

Article Type: Letter to the Editor

Vernal Keratoconjunctivitis and immune mediated diseases: one unique way to symptom control?

Francesca Occasi 1. MD.

Anna Maria Zicari 1. Professor, MD.

Laura Petrarca 1. M.D.

Marcella Nebbioso 2. Professor, MD.

Guglielmo Salvatori 3. M.D.

Marzia Duse 1. Professor, MD.

1 “Sapienza” University of Rome, Department of Pediatrics, Rome, Italy .

2 “Sapienza” University of Rome, Department of Sense Organs, Rome, Italy .

3 “Bambino Gesù” Children's Hospital, Department of Medical and Surgical Neonatology, Rome, Italy .

In relation to this manuscript we declare that there are no conflict of interest or financial support.

Corresponding author:

Occasi Francesca

“Sapienza” University of Rome

Work address: Viale Regina Elena , 324- 00161 Rome, Italy

Mail: occasi.f@gmail.com

+39 06 49979333

Fax. +39 06 49979377

Key words: Vernal Keratoconjunctivitis, omalizumab, Asthma, Atopic dermatitis, Children.

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/pai.12350

This article is protected by copyright. All rights reserved.

Vernal Keratoconjunctivitis and immune mediated diseases: one unique way to symptom control?

To the Editor:

We report the case of a 15-year old boy affected by Vernal keratoconjunctivitis (VKC), asthma and atopic dermatitis (AD) treated with omalizumab with the control not only of respiratory and cutaneous symptoms but also of ocular manifestation.

A 15-year old adolescent suffering from persistent allergic asthma with a seven years history of severe ocular itching, discharge, irritation and mild photophobia increasing during the summer, not responding to topical antihistamines, came to our attention at the Pediatric Department of the “Policlinico Umberto I” hospital in Rome. A severe atopic dermatitis since the second month of age, firstly presenting as a diaper dermatitis, then involving the folds of the limbs, and finally the face and the neck, especially the perioral and the periocular areas, was also referred. No family history of atopic or autoimmune diseases was recorded.

On our first examination skin prick tests were positive for mites, lolium pratense, cypress and betulaceae and he presented a severe facial dermatitis, mainly involving the perioral and the periocular skin, with several lesions due to scratching (Figure 1). On ophtalmological evaluation he showed intense conjunctival hyperemia and the upper palpebral conjunctiva presented giant papillae in both eyes (Fig. 2a). A corneal center ulcer involving the left eye (Fig. 3a) with intense pain, photophobia, and scarce visual acuity was found. In fact, best corrected visual acuity (BCVA) was 20/40 in left eye and 20/20 in right eye with Snellen chart.

The adolescent underwent a topic therapy with vancomycin, fusidic acid and atropine 1% for 2 months followed by the topical administration of artificial tears with 1% cyclosporine (1drop/eye twice daily; prepared strictly respecting sterility criteria, by the Chemistry Service Institute at the “Sapienza” University of Rome, following a formulation including one part of commercially available cyclosporine solution for intravenous infusion -Sandimmun_Novartis Farma S.p.A.S.S., Varese, Italy-, diluted in aqueous vehicle -Vismed Light_TRB Chemedica, Haar/Munich, Germany) for 45 days resulting in a resolution of the shield ulcer in a corneal scar of the optical zone (Fig. 3b) and an improvement of BCVA to 20/20 with Snellen chart also in the left eye. Moreover, concerning asthma, due to a poor control of symptoms (FEV1= 65.6%) with severe exacerbation in the previous 12 months, despite the daily therapy

with inhaled long-acting beta-agonist and corticosteroids, a sub-cutaneous therapy with omalizumab (Novartis, Basel, Switzerland) was started at a dose of 600 mg every two weeks.

After three months of treatment asthma control was reached, a complete resolution of VKC (Fig 2b) and atopic dermatitis (Fig 1b) was observed, thus, the topical cyclosporine administration was interrupted autonomously. Of note, after the exposition to a high concentration of pollen and intense light during a football match the patient experienced a recurrence of all the ocular, cutaneous and respiratory symptoms and the topical treatment with 1% of cyclosporine has been resumed together with 4 application per day of fusidic acid and a systemic therapy with 10 mg of cetirizine and 10 mg for 3 days of prednisone (followed by 5 mg for 2 days). Again, after only 6 days of therapy an improvement of the ocular and respiratory symptoms has been found and after one month a complete resolution of the dermatitis has been noticed.

We report the case of a young male affected by VKC associated with severe atopic dermatitis and uncontrolled asthma, two immunological diseases mediated by Immunoglobulin E.¹ VKC is a rare and chronic relapsing condition involving conjunctiva and/or corneal tissue, occurring mainly in children and adolescents, in dry and hot climates which can lead to visual loss.

Although an Ig-E mediated mechanism underlying this condition has been a matter of debate for a long time, its immunopathogenesis remains still unclear, probably multifactorial, involving both Th1 and Th2- mediated response and an association with DQB1*05 allele has been described.² In this perspective, only 50% of children with VKC show a clear allergic sensitization. Moreover, this apparently “isolated” disease underlie an immune-mediated dysregulation associated not only to a local inflammation, but also to a systemic inflammatory response related to an outward and inward passage of inflammatory cells and mediators as confirmed by the increased serum level of both HMGB1 and circulating sRAGE in patients affected by VKC.³

Omalizumab, a recombinant humanized monoclonal antibody, is used as add on therapy, for the treatment of asthma. In fact it has been approved as for patients higher than 6 years old suffering from moderate to severe uncontrolled allergic asthma.⁴ Its mechanism of action includes the binding to free IgE, reducing the expression of the IgE receptor and controlling

the release of soluble mediators.⁵ Two authors reported the effect of Omalizumab on VKC in patients affected also by AD, asthma. Taillè et al.⁶ reported in a 35 year-old patient a rapid improvement of conjunctivitis with a reduction of oral steroid use and an improvement in patient's quality of life while an improvement in respiratory and cutaneous symptom after few months of treatment, and in ocular symptoms after nine month, was documented by Sanchèz et al.⁷ in a 15 year-old girl also receiving topic tacrolimus.

In the present case the administration of omalizumab lead to a complete control of VKC which had only been partially controlled by the topic therapy with 1% cyclosporine and this effect on ocular symptoms was associated with the improvement of asthma and atopic dermatitis. Moreover, soon after pollen and intense light exposure the patient experienced an exacerbation of all manifestations. The clinical evidence of a strong relationship between ocular, cutaneous and respiratory symptoms suggests that the local and systemic inflammation underlying VKC could be able to trigger the onset of skin and respiratory symptoms. We speculate that omalizumab, controlling the IgE mediated inflammation, could indirectly lead to a reduction of the inward inflammatory mediators influencing VKC exacerbations.

In conclusion, according to our knowledge, this is the first report, suggesting that asthma, AD and VKC, although probably associated with different immunopatogenic mechanism, might conduct to a wider common immune mediated inflammation which could, hence, influence clinical remissions and exacerbations.

Occasi F., M.D., Department of Pediatrics, Policlinico Umberto I – “Sapienza” University of Rome, Italy

Zicari AM., Professor, M.D., Department of Pediatrics, Policlinico Umberto I – “Sapienza” University of Rome, Italy

Petrarca L., M.D., Department of Pediatrics, Policlinico Umberto I – “Sapienza” University of Rome, Italy

Nebbioso M., Professor, M.D., Department of Sense organs, Policlinico Umberto I – “Sapienza” University of Rome, Italy

Salvatori G., M.D., Department of Medical and Surgical Neonatology, “Bambino Gesù” Children's Hospital, Rome, Italy .

Duse M., Professor, M.D., Department of Pediatrics, Policlinico Umberto I – “Sapienza” University of Rome, Italy

References:

1. Platts-Mills Thomas AE. The role of immunoglobulin E in allergy and asthma. American journal of respiratory and critical care medicine 2001; 164: S1-S5.
2. Zicari AM, Mora B, Lollobrigida V, Occasi F, Cesoni Marcelli A, Megiorni F, et al. Immunogenetic investigation in vernal keratoconjunctivitis. *Pediatr Allergy Immunol* 2014 ;25:508-10.
3. Zicari AM, Zicari A, Nebbioso M, Mari E, Celani C, Lollobrigida V, et al. High-mobility group box-1 (HMGB-1) and serum soluble receptor for advanced glycation end products (sRAGE) in children affected by vernal keratoconjunctivitis. *Pediatr Allergy Immunol* 2014 ;25:57-63.
4. Bousquet J, Siergiejko Z, Swiebocka E, Humbert M, Rabe KF, Smith N et al. Persistency of response to omalizumab therapy in severe allergic (IgE-mediated) asthma. *Allergy* 2011;66:671–678.
5. Baena-Cagnani CE, Gomez RM. Current status of therapy with omalizumab in children. *Curr Opin Allergy Clin Immunol*. 2014;14:149-54.
6. Taillé C, Doan S, Neukirch C, Aubier M. Omalizumab for severe atopic keratoconjunctivitis. *BMJ Case Rep*. 2010. doi: 10.1136/bcr.04.2010.2919.
7. Sánchez J, Cardona R. Omalizumab. An option in vernal keratoconjunctivitis? *Allergol Immunopathol (Madr)*. 2012;40:319-20. doi: 10.1016/j.aller.2011.08.002.

Figure legends:

Figure 1.

Atopic dermatitis before (a) and after (b) treatment with omalizumab.

Figure 2.

Giant papillae of the upper palpebral conjunctiva before (a) and after treatment with topical cyclosporine 1% and omalizumab (b).

Figure 3.

The corneal center ulcer involving the left eye (a) and the corneal scar in optical area after topic therapy with vancomycin, fusidic acid and atropine 1% followed by the topical administration of artificial tears with 1% cyclosporine (b).







