattern in the mid-dermis; and (iii) fragmented elastic fibers separating collagen bundles on hematoxylin and eosin staining (Fig. 2a,b). Verhoeff–Van Gieson staining was performed to detect elastic fibers, and it revealed numerous thin, wavy, elongated, and fragmented elastic fibers that stained brown to black between the collagen bundles (Fig. 2c). Melan-A staining was also performed to differentiate cutaneous depigmented disorders due to the loss of melanocytes (such as vitiligo); however, it showed normally positive reactions in the epidermal melanocytes of the basal layer (Fig. 2d). Based on the aforementioned findings, she was diagnosed with facial linear focal elastosis (LFE). The patient refused therapeutic intervention.

LFE is a rare dermal elastosis clinically characterized by several asymptomatic, indurated, palpable, yellow, linear band-like plaques typically presenting in a horizontally parallel arrangement across the back.^{1,2} Although LFE has locational predilection for the back, some LFE cases have been reported to be encountered on other atypical sites, including the lower extremities,³ shoulders,⁴ and face.⁵ Facial LFE appears to be extremely rare because only one case has been previously reported.⁵ Furthermore, the solitary distribution and whitish color of the skin lesion observed in this case were rare for LFE (Fig. 1a,b). Although the previously reported case of facial LFE also presented as a solitary lesion, it had irregular hyperpigmentation compared with the white lesion noted in this case.⁵

Histopathological findings of typical LFE include focal increase in or aggregation of elastic fibers in the dermis with an unaffected epidermis and basophilic materials of degenerated and fragmented elastic fibers separating normal or hypertrophic collagen bundles.^{1,2} Elastic tissue staining, including Verhoeff–Van Gieson or Weigert staining, exhibits increased and fragmented elastic fibers between dermal collagen bundles in LFE.² Furthermore, this case showed these typical histopathological findings, leading to the confirmed diagnosis of LFE (Fig. 2a–c).

Striae distensae (SD), late-onset focal dermal elastosis, and dermatofibrosis lenticularis disseminata (DLD) need to be distinguished from LFE.^{1,2,5} SD presents with dermal rarefaction owing to the rupture of collagen bundles and absence of dermal elastosis.^{2,5} The presence of dermal elastosis differentiated our case from SD. Late-onset focal dermal elastosis presents with papular lesions typically occurring on the neck and flexural creases.² This was ruled out in our patient because she had a linear plaque over the face. DLD is an inherited connective tissue nevus of the elastin type, characterized by round-to-oval skin-colored papules.^{1,5} In this case, the lesion that appeared in the woman was less likely