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OBSERVATION

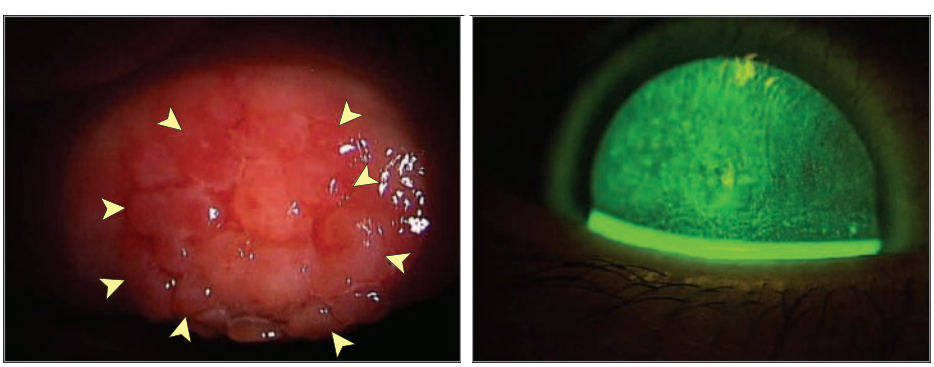
Treatment of Vernal Keratoconjunctivitis Using Upadacitinib

Vernal keratoconjunctivitis (VKC) is a severe and chronic ocular allergic disease that predominantly affects children. Clinically, VKC is characterized by the formation of giant papillae on the upper palpebral conjunctiva and corneal damage caused by potent type 2 and eosinophilic inflammation, resulting in vision loss. As severe cases are often refractory to topical treatment using steroids or immunosuppressants, the development of novel therapeutic strategies is imperative.[1-3] Janus kinase (JAK), an intracellular tyrosine kinase, regulates cytokine signaling pathways. Currently, JAK inhibitors are used to treat atopic dermatitis (AD).[4] This report presents a case of improvement of VKC associated with initiation of an oral JAK inhibitor upadacitinib.

Report of a Case | A 13-year-old girl presented with exacerbation of symptoms including photophobia, itchy eyes, and pain in her right eye. Slitlamp examination revealed giant papillae on the upper tarsal conjunctiva and superficial punctate keratitis in the right eye (**Figure 1**). Her best-corrected visual acuity was 20/63 OD and 20/16 OS. She had previously been diagnosed with VKC associated with AD at 9 years old and for 4 years was treated with eye drops containing tacrolimus, cyclosporine, steroids, and antiallergic agents. Despite topical treatment with eye drops, the giant papillae on the tarsal conjunctiva continued to worsen and resolve seasonally. Corneal lesions such as a shield ulcer and superficial punctate keratitis in her right eye persisted for 3 months. AD was observed on her skin, including the face, and was treated with tacrolimus ointments, steroid ointments, and a moisturizer. As the patient's AD was severe with persistent skin rash refractory to treatment with topical medications, oral upadacitinib (15 mg/d) was administered for AD. Scores for the Eczema Area and Severity Index and the Investigator's Global Assessment before and 2 weeks after upadacitinib treatment improved from 28.0 to 1.2 and 3 to 2, respectively. The pain and itching in the right eye improved within a month after upadacitinib administration. Additionally, the giant papillae gradually flattened, and corneal lesions improved after upadacitinib administration. After 3 months of oral upadacitinib administration, the giant papillae and punctate epithelial keratitis resolved completely (**Figure 2**A and B), and vision improved to 20/16 OD. After 11 months of treatment, upadacitinib dosage was increased to 30 mg/d owing to the exacerbation of AD. After more than 14 months of upadacitinib treatment, no recurrence of giant papillae or corneal damage was observed with topical treatment of only antiallergic eye drops (Figure 2C and D), and visual acuity was maintained at 20/16 OD and 20/20 OS.

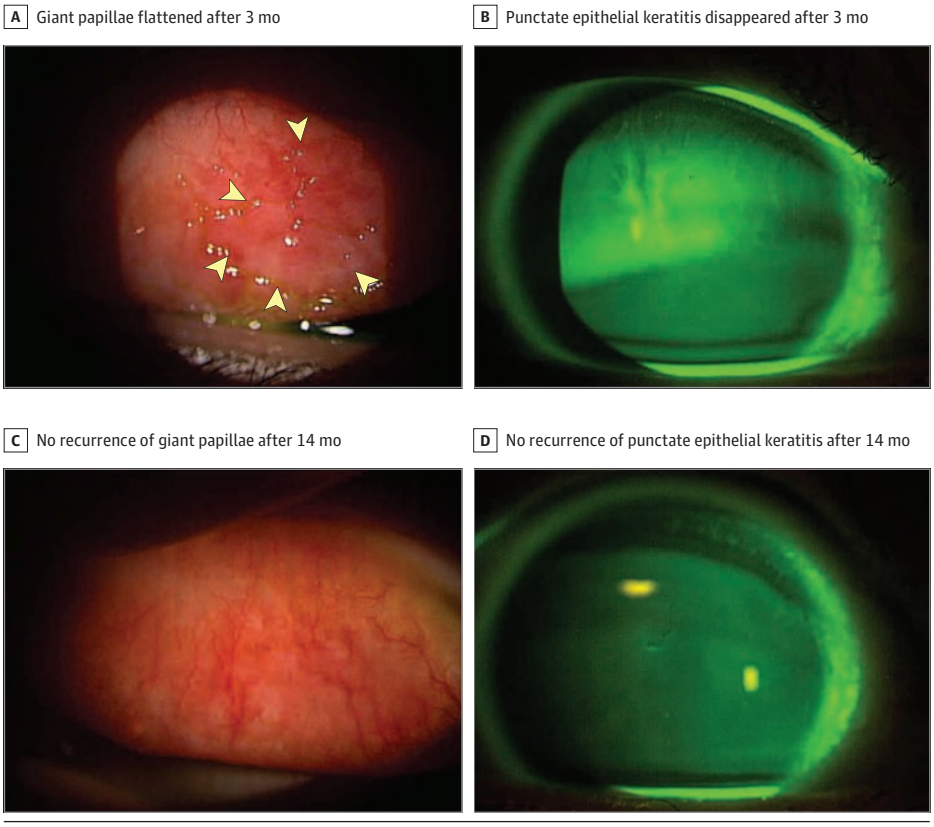
Discussion | Keratoconjunctivitis has been reported to improve during treatment of AD by upadacitinib. Hayama et al[5] reported improvement of dupilumab-associated conjunctivitis after switching to upadacitinib in a patient with AD. Ghiglioni et al[6] were the first to show the improvement of atopic keratoconjunctivitis during treatment with upadacitinib. In this case involving VKC resistant to topical treatment, the giant papillae of conjunctiva and corneal lesions resolved within 3

Figure 1. Slitlamp Images for Upper Tarsal Conjunctiva and Cornea With Fluorescein Staining Before Upadacitinib Administration



Giant papillae on the upper tarsal conjunctiva (arrowheads) (A) and superficial punctate keratitis (B) were apparent before upadacitinib administration.

Figure 2. Slitlamp Images for Upper Tarsal Conjunctiva and Cornea With Fluorescein Staining After Upadacitinib Administration



Giant papillae flattened (arrowheads) (A) and punctate epithelial keratitis (B) disappeared completely after 3 months of oral administration of upadacitinib. C, No recurrence of giant papillae or corneal damage was observed for the next 14 months.

months following initiation of oral upadacitinib, without recurrence for the next 14 months. To the best of our knowledge, this report is the first to describe this effect in association with initiation of upadacitinib in patients with VKC associated with AD. Important cytokines for ocular allergic inflammation including type 2 cytokines interleukin 4 and interleukin 13 and epithelium-derived cytokine thymic stromal lymphopoietin signal through the JAK1 pathway.[4] As upadacitinib is a selective JAK1 inhibitor, this case suggests that cytokine signaling through the JAK1 pathway may play critical roles in VKC pathogenesis. Although this single-case report cannot prove a cause-and-effect relationship and further studies and clinical trials would be needed to determine its efficacy, upadacitinib is a potential novel therapeutic agent against VKC, especially in cases with AD.

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