

### Omalizumab in the treatment of aspirin-exacerbated respiratory disease

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#### Clinical Implications

- Omalizumab, in a case of severe aspirin-induced asthma, rapidly reduced asthma symptoms, improved lung function, enhanced quality of life, and restored tolerance to both aspirin and alcohol even though this is not considered to be an IgE-mediated condition.

#### TO THE EDITOR:

Aspirin-induced asthma with polyposis (Samter's triad), also referred to as aspirin-exacerbated respiratory disease (AERD), is a distinct clinical entity characterized by aspirin-induced respiratory reactions, asthma, eosinophilia, and nasal polyposis.<sup>1</sup> It is frequently accompanied by respiratory intolerance reactions to alcohol ingestion.<sup>2</sup>

AERD is considered not to be IgE mediated but to result from the production of high levels of leukotrienes as a consequence of an impaired cyclooxygenase enzyme pathway.<sup>3</sup> Ingestion of aspirin or nonsteroidal anti-inflammatory drugs exacerbates this condition by further inhibiting cyclooxygenase enzyme.<sup>4</sup> Treatment is usually difficult and includes a complex aspirin desensitization schedule.<sup>1</sup> However, 2 recent case reports of single patients have indicated that omalizumab (anti-IgE) may be an effective therapy for AERD.<sup>5,6</sup> Furthermore, omalizumab has been reported to be effective in both allergic and nonallergic patients with nasal polyps and asthma.<sup>7</sup>

Here, we report successful omalizumab therapy of a 55-year-old woman in our outpatient consultancy service in Berlin. She had asthma since 1984 and had experienced more than 50 exacerbations in the 5 years before attending the clinic. She had been hospitalized twice with anaphylaxis, the symptoms of which included an urticarial rash, marked rhinorrhea, breathlessness, cough, and hypotension, following ingestion of a single tablet of aspirin. Also, ingestion of even a small amount of alcohol caused severe bronchoconstriction. Her FEV<sub>1</sub> was 57% of her predicted value, and her asthma control test<sup>8</sup> score was 5 points. She had no family history of allergy, a total IgE level of 218 kU/L, and negative skin prick test responses to house dust mite, animals, and common pollen allergens. The histamine skin prick test result was positive. *In vitro* tests for specific IgE were not performed. She also suffered from chronic sinusitis and polyposis for which she had had 3 nasal polypectomies. Her asthma was poorly controlled despite daily treatment with inhaled fluticasone propionate (2000 µg), prednisolone (70-120 mg), and tiotropium bromide (18 µg).

Dosing with omalizumab, 450 mg monthly, was started 2 years ago, the dose being calculated from her weight and pre-treatment total serum IgE level. The patient reported that even on the first night after her first injection, she experienced an

unbroken night's sleep for the first time in several years. Objective tests performed 3 weeks after her first injection showed her % predicted FEV<sub>1</sub> to be increased from 57% to 80% and her asthma control test score from 5 to 21 points. Double-blind, placebo-controlled oral provocation tests to aspirin and alcohol were performed 2 months after starting omalizumab therapy. The aspirin provocation test schedule was as follows: placebo at 08.00 AM, aspirin 125 mg at 12.30 PM, aspirin 250 mg at 14.30 PM, and aspirin 500 mg at 16.30 PM. For the alcohol provocation test, the stated volumes of absolute alcohol were diluted in approximately 100 mL fruit juice. The provocation schedule was as follows: fruit juice (placebo) at 11:00 AM, 11.30 AM, and 12.00 noon and alcohol 1 mL at 14:30 PM, 3 mL at 15.00 PM, and 6 mL at 15.30 PM. No respiratory symptoms were observed with either provocation test, and the patient felt well all day.

After 1 year, the dose of omalizumab was reduced to 150 mg monthly. She remained symptom free and could take aspirin and enjoy drinking alcohol without unwanted effects. Also, she has reduced her daily pharmacotherapy to inhaled fluticasone propionate (1000 µg), oral prednisolone (5 mg), and tiotropium bromide (18 µg). No adverse reactions to omalizumab have been reported.

In May this year, the patient stopped omalizumab therapy for personal reasons but her original symptoms began to reemerge over the following 2 months. In July, she underwent nasal provocation with aspirin. Nasal provocation with 40 µL 0.9% NaCl caused a small rise in peak inspiratory nasal flow (PINF) from a baseline of 212 L/min to 241 L/min. However, following provocation 30 minutes afterwards with 16 mg lysine-aspirin, her PINF fell by 43% to 120 L/min 10 minutes later. Omalizumab therapy was then reintroduced at 150 mg monthly after which she again became symptom free. In October, she underwent further nasal provocation. This time, installation of lysine-aspirin, 16 mg, produced only an 8% fall in the PINF from a baseline of 208 L/min to 196 L/min 10 minutes later, demonstrating a clear loss of aspirin sensitivity.

The mechanism underlying omalizumab's reversal of AERD and the associated alcohol intolerance, a condition that is traditionally not considered to be IgE mediated, is not clear. In contrast to asthma, in which omalizumab may take several months to become fully effective,<sup>9</sup> the onset of action of omalizumab in this patient was very rapid.

In conclusion, a patient with severe AERD was successfully treated with omalizumab. Omalizumab produced a clear improvement in quality of life and a reduction in asthma symptoms, improved the lung function, and restored tolerance to both aspirin and alcohol. Further studies of the use of omalizumab in the treatment of AERD appear warranted.

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Conflict of interest: The authors declare that they have no relevant conflicts of interest.

Received for publication December 18, 2014; revised January 16, 2015; accepted for publication January 20, 2015.

Available online January 30, 2015.

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2213-2198

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<http://dx.doi.org/10.1016/j.jaip.2015.01.012>**REFERENCES**

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