

Omalizumab in Patient With Aspirin Exacerbated Respiratory Disease and Chronic Idiopathic Urticaria

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Summary. Aspirin hypersensitivity associated with chronic rhinosinusitis—with or without nasal polyposis—and asthma resistant to conventional therapy defines the aspirin-exacerbated respiratory disease (AERD). We describe the case of a 15-year-old female patient with adverse reaction to aspirin, chronic rhinosinusitis, and severe asthma. She also experienced chronic idiopathic urticaria worsened by non-steroidal anti-inflammatory drug administration. AERD was diagnosed based on clinical history and symptoms. Given the poor responsiveness to standard therapy for respiratory and cutaneous symptoms, omalizumab was administered for 24 weeks with control of respiratory symptoms and short term improvement of cutaneous symptoms.

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INTRODUCTION

Aspirin-exacerbated respiratory disease (AERD), is characterized by non-allergic hypersensitivity to non-steroidal anti-inflammatory drugs (NSAIDs) and chronic upper and lower respiratory symptoms. Chronic eosinophilic rhinosinusitis (with or without nasal polyposis) and bronchial asthma are the most common symptoms that are usually exacerbated by NSAID exposure.¹ Avoidance of NSAIDs does not ensure disappearance of the airway inflammation, so asthma and nasal polyposis usually continue to progress and persist for life. Despite the absence of atopic state, affected patients may present with other allergic conditions and anaphylaxis and urticaria are often described.¹

Aspirin challenge test can be performed for confirmation. Drug avoidance is the recommended treatment and desensitization is suggested in particular conditions.¹ Chronic idiopathic urticaria (CIU) is characterized by itchy hives, angioedema, or both, lasting for a period of 6 weeks or longer without identifiable causes. Second-generation H₁ antihistamines are recommended as first-line treatment but if symptoms persist, third-line therapy as anti IgE treatment (omalizumab) has been shown to be very effective.²

CASE REPORT

We report the case of a 15-year-old female patient who was referred to the Respiratory Unit of Bambino Gesù

Children Hospital at Rome (Italy) for chronic rhinosinusitis, asthma, and CIU. She had a family history of atopy and personal history of aspirin adverse reactions characterized by significant worsening of asthma and urticaria following aspirin intake at therapeutic dosage. No seasonal worsening of respiratory symptoms was reported. Total IgE (81 kU/L), skin prick tests, and IgE for common foods and aeroallergens were negative. Bronchial levels of fractional exhaled nitric oxide (FeNO) were elevated (93 ppb) and baseline spirometric parameters demonstrated forced expiratory volume in the 1 sec

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Conflict of interest: None.

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(FEV1) of 92% of the predicted value and a positive bronchodilator test (increase in FEV1 of 15%).

A step-up therapy with inhaled budesonide (800 mcg/die) and formoterol and oral montelukast were attempted for asthma control in the last year. Oral loratadine and intranasal fluticasone furoate were prescribed for urticaria and rhinosinusitis control, respectively. Despite good medication adherence the patient required frequent courses of systemic corticosteroids (prednisolone 1 mg/kg/day) given the poor control of respiratory symptoms and associated anosmia.

Blood examination revealed an increase of peripheral eosinophils (12.2%, 1268 mmc). Nasal sinus computed tomography (CT) showed pansinusitis with nasal polyposis. Nasal nitric oxide (nNO), ciliary motility, and ultrastructural study on nasal brushing were normal. Sweat testing and extended genetic analysis for cystic fibrosis (CF) were negative. Nasal polypectomy was performed and inflammatory eosinophilic infiltrate was detected on histologic examination.

In view of poor control of respiratory symptoms and peripheral and mucosal eosinophilia, the patient was screened for autoimmune disease: levels of pANCA, cANCA, ANA, C3, C4, and chest CT images were normal. A diagnosis of Churg Strauss syndrome became less plausible as only three of six criteria proposed by the American College of Rheumatology (ACR) were satisfied.

Given the history of aspirin adverse reaction and the clinical picture suggestive of ASA triad (sinusitis, nasal polyposis, and asthma resistant to conventional treatment), AERD was suspected.

Oral challenge with NSAIDs was not performed because of safety concerns in view of severity of respiratory symptoms described after aspirin ingestion. Considering the clinical setting and the poor response to standard treatment, we proposed anti-IgE therapy with a dual purpose: to control asthma symptoms and to prevent urticaria.

Following written informed consent and basal evaluation of peripheral eosinophils, total IgE, bronchial FeNO, FEV1, UAS7 (Urticaria Activity Score 7), and ACT (Asthma Control Test), omalizumab was started at the dosage of 300 mg suggested for CIU and the subcutaneous administration was performed every 4 weeks for 6 months.

During and at end of the treatment the patient was essentially free of both respiratory and cutaneous symptoms and did not require systemic corticosteroid therapy. At monthly periodical evaluation, we observed a reduction of peripheral eosinophil count (8%, 930 mmc) and significant and sustained reduction of bronchial FeNO from 93 ppb at baseline to 21 ppb (± 2.6 SD) at the following visits. An increase of FEV1 from baseline (92%) to 102% after the fifth dose administration was noted (Fig. 1). UAS7 and ACT scores improved from the baseline after the first and second dose administration (Fig. 2). Nevertheless, the patient experienced relapse of cutaneous symptoms just after 1 month of discontinuation of therapy and systemic corticosteroid therapy was required.

DISCUSSION

Aspirin hypersensitivity is a feature of AERD that is characterized by severe asthma for which standard therapy fails in obtaining accurate control.¹

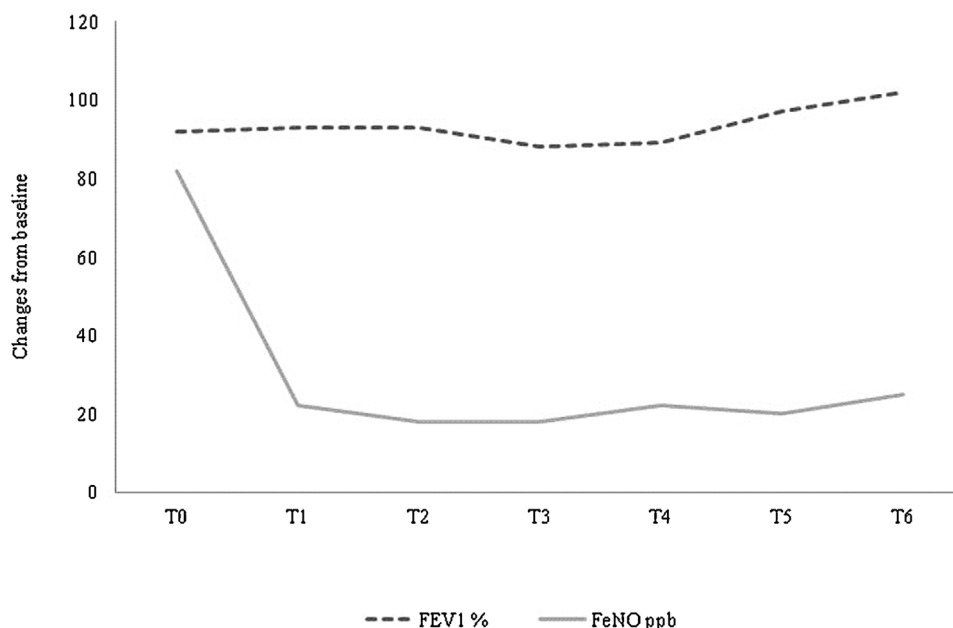


Fig. 1. Baseline and periodical evaluation of bronchial FeNO (continuous line) and FEV1 (dashed line) during omalizumab treatment.

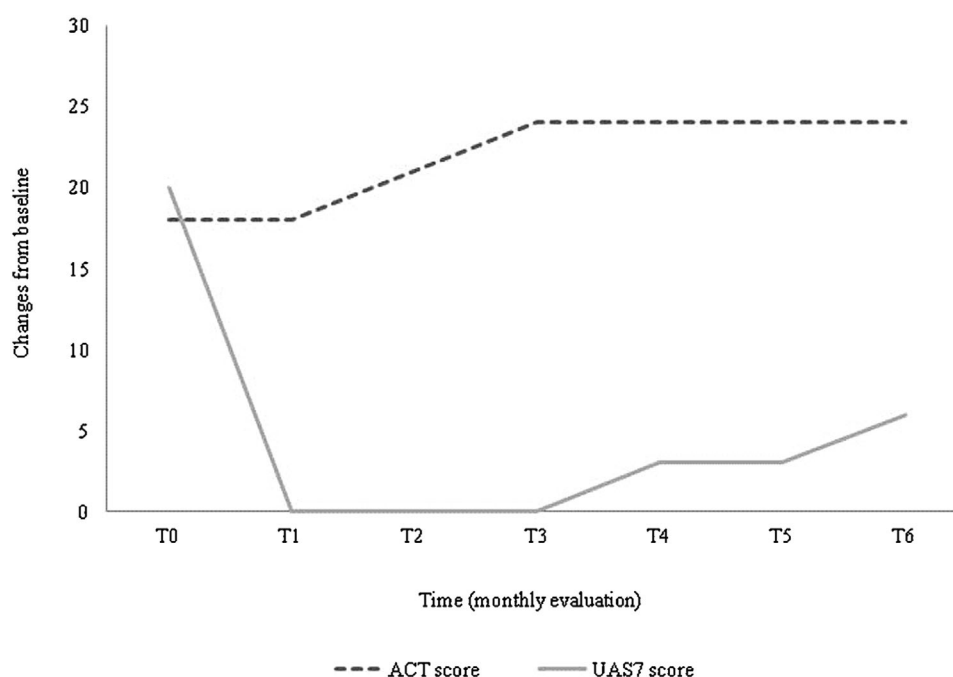


Fig. 2. Baseline and periodical evaluation of ACT (dashed line) and UAS7 (continuous line) score during omalizumab treatment.

The association of AERD and urticaria is frequent in clinical practice. To date, severe allergic asthma and CIU represent the only therapeutic indications for omalizumab therapy for which data of efficacy are available.

Only few reports describe the use of omalizumab in patients with AERD in which it was instrumental in achieving and maintaining aspirin desensitization.³ Other papers describe respiratory improvements after anti-IgE therapy⁴; the effect is related to the down-regulation of high-affinity IgE Fc receptors on mast cells resulting in the inhibition of mast cell activation and leukotriene overproduction with low urinary LTE₄ and PGD₂M levels in treated patients.⁵

We present the case of a female patient with AERD complicated by the coexistence of severe asthma and CIU treated with omalizumab for 24 weeks.

At the end of therapeutic cycle, peripheral eosinophil count is reduced. This phenomenon probably reflects the reduced mucosal eosinophil infiltration leading to lower bronchial exhaled NO. Although the slight FEV1 increase could be an expression of intra-individual variability, we interpreted the data as expression of improvement of respiratory inflammation documented by the increase of ACT score from baseline and the lack of need for systemic corticosteroid therapy persisting even after treatment discontinuation. Inhibition of cutaneous mast cell activation explains amelioration of CIU symptoms demonstrated

by the reduction of UAS7 score from the baseline. This effect was not maintained after discontinuation of omalizumab treatment. In conclusion, the present case describes limited short term effects of omalizumab on control of cutaneous symptoms of AERD. Further studies are required to investigate its long term effects.

REFERENCES

1. Palikhe S, Kim JH, Park HS. Update on recent advances in the management of aspirin exacerbated respiratory disease. *Yonsei Med J* 2009;50:744–750.
2. Zuberbier T, Aberer W, Asero R, Bindslev-Jensen C, Brzoza Z, Canonica GW, Church MK, Ensina LF, Giménez-Arnau A, Godse K, et al. The EAACI/GA 2LEN/EDF/WAO guidelines for the definition, classification, diagnosis, and management of urticaria: the 2013 revision and update. *Allergy* 2014;69: 868–887.
3. Guillén D, Bobolea I, Calderon O, Fiandor A, Cabañas R, Heredia R, Quirce S. Aspirin desensitization achieved after omalizumab treatment in a patient with aspirin-Exacerbated urticaria and respiratory disease. *J Investig Allergol Clin Immunol* 2015;25:133–162.
4. Aksu K, Kurt E. Aspirin tolerance following omalizumab therapy in a patient with aspirin-exacerbated respiratory disease. *Allergol Immunopathol (Madr)* 2013;41:208–210.
5. Hayashi H, Mitsui C, Nakatani E, Fukutomi Y, Kajiwaru K, Watai K, Sekiya K, Tsuburai T, Akiyama K, Hasegawa Y, et al. Omalizumab reduces cysteinyl leukotriene and 9a, 11b-prostaglandin F2 overproduction in aspirin-exacerbated respiratory disease. *J Allergy Clin Immunol* 2016;137:1585–1587.