

Angioedema: A potential complication of dupilumab in atopic dermatitis

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Abstract

Dupilumab is a relatively new and quite effective medication for recalcitrant atopic dermatitis in patients over 6 years of age. Here, we present a 12-year-old girl with progressively worsening episodic facial swelling and erythema while treated with dupilumab. This case highlights the possibility of angioedema as an adverse effect of dupilumab treatment.

KEYWORDS

angioedema, atopic dermatitis, biologic, drug reaction, dupilumab

1 | INTRODUCTION

Dupilumab is an IL-4R α antagonist indicated for the treatment of moderate-to-severe recalcitrant atopic dermatitis in patients 12 years and older. The most common adverse events reported in adolescents and adults include conjunctivitis, keratitis, blepharitis, nasopharyngitis, headaches, injection site reactions, and herpes simplex viral infections.^{1,2} To our knowledge, angioedema has not been described as a side effect of dupilumab. Drug-induced allergic angioedema is a type I hypersensitivity reaction mediated by histamine and IgE. Presentation involves swelling of mucosal and submucosal tissue of the face, lips, tongue, and other parts of the body such as hands, feet, and genitalia. Patients may develop urticaria, gastrointestinal symptoms, and, in severe cases, respiratory symptoms.³ Herein, we report a novel case of angioedema in a pediatric patient treated with dupilumab.

2 | CASE REPORT

A 12-year-old girl with severe, recalcitrant atopic dermatitis (AD), asthma, and food allergies presented with worsening recurring facial edema following treatment with dupilumab over several months. In the past, her AD was inadequately controlled, requiring prednisone courses, high potency topical steroids, and systemic cyclosporine and had resulted in numerous hospitalizations for flares and secondary infections. At the time of presentation, she had been treated

with dupilumab for three months with marked improvement in her AD but with progressively worsening episodic facial swelling. Previously, one month after initiation of dupilumab, the patient's mother contacted the on-call physician to report that the patient had developed pruritic hives on her face, swelling of her cheeks and lips, and gastrointestinal cramping. At this time, her mother reported that the patient's last dose of dupilumab was 1 week prior and mother denied any known temporal association or other precipitating event. The patient's mother denied episodes of facial swelling prior to starting dupilumab. The patient denied dyspnea or wheezing and was successfully treated with oral antihistamines. At the next clinic evaluation, the patient continued to complain of rash on her face and swelling of her lips and cheeks, though was noted to have near complete resolution of her AD. Physical examination at this visit showed erythematous, edematous plaques on left cheek and upper cutaneous lip. The patient was offered biopsy and/or prednisone as well as alternative treatment of AD due to concern for angioedema. After extensive discussion of risk and benefits, family opted for continuation of dupilumab given patient's dramatic improvement as well as an oral short steroid taper starting at 1.0 mg/kg/d. Two weeks following that office visit, the patient presented to the emergency department with worsening swelling around her eyes and lips, facial erythema, and pruritus of her hands but no dyspnea or wheezing which again improved with an oral antihistamine. At next follow-up, the patient reported waxing and waning facial swelling. Her mother reported that within a day of receiving a dupilumab injection, the patient would develop facial redness and swelling of her lips, cheeks,

and eyes. She reported that these episodes typically lasted for a week and seemed to worsen with each subsequent exposure to dupilumab. Photographs on the mother's cell phone showed peri-orbital and labial edema with bright erythema of the skin. A mutual decision was made to discontinue dupilumab and begin mycophenolate therapy. In the four months since discontinuing dupilumab, the patient has not had any recurrent episodes of facial swelling.

3 | DISCUSSION

Dupilumab is a relatively new and quite effective medication for atopic dermatitis, and cases of new-onset facial dermatoses following dupilumab treatment have been emerging. Numerous studies and case reports have proposed that the IL-4 receptor blockade from dupilumab may unmask an allergic contact dermatitis (ACD) and thus be a mechanism of these new dermatoses.⁴ Patients in these emerging reports typically had new-onset erythematous or eczematous dermatitis of the face without facial edema, extensive pruritus, or urticaria.⁴⁻⁶ Unlike these cases, our patient presented with recurrent facial erythema and edema and experienced episodic urticaria, pruritus, and gastrointestinal cramping. The development of her facial edema and erythema quickened and worsened with subsequent dupilumab injections, which is consistent with sensitization in allergic angioedema. Her history, examination, and response to therapy support allergic angioedema induced by dupilumab. This case highlights the possibility of angioedema as an adverse effect of dupilumab. As dupilumab's use expands, monitoring for its potential adverse effects should also.

CONFLICTS OF INTEREST

The authors have no conflicts of interest relevant to this article to disclose.

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