Dupilumab Associated with Uveitis: A Case Report

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Background

Atopic dermatitis (AD) is a chronic inflammatory skin disease mediated by T helper 2 (Th2) cytokines interleukins 4 (IL-4) and/or IL-13.[1] Dupilumab is a monoclonal antibody that inhibits signaling of IL-4 and IL-13 via IL4-receptor a blockade.[2] Dupilumab resulted in significant improvement in AD signs and symptoms and health-related quality of life in patients with moderate to severe AD.[3]

Overall, dupilumab was found to have good long-term safety and efficacy[4]. There most commonly reported eye complications during dupilumab treatment were 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 one case of reactivation of herpes simplex virus uveitis.[6] Here, we report a novel case of uveitis in a patient taking dupilumab for moderate-severe AD.

To our knowledge, there have been no reports of uveitis occurring while on dupilumab in a patient without a previous history of uveitis.

Case Report

A 50-year-old female with a significant medical history for Graves' disease, left eye congenital blindness, inactive discoid lupus with scarring alopecia of the scalp, and vitiligo was diagnosed with adult-onset AD. At age 55, after failing numerous treatment, subcutaneous dupilumab was started with 600 mg loading dose followed by 300 mg every other week. She achieved almost clear skin with a drastic reduction in AD signs, symptoms and quality of life.

At age 57 years (after >1 year on dupilumab) she started experiencing redness and pain in her right eye and was diagnosed with uveitis by ophthalmology and started on corticosteroid eye drops. An autoimmune workup was pursued. Anti-nuclear antibody (ANA) was elevated at 1:320 with a speckled and homogenous pattern. Otherwise, her labs were within normal limits. Within 2 months, adalimumab was started to treat the uveitis, prednisone was tapered and discontinued, and dupilumab was discontinued.

Over the following months, her uveitis improved, but her AD symptoms worsened, with generalized xerosis, and ill-demarcated erythematous and hyperpigmented plaques on the dorsal hands, digits, wrists, back, forearms and lower extremities, covering approximately 30% of her body surface area. Narrow-band ultraviolet B therapy was started, though she had an inadequate response. Dupilumab was therefore resumed. Within one month of restarting dupilumab, the uveitis recurred. Dupilumab was again discontinued.

Discussion

- Most cases of uveitis are attributable to autoimmune diseases, infections, and medications.[7]
- Based on Naranjo score of 5, it is "probable" that dupilumab caused the uveitis in this case due to the following: 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 re-introduced (+2).[8]
- Patients who are started on dupilumab should be monitored for ophthalmologic complications, especially those with a history of eye disease.
- Eye pain warrants ophthalmologic evaluation, as it may indicate keratitis or uveitis.
- Further elucidation of adverse-event profile and the mechanisms of ophthalmic adverse-events, e.g. uveitis, are needed.

References

1.Gandhi, N.A., B.L. Bennett, N.M. Graham, et al., *Targeting key proximal drivers of type 2 inflammation in disease.* Nat Rev Drug Discov, 2016. **15**(1): p. 35-50.
2.Guttman-Yassky, E., R. Bissonnette, B. Ungar, et al., *Dupilumab progressively improves systemic and cutaneous abnormalities in patients with atopic dermatitis.* J Allergy Clin Immunol, 2019. **143**(1): p. 155-172.
3.Simpson, E.L., *Dupilumab Improves General Health-Related Quality-of-Life in Patients with Moderate-to-Severe Atopic Dermatitis: Pooled Results from Two Randomized, Controlled Phase 3 Clinical Trials.* Dermatol Ther (Heidelb), 2017. **7**(2): p. 243-248.
4.Deleuran, M., D. Thaçi, L.A. Beck, et al., *Dupilumab shows long-term safety and efficacy in patients with moderate to severe atopic dermatitis enrolled in a phase 3 open-label extension study.* Journal of the American Academy of Dermatology, 2020. **82**(2): p. 377-388.
5.Akinlade, B., E. Guttman-Yassky, M. de Bruin-Weller, et al., *Conjunctivitis in dupilumab clinical trials.* Br J Dermatol, 2019. **181**(3): p. 459-473.
6.Ivert, L.U., C.F. Wahlgren, L. Ivert, et al., *Eye Complications During Dupilumab Treatment for Severe Atopic Dermatitis.* Acta Derm Venereol, 2019. **99**(4): p. 375-378.
7.London, N.J.S., S.J. Garg, R.S. Moorthy, et al., *Drug-induced uveitis.* Journal of Ophthalmic Inflammation and Infection, 2013. **3**(1): p. 43.
8.Naranjo, C.A., U. Busto, E.M. Sellers, et al., *A method for estimating the probability of adverse drug reactions.* Clin Pharmacol Ther, 1981. **30**(2): p. 239-45.