Aspirin-Exacerbated Respiratory Disease as an Endotype of Chronic Rhinosinusitis

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KEYWORDS

• Chronic rhinosinusitis • Chronic rhinosinusitis with nasal polyps • CRSwNP
• Aspirin-exacerbated respiratory disease • AERD • Samter disease • Samter triad

KEY POINTS

- Clinically, patients with aspirin-exacerbated respiratory disease (AERD) can be distinguished from those with chronic rhinosinusitis with nasal polyps (CRSwNP) and asthma by the development of respiratory symptoms following the ingestion of a COX-1 inhibitor. However, clinical history alone may not always be sufficient to confirm the diagnosis of AERD.
- In the absence of COX-1 inhibitors, patients with AERD on average still have worse upper and lower respiratory tract disease than those patients with CRSwNP with or without asthma.
- Nasal polyps from patients with AERD and CRSwNP are both defined by a predominant type-2 inflammatory environment but there appears to be significantly increased levels of eosinophil and mast cell degranulation occurring in AERD.
- Mechanistically, AERD, unlike CRSwNP, is characterized by platelet activation as well as a dysregulation in arachidonic acid metabolism.

Disclosures: W.W. Stevens has no financial conflicts of interest. R.P. Schleimer has served as a consultant with several pharmaceutical companies with interest in CRS, including AstraZeneca, Genentech, GSK, Intersect ENT, Merck, Regeneron, and Sanofi. R.P. Schleimer is a founder, shareholder, and advisor for Allakos.
Funding: This work was supported by Chronic Rhinosinusitis Integrative Studies Program (U19-AI106683) and by the National Institutes of Health grants T32 AI083216, R37 HLO68546, RO1 HL0788860 and R01 AI104733.
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Immunol Allergy Clin N Am 36 (2016) 669–680
http://dx.doi.org/10.1016/j.iac.2016.06.004 **immunology.theclinics.com**
0889-8561/16/$ – see front matter © 2016 Elsevier Inc. All rights reserved.

INTRODUCTION

Chronic rhinosinusitis with nasal polyps (CRSwNP) and aspirin-exacerbated respiratory disease (AERD) are both conditions characterized by the presence of chronic sinonasal inflammation and nasal polyps. Numerous groups have labored to describe the clinical features of these diseases as well as investigate the underlying mechanisms that could be driving their overlapping but distinct pathophysiologic mechanisms. However, there are few head-to-head studies directly comparing the sinonasal inflammatory environment of CRSwNP with that of AERD. As a result, the relationship between CRSwNP and AERD remains incompletely defined.

CLASSIFICATION

To further understand the relationship between CRSwNP and AERD, it is important to review the clinical criteria needed to make the diagnosis of each condition. Per the consensus guidelines, patients with CRSwNP must present with greater than 12 weeks of rhinorrhea, facial pressure or pain, nasal congestion, and/or a reduction in sense of smell.[1,2] Additionally, there must be objective evidence of nasal polyps and mucosal disease visualized on sinus computed tomography (CT) imaging or nasal endoscopy. CRSwNP can exist without medical comorbidities but more often is observed with other chronic conditions, such as asthma, hay fever, cystic fibrosis, or eosinophilic granulomatosis with polyangiitis.

The clinical diagnosis of AERD is based on evolving criteria. In 1922, Widal published the first study describing a patent with asthma, nasal polyps, and sensitivity to aspirin. Later, Samter and Beers[3] described a cohort of aspirin-sensitive patients of whom 85% had only respiratory symptoms and 51% had nasal polyps. In this report, it was noted "that every patient does not necessarily present with every potential component of the syndrome." Furthermore, later studies suggested that patients with AERD first developed upper respiratory tract symptoms that progressed to involve the lower respiratory tract and then last acquired the aspirin intolerance.[4] In 2001, the term "aspirin-exacerbated respiratory disease" was termed by Stevenson and colleagues[5] to emphasize that these patients had underlying respiratory disease that was worsened but not induced by aspirin. Additionally, over the course of time, it was also discovered that all medications that inhibit the cyclooxygenase-1 (COX-1) enzyme, not just aspirin, could elicit upper and lower respiratory tract symptoms in patients with AERD.

Given this history, it is not surprising that different terminologies are still used to define the same or related clinical phenotypes (eg, Samter disease, Samter triad, AERD, nonsteroidal anti-inflammatory disease–exacerbated respiratory disease, aspirin-intolerant asthma). However, even when the same terminology is used, there can be variations in the clinical features of the study cohort. For example, AERD has been investigated in patients with asthma and aspirin intolerance as well as in patients with asthma, aspirin intolerance, and CRSwNP. How the presence (or absence) of sinonasal inflammation might influence the overall disease pathology is not known. As a result, it is not clear whether these 2 groups are distinct subsets or rather part of a disease continuum. Unless otherwise specified, this review defines AERD as the presence of the triad of CRSwNP, asthma, and worsening of upper and lower respiratory tract symptoms following the ingestion of COX-1 inhibitors.

EPIDEMIOLOGY

By definition, all patients with AERD have CRSwNP; however, not all patients with CRSwNP have AERD. It is estimated that only approximately 10% of patients with

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