

Letters

OBSERVATION

Omalizumab Treatment of Vernal Keratoconjunctivitis

Vernal keratoconjunctivitis (VKC) is a severe ocular, chronic, relapsing disease that can result in loss of visual acuity and blindness. Treatment with topical antihistamines, mast-cell stabilizers, corticosteroids, or even topical immunosuppressors (ie, cyclosporine or tacrolimus) frequently does not improve VKC symptoms, and partial control of symptoms with oral corticosteroids can induce severe adverse events with long-term use.¹ Omalizumab is a humanized monoclonal antibody directed toward IgE and is approved for treating severe allergic asthma and severe chronic idiopathic urticaria.²

Report of Cases | We herein describe 2 clinical cases of patients with severe VKC who benefited from subcutaneous treatment with omalizumab. Improvement also was documented by cytologic reduction of eosinophil levels in a conjunctival smear.

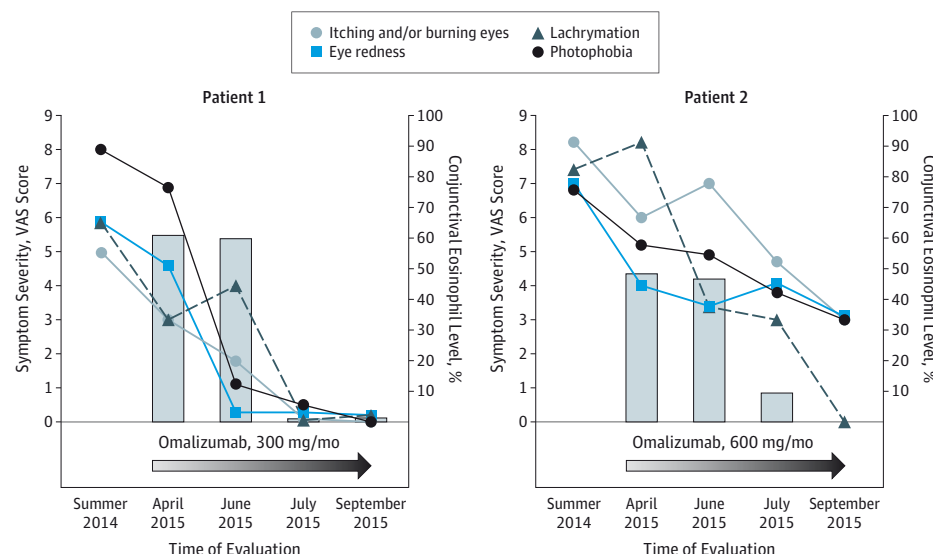
A girl in her first decade of life (patient 1) and a man in his third decade of life (patient 2) each had severe VKC that was unresponsive to treatment with topical antihistamines, mast-cell stabilizers, corticosteroids, cyclosporine, and tacrolimus and was partially and temporarily responsive to treatment with oral corticosteroids. Patient 1 underwent systemic administration of subcutaneous omalizumab, 300 mg/mo (considered the minimal effective dose in a previous similar pediatric case report³), and patient 2, 600 mg/mo (calculated according to the standards approved by the US Food and Drug Administration (<http://www.fda.gov/downloads/drugs/developmentapprovalprocess>

[/howdrugsaredevelopedandapproved/approvalapplications/therapeuticbiologicapplications/ucm113454.pdf](http://howdrugsaredevelopedandapproved/approvalapplications/therapeuticbiologicapplications/ucm113454.pdf)) and the European Medicines Agency (http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000606/WC500057298.pdf) for patients with asthma based on weight and total serum IgE level. Both patients were treated for 6 consecutive months from April to September 2015. Compassionate treatment with omalizumab was approved by the institutional ethical committee of Azienda Ospedaliero Universitaria Policlinico-Vittorio Emanuele Hospital; the parents (for patient 1) or the patient (for patient 2) provided written informed consent for compassionate treatment and publication of clinical data. Neither patient was sensitized to any airborne or food allergens. Patient 2 had concomitant atopic dermatitis since childhood. Neither patient had concomitant asthma.

Ophthalmologic examination with assessment of the superior tarsal conjunctiva was performed at every visit. Each ocular symptom (burning and/or itching, redness, lachrymation, and photophobia) was evaluated using a visual analog scale (VAS) ranging from 0 to 9, with higher scores indicating worse symptoms. Conjunctival scrape smears for cytologic examination were obtained at each visit.

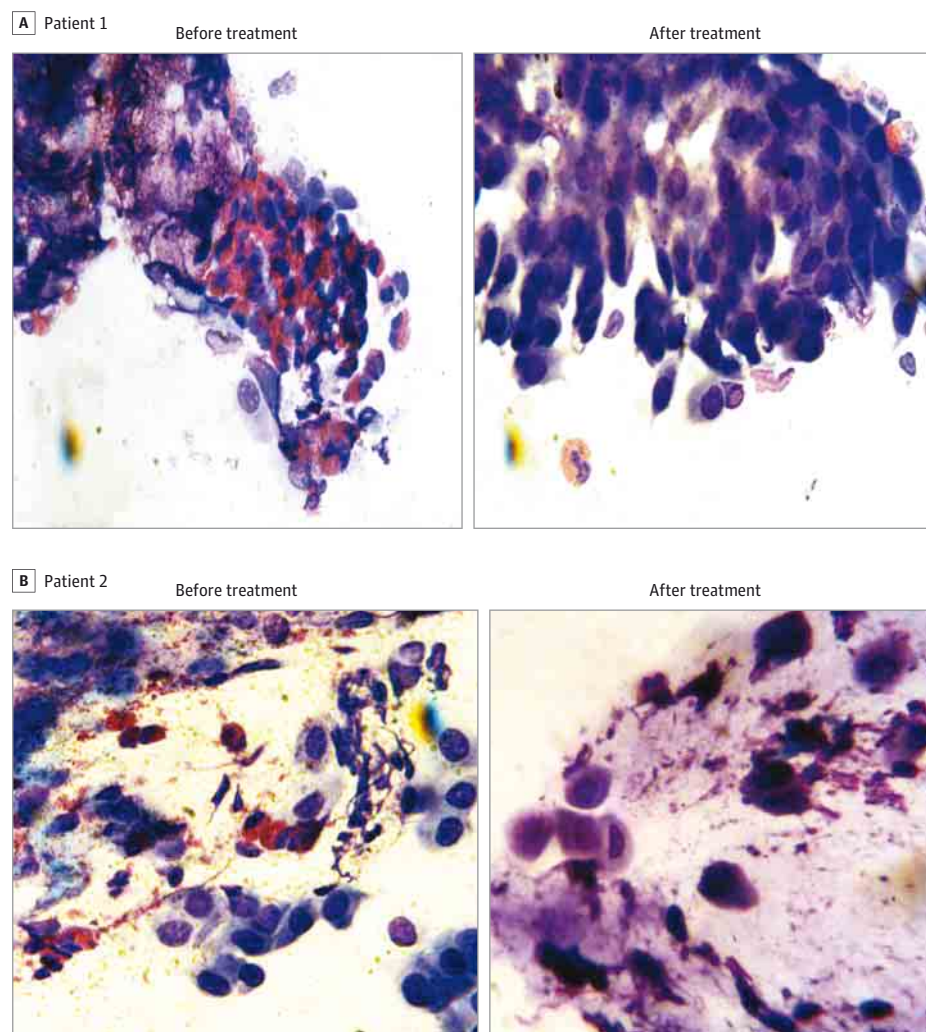
During omalizumab treatment, both patients experienced improved VKC symptoms (reduction in the VAS for each symptom and in the need for topical antihistamines as rescue drugs) (Figure 1), physical examination findings (eye redness and cobblestone papillae were abolished; unfortunately, images were not obtained), and conjunctival cytologic findings (eosinophil levels decreased from 69% to 3% in patient 1 and from 51% to 0% in patient 2 after 6 months

Figure 1. Clinical and Cytologic Results of Omalizumab Treatment



Changes in the visual analog scale (VAS) (range, 0 to 9; higher scores indicate worse symptoms) for ocular symptoms and in conjunctival eosinophil levels (bars) before and during omalizumab treatment in 2 patients with severe vernal keratoconjunctivitis. Both patients underwent subcutaneous treatment for 6 months. To convert eosinophil levels to a proportion of 1, multiply by 0.01.

Figure 2. Results of Conjunctival Cytologic Examination



Conjunctival scrape smears for cytologic examination were obtained from each patient at each visit. The eosinophil level in patient 1 was 68% before and 3% after omalizumab treatment; in patient 2, the eosinophil level was 51% before and 0% after omalizumab treatment (to convert eosinophil levels to a proportion of 1, multiply by 0.01) (May-Grünwald-Giemsa, original magnification $\times 1000$).

of treatment [to convert to a proportion of 1, multiply by 0.01]) (Figure 1 and Figure 2). All these improvements were maintained until the end of the summer. In the past, summer was associated with worsening symptoms. The patients experienced no adverse effects during the 6-month treatment period. An improvement in patient 2's atopic dermatitis was not identified.

Discussion | To our knowledge, only 2 other cases of VKC^{3,4} and 7 cases of atopic keratoconjunctivitis^{5,6} (all with concomitant severe asthma) treated with omalizumab are described in the literature. Our 2 cases may be the first reports of severe VKC not associated with severe asthma treated successfully with omalizumab. Improved symptoms and ophthalmologic examination findings were also documented using cytologic examination of conjunctival smears. We suggest that this diagnostic technique be used more often in clinical practice, particularly for diagnosing and monitoring patients with conjunctival eosinophilic inflammatory diseases, such as VKC or atopic keratoconjunctivitis.

Both clinical cases strengthen the observation that omalizumab can be effective in patients with VKC without concomitant asthma. Further studies and specific trials should be designed to confirm or refute our observation of the effectiveness of omalizumab in patients with severe VKC.

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Central Retinal Vein Occlusion Noted 2 Days After Use of Phendimetrazine as an Appetite Suppressant

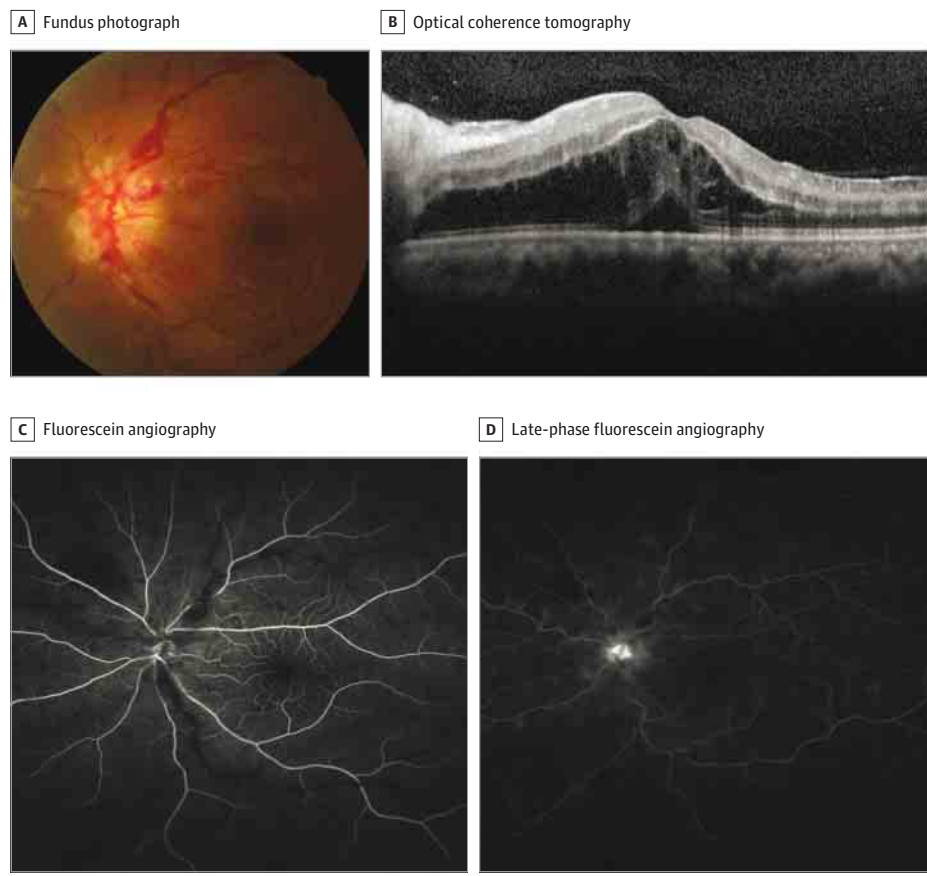
Phendimetrazine behaves as a sympathomimetic amine and is used as an appetite suppressant.¹ We present a case of central retinal vein occlusion (CRVO) that developed after taking phendimetrazine for 2 days. The purpose of this case report is to draw attention to the potential for sight-threatening complications in patients receiving phendimetrazine, although the event could have been coincidental to its use.

Report of a Case | A woman in her 40s presented with sudden painless loss of vision in her left eye for 3 days. Two days prior to the symptom development, she had begun to take phendimetrazine at a dose of 35 mg twice a day, to lose weight. She ceased taking the medication after the onset of symptoms. She had no relevant history of medical illness, except for pregnancy-induced hypertension 10 years ago, and had no known drug allergies.

On ophthalmologic examination, corrected visual acuity was 20/20 OD and 20/63 OS. Intracocular pressures were 16 mm Hg OD and 17 mm Hg OS. Her pupils were reactive and did not show any relative afferent papillary defect. Slitlamp examination revealed no abnormal findings in the anterior segments. Fundus examination showed optic nerve head swelling and dilated and tortuous vascular changes with multiple dot and flame-shaped hemorrhages in her left eye. The right fundus appeared normal. Optical coherence tomography showed severe macular edema, mainly in the outer layer and subretinal space, with a central subfield thickness of 629 μ . Fluorescein angiography revealed nonischemic CRVO of her left eye (Figure 1).

On physiologic examination, her blood pressure (BP) was 166/103 mm Hg, and her pulse rate was 67 beats per minute. Because she had vague chest discomfort and headache, she was evaluated by a cardiologist and a neurologist by electrocardiography, chest radiography, computed tomography, and

Figure 1. Patient's Left Eye at First Visit



C, fluorescein angiography in the retinal arteriovenous phase. The arteriovenous transit time was delayed to about 24 seconds.
D, Fluorescein angiography in the late phase.