

Clinical Communications

Mepolizumab does not prevent all aspirin-induced reactions in patients with aspirin-exacerbated respiratory disease: A case series

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Clinical Implications

- Aspirin-exacerbated respiratory disease is characterized by nonsteroidal anti-inflammatory drug-induced respiratory reactions in patients with nasal polyposis and asthma. Mepolizumab, an anti-IL-5 antibody, is often used as an adjunct asthma treatment for patients with aspirin-exacerbated respiratory disease. Our data suggest that patients with aspirin-exacerbated respiratory disease can still develop aspirin-induced reactions while on mepolizumab.

Aspirin-exacerbated respiratory disease (AERD) is a syndrome that includes nasal polyposis, asthma, and nonsteroidal anti-inflammatory drug sensitivity. This clinical triad is seen in about 7% of adults with asthma, and in about 15% of those with severe asthma,¹ with the average age of onset being 34 years. A positive aspirin-induced reaction during a provocative aspirin challenge is the current standard for confirmative diagnosis.² Aspirin desensitization, followed by initiation of daily high-dose aspirin therapy, is often used to help reduce nasal polyposis and asthma symptoms in these patients.³ More recently, biologics, such as mepolizumab, have also been used on their own or as an adjunct with high-dose aspirin.⁴ Mepolizumab is a fully humanized mAb against IL-5, which is the main cytokine responsible for the maturation, activation, and survival of eosinophils,⁵ and is Food and Drug Administration–approved for the treatment of uncontrolled eosinophilic asthma.⁶ However, the effects of anti-IL-5 treatment on the severity of aspirin-induced reactions are unknown. Using a retrospective chart review of patients at the Brigham and Women's AERD clinic, we describe 3 patients with AERD who all developed clinically observed reactions during oral aspirin challenge/desensitization while on mepolizumab.

Patient 1 was a 48-year-old white woman diagnosed with AERD in 2016 who had had 2 sinus surgeries before the aspirin desensitization, with the last surgery occurring 23 months before her aspirin desensitization. Her daily medications included montelukast 10 mg oral nightly, zileuton 1200 mg oral twice a day, and an oral antihistamine, as well as monthly injections of mepolizumab, which she had been on for 3 months at the time of desensitization. Since starting the mepolizumab she reported mild improvement in her asthma but continued to be completely anosmic, with bilateral nasal polyps present on examination. Her baseline FEV₁ and forced vital capacity were 1.81 L/72%

predicted and 2.44 L/78% predicted before the challenge, respectively. Before the desensitization, she stopped the montelukast, zileuton, and antihistamines. During the desensitization, the patient developed nasal congestion, headache, itching, and rhinorrhea, with a drop of 12% from baseline in her FEV₁, with a provocative aspirin dose of 162 mg inducing symptoms 32 minutes after ingestion.

Patient 2 was a 49-year-old white woman diagnosed with AERD in the early 1990s who had 4 sinus surgeries before desensitization, the most recent of which occurred at least 10 years before the aspirin desensitization. Her daily medications included daily inhaled corticosteroids with a long-acting β -agonist, tiotropium, fexofenadine, and diphenhydramine, as well as monthly injections of mepolizumab, which she had been on for 13 months at the time of desensitization. Since starting mepolizumab she reported fewer asthma exacerbations, but she continued to have poor control of her baseline asthma symptoms. She also remained anosmic, with bilateral nasal polyps present on examination. Her baseline FEV₁ and forced vital capacity were 1.84 L/60% predicted and 2.50 L/65% predicted, respectively. Before the desensitization, her antihistamines were stopped. During the aspirin desensitization, the patient developed pruritus, hives, and audible wheezing on chest auscultation, without a change in her FEV₁. The provocative aspirin dose was 40 mg, inducing symptoms 15 minutes after ingestion.

Patient 3 was a 38-year-old African woman diagnosed with AERD in 2016 with 1 previous sinus surgery, 7 months before desensitization. Her daily medications included an inhaled corticosteroid with a long-acting β -agonist, an additional daily inhaled corticosteroid, and montelukast, as well as monthly injections of mepolizumab, which she had been on for 6 months at the time of desensitization. She reported very little symptomatic improvement from the mepolizumab and had continued anosmia. Her baseline FEV₁ was 2.22 L/67% predicted, and her baseline forced vital capacity was 2.91 L/71% predicted. During the desensitization, she developed pruritus, severe abdominal pain, nausea, intractable vomiting, and wheezing, with a decrease of 11% in her FEV₁. She was treated with intramuscular epinephrine due to the severity of her symptoms and the desensitization was stopped. The provocative aspirin dose was 40.5 mg, inducing symptoms less than 30 minutes after ingestion. A tryptase, drawn 7 hours after the onset of symptoms, was 19 ng/mL.

On the basis of this small case series, we conclude that patients with AERD can still develop aspirin-induced reactions, including severe and systemic symptoms, despite monthly anti-IL-5 treatment with mepolizumab. Therefore, continued aspirin and nonsteroidal anti-inflammatory drug avoidance in patients with AERD who are treated with mepolizumab is recommended unless the patients have successfully completed an aspirin desensitization. A larger prospective study would be needed to conclusively determine the effect of mepolizumab treatment on the positive and negative predictive diagnostic value of provocative aspirin challenges in patients with suspected AERD.

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REFERENCES

1. Rajan JP, Wineinger NE, Stevenson DD, White AA. Prevalence of aspirin-exacerbated respiratory disease among asthmatic patients: a meta-analysis of the literature. *J Allergy Clin Immunol* 2015;135:676-681.e671.
2. Lee RU, Stevenson DD. Aspirin-exacerbated respiratory disease: evaluation and management. *Allergy Asthma Immunol Res* 2011;3:3.
3. McMains KC, Kountakis SE. Medical and surgical considerations in patients with Samter's triad. *Am J Rhinol* 2006;20:573-6.
4. Tuttle KL, Buchheit KM, Laidlaw TM, Cahill KN. A retrospective analysis of mepolizumab in subjects with aspirin-exacerbated respiratory disease. *J Allergy Clin Immunol Pract* 2018;6:1045-7.
5. Abonia JP, Putnam PE. Mepolizumab in eosinophilic disorders. *Expert Rev Clin Immunol* 2011;7:411-7.
6. Choy MS, Dixit D, Bridgeman MB. Mepolizumab (Nucala) for severe eosinophilic asthma. *P & T* 2016;41:619-22.