A case report of uveitis secondary to dupilumab treatment for atopic dermatitis

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Key words: adverse effect; atopic dermatitis; dupilumab; eczema; treatment; uveitis.

INTRODUCTION

Atopic dermatitis (AD) is a chronic inflammatory skin disease mediated by the helper T cell type 2 cytokines interleukin 4 (IL-4) and/or IL-13.[1] Dupilumab is a monoclonal antibody that inhibits signaling of IL-4 and IL-13 via IL-4 receptor blockade.[2] Dupilumab treatment results in significant improvement in AD signs and symptoms and health-related quality of life in patients with moderate to severe AD.[3]

Overall, dupilumab has been found to have good long-term safety and efficacy.[4] The most commonly reported adverse events are ophthalmic complications, including dryness, pruritus, blepharitis, conjunctivitis, and keratitis.[4] Here, we report a novel case of uveitis in a patient taking dupilumab for moderately severe AD.

Abbreviations used:

AD: atopic dermatitis
IL: interleukin

CASE REPORT

A 55-year-old woman presented with a 5-year history of a worsening, intensely pruritic dermatitis affecting the neck, trunk, and bilateral upper and lower extremities, including flexural distribution. Exacerbating factors included stress, heat, sweating, and sunlight. Her past medical history was significant for Graves disease, left eye congenital amblyopia (cortical blindness), inactive discoid lupus with scarring alopecia of the scalp, and vitiligo. She denied a prior history of atopy, including childhood AD, asthma, and allergies. A biopsy of the right arm revealed spongiotic dermatitis with eosinophilia and mild lymphocytic atypia consistent with eczematous dermatitis. A diagnosis of adult-onset AD was made.

Prior treatments consisted of topical clobetasol propionate ointment 0.05%, triamcinolone acetonide ointment 0.1%, desoximetasone ointment 0.05%, fluocinide ointment 0.05%, oral mycophenolate mofetil 1000 mg twice daily, and >10 courses of tapering doses of oral prednisone, all of which produced minimal improvement. At age 55 years, subcutaneous dupilumab was started with a 600-mg loading dose, followed by 300 mg every other week. The AD was moderately severe (investigator's global assessment = 3, body surface area = 20%, numeric rating scale-itch = 9 of 10), with no lesions affecting the face or eyelids prior to initiating dupilumab. The patient achieved almost clear skin with a drastic reduction in all AD signs (investigator's global assessment = 1, body surface area < 1%) and symptoms (numeric rating scale-itch = 1) and improvement in quality of life.

At age 57 years (after >1 year on dupilumab), the patient started experiencing redness and pain in the right eye. Slit-lamp examination of the right eye by an ophthalmologist showed pigment on the endothelium of the cornea, inflammatory cells within the

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Funding sources: None.
Conflicts of interest: None disclosed.
IRB approval status: Not applicable.

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JAAD Case Reports 2021;7:98-9.
2352-5126

https://doi.org/10.1016/j.jdcr.2020.11.012

anterior chamber of the eye, posterior synechiae of the iris, and mild nuclear sclerosis of the crystalline lens. The left eye initially showed pigment on the endothelium of the cornea, mild nuclear sclerosis, and no signs of intraocular inflammation. No new defects were observed in visual acuity (20/30 in the right eye), pupillary reactivity, intraocular pressure (10 mmHg and 11 mmHg in the right and left eye, respectively), or eye motility. A diagnosis of anterior uveitis of the right eye was made, and corticosteroid eye drops were started. However, the symptoms worsened within several weeks, with worsening visual acuity and new-onset floaters and flashes in the right eye. Examination demonstrated bilateral thickening of the choroid and serous retinal detachments, at that time constituting a panuveitis of both eyes. Oral prednisone, 60 mg, was started and was tapered slowly over the following several months.

Laboratory evaluation performed immediately after the diagnosis of uveitis revealed elevated antinuclear antibody (1:320 with a speckled and homogenous pattern), comprehensive metabolic panel, serum protein electrophoresis, erythrocyte sedimentation rate, C-reactive protein, antineutrophil cytoplasmic antibodies, and vitamin D levels within normal limits. There were no other laboratory or physical findings consistent with a diagnosis of systemic lupus or other connective tissue disease. Two months after the diagnosis of uveitis was made, as the patient's symptoms did not fully resolve despite the tapered dose of prednisone, adalimumab was added. Dupilumab was discontinued.

After 2 months of biweekly subcutaneous injections of adalimumab, the uveitis completely resolved, with no signs evident on slit-lamp examination and no reported symptoms. However, the AD worsened, with severe pruritus, moderate skin pain, severe sleep disturbance, generalized xerosis, and ill-demarcated erythematous and hyperpigmented plaques on the dorsal surface of the hands, digits, wrists, back, forearms, and lower extremities, covering >30% of total body surface area. Narrowband ultraviolet B therapy produced an inadequate response, and dupilumab was therefore resumed. Within 1 month of restarting dupilumab, signs and symptoms of AD rapidly improved, but the uveitis recurred. Dupilumab was again discontinued, with consequent resolution of the uveitis.

DISCUSSION

A 50-year-old female patient with a diagnosis of adult-onset AD experienced new-onset uveitis during treatment with dupilumab that improved with drug cessation. The most commonly reported eye complications during dupilumab treatment are conjunctivitis, with an incidence of 10%-20% in phase 2 and 3 clinical trials[5] and as high as 70% in a real-world Swedish case series, and 1 case of reactivation of herpes simplex virus uveitis.[6] To our knowledge, there have been no reports of new-onset uveitis occurring during dupilumab treatment.

Most cases of uveitis are attributable to autoimmune diseases, infections, or medications.[7] Based on the calculated Naranjo scale of 5, it is "probable" that dupilumab caused the uveitis in this case, for the following reasons: the adverse event appeared after the suspected drug was administered (+2), the adverse reaction improved when the drug was discontinued (+1), and the adverse reaction reappeared when the drug was reintroduced (+2).[8] Patients who are started on dupilumab should be monitored for ophthalmologic complications, especially those with a history of eye disease. Based on our anecdotal experience, patients with mild ophthalmologic complications, such as dryness or pruritus, may not require ophthalmologic monitoring. The presence of eye pain warrants ophthalmologic evaluation, as it may indicate keratitis or uveitis. Further elucidation of dupilumab's adverse-event profile and the mechanisms of ophthalmic adverse events, such as uveitis, is needed.

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