Aspirin-Exacerbated Respiratory Disease

Evan S. Walgama, MD, Peter H. Hwang, MD*

KEYWORDS

• Aspirin-exacerbated respiratory disease • Chronic rhinosinusitis • Nasal polyposis • Sinus surgery

KEY POINTS

- AERD is a well-recognized subtype of difficult-to-control CRS. It has specific biomarkers and disease-specific treatment considerations.
- The clinical hallmark of AERD is an acquired sensitivity to ingestion of aspirin and other cyclooxygenase-1 (COX-1) inhibitors.
- Familiarity with aspirin desensitization is essential for sinus surgeons, although it is often performed by medical allergists.

INTRODUCTION

Aspirin-exacerbated respiratory disease (AERD) is an inflammatory condition characterized by the triad of asthma, rhinosinusitis, and sensitivity to aspirin. AERD is also referred to as Samter triad, and beyond these two designations, the literature has used several others including aspirin triad, aspirin-sensitive asthma, aspirin-induced asthma, and aspirin-intolerant asthma. For this article, AERD is the preferred nomenclature.

AERD is one of the best characterized subtypes of rhinosinusitis.[1] Disordered eicosanoid metabolism, the pathophysiologic mechanism underlying AERD, is unique to this disorder. The rhinosinusitis of AERD is typically severe and, among currently defined subtypes, one of the more difficult to control. Fortunately, there are specific treatment options available to patients with aspirin sensitivity, including aspirin desensitization, which may ameliorate the severity of upper and lower airway inflammatory disease.[2–7] In this sense AERD is a prototype for the application of precision medicine principles; it is a well-defined subtype of chronic rhinosinusitis (CRS) with individualized treatment strategies tailored to the underlying pathophysiologic mechanism.

Disclosure Statement: No disclosures (E.S. Walgama); Consultant: Olympus, Intersect, Arrinex, Sinuwave (P.H. Hwang).
Department of Otolaryngology/Head and Neck Surgery, Stanford School of Medicine, Stanford Sinus Center, 801 Welch Road, Palo Alto, CA 94304, USA
* Corresponding author.
E-mail address: hwangph@stanford.edu

Otolaryngol Clin N Am 50 (2017) 83–94
http://dx.doi.org/10.1016/j.otc.2016.08.007
oto.theclinics.com

With a proliferation of novel biologic agents to address specific components of the inflammatory cascade, AERD may serve as a model for how other types of difficult-to-control CRS are treated in the future.

CLINICAL PRESENTATION

AERD is an acquired disorder that typically presents in the third or fourth decade.[8,9] Patients usually do not report a previous history of atopy, rhinitis, or asthma, and may offer a history of tolerating aspirin or nonsteroidal anti-inflammatory drugs well into adulthood. This disorder affects approximately 0.5% of the population, and females twice as often as males.[10] Obesity and smoking are risk factors that are more associated with AERD than aspirin-tolerant asthma.[10]

The hallmark of AERD is an acquired sensitivity to ingestion of aspirin and other cyclooxygenase (COX)-1 inhibitors. Patients with AERD develop symptoms 30 to 120 minutes after ingestion of aspirin, resulting from proinflammatory effects of dysregulated cysteinyl leukotrienes on the upper and lower respiratory tracts (increased vascular permeability, bronchoconstriction, and eosinophil chemotaxis and activation). Patients typically experience acute onset of nasal congestion, conjunctivitis, throat tightness, and exacerbation of asthma. There can also be an associated anaphylactic-like reaction characterized by urticaria, gastrointestinal disturbance, or hypotension.[11] Because the drug reaction is not IgE-mediated, it is not considered true anaphylaxis. The severity of symptoms is variable, from minimal wheezing to severe respiratory compromise.

In the absence of an acute exposure to aspirin, patients who develop AERD still experience progressive upper and lower respiratory inflammatory symptoms because of abnormally elevated circulating levels of cysteinyl leukotrienes. The syndrome may unfold over a few years, with the first symptom to present usually being rhinitis.[8] The rhinitis is often reported to have originated as a "cold that never went away." It is associated with a clear discharge and may be resistant to standard therapies. Rhinitis progresses to CRS in 60% to 90% of cases.[8] CRS associated with AERD is characterized by hyperplastic mucosal remodeling with prominent eosinophilia, and ultimately, nasal polyposis.

An average of 2 years later, patients develop asthma.[8] Patients frequently have no prior history of childhood asthma or any prior problems with reactive airway disease. The asthma of AERD is typically moderate-severe to severe, by current classification standards. It is often difficult to control; compared with patients with aspirin-tolerant asthma, patients with AERD are more likely to have severe asthma, to require intensive care unit admission for asthma, to need oral steroids for asthma exacerbation, and to receive high-dose inhaled steroids for asthma control.[12] However, sometimes asthma is absent.[4]

Aspirin intolerance can develop at any point during this time course but frequently is the last part of the triad to develop. This happens on average 4 years after the onset of asthma.[8] Because most patients with CRS and comorbid asthma do not have aspirin sensitivity, taking a careful history regarding aspirin tolerance is important to discern patients with AERD from those without AERD. Still, in patients with asthmatic rhinosinusitis who have no history of adverse reaction to aspirin, 15% have a positive oral aspirin challenge.[8] Conversely, for patients with asthmatic rhinosinusitis who do report a history of adverse reaction to aspirin, 14% have a negative oral aspirin challenge.[13] Patients who report recurrent adverse reactions to aspirin, or who had a previous severe reaction to aspirin, have fewer negative oral aspirin challenges.