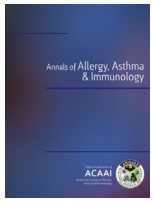
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Letter

Resolution of alcohol-induced respiratory symptoms following aspirin desensitization in aspirin-exacerbated respiratory disease

An enigmatic disease process, aspirin-exacerbated respiratory disease (AERD) continues to exhibit new facets as the understanding of this condition evolves. First described by Beers and Samter in 1968, the prevalence of AERD is estimated to be 5% to 10% of adults with asthma.[1] The pathogenesis of AERD remains incompletely understood as does its emerging association with alcohol-induced respiratory reactions. The earliest cases of alcohol-induced respiratory reactions were described in a controlled challenge study that described severe bronchospasm in patients with asthma after ingestion of sulfite-containing red wine in 1986.[2,3] The AERD and alcohol-induced respiratory reactions were more firmly linked in a 2002 study in which 316 of 11,933 randomly sampled patients had alcohol-induced nasal symptoms, 17% of whom developed concomitant aspirin and nonsteroidal anti-inflammatory drug intolerance.[4] More recently, a 2014 questionnaire-based study by Cardet et al[1] assessed 4 clinical types (aspirin challenge-confirmed AERD, aspirin-tolerant asthma, aspirin tolerance with chronic rhinosinusitis, and a healthy control) and found the prevalence of alcohol-induced reactions to be highest in patients with AERD. Notably, they commented that alcohol-related respiratory symptoms in 63% of patients with AERD showed improvement after aspirin desensitization, but the degree of tolerance was not characterized. We present the first reported case of a patient with confirmed AERD and alcohol-induced respiratory reaction who developed complete resolution of alcohol-induced symptoms with aspirin-desensitization therapy.

A 56-year-old man had a history of facial flushing and profuse rhinorrhea with ingestion of alcoholic beverages, which arose concurrently with his diagnosis of severe recurrent nasal polyposis, moderate persistent asthma, allergic rhinitis, anosmia, and ageusia. The severity of symptoms related to his nasal polyps required him to undergo multiple polypectomies with a frequency of surgery of almost every 2 years. He first noted symptoms to ibuprofen 5 years before presentation, followed by an aspirin-related reaction, and subsequently avoided all nonsteroidal anti-inflammatory drugs. In these instances, he related symptoms of cephalic flushing, profuse rhinorrhea, and epiphora mirroring his symptoms with alcohol ingestion. According to spirometry and history, he had moderate persistent asthma that was well controlled with medium-dose inhaled fluticasone and salmeterol.

In preparation for an aspirin challenge, montelukast was added to his asthma control regimen. He underwent an aspirin challenge and desensitization using the intranasal ketorolac protocol,[5] which elicited strong upper respiratory symptoms and a reversible decrease in forced expiration volume in 1 second greater than 10% from baseline. Although his change in forced expiration volume in 1 second did not meet strict criteria, given his pretreatment with montelukast and the development of typical upper respiratory symptoms, he was characterized as experiencing a positive challenge. Since completing successful aspirin desensitization, he has remained on 650 mg of aspirin twice daily and has regained his sense of smell and taste. His montelukast was discontinued after the challenge. Significantly, he self-challenged to wine, grain liquor, and beer without any symptoms and continues to tolerate these beverages without issue.

The etiology of the association between alcohol-induced respiratory symptoms and AERD is unknown; current thought centers on dysregulation of the arachidonic acid pathway.[1,6–8] For AERD, the medical literature focuses on aberrancies in the arachidonic acid pathway compounded by cyclooxygenase-1 inhibition, which favor the activity of 5-lipoxygenase and cysteinyl leukotriene (Cys-LT) production largely unchecked by prostaglandin E_2. The Cys-LTs are known inflammatory mediators and particularly increases in leukotriene E_4 have been found in patients with AERD challenged with aspirin.[6,9] There also appears to be a direct relation between the amount of urinary Cys-LTs and severity of respiratory symptoms.[9] Conversely, prostaglandin E_2 serves as an immunoregulator because it suppresses the function of inflammatory mediators such as Cys-LTs. A possible correlation with alcohol-related symptoms has been suggested by an overproduction of Cys-LTs in urine studies of intoxicated subjects.[1] Unfortunately, further links in the biochemical properties of patients with AERD and alcohol-induced respiratory symptoms have not yet been made.

This case lends clinical evidence bolstering the idea of a common pathway for AERD and respiratory symptoms from alcohol consumption in this subset of patients, because these resolved after aspirin desensitization. It remains to be seen whether these conditions truly represent the same clinical entity or perhaps an overlap syndrome of related processes. Another consideration is the possibility of a nonspecific increase in bronchial reactivity to multiple agents in patients with AERD as suggested by literature on corticosteroids in aspirin-sensitive patients with asthma.[10] The primary limitation in further investigation is that the prevalence of AERD in patients who develop alcohol-induced respiratory symptoms is unknown. Although widely recognized in the allergy community, AERD remains relatively obscure in primary care. A substantial amount of cases are probably unrecognized and treated as isolated asthma. Another limitation is a lack of diagnostic and screening modalities other than history. The importance of identifying an AERD-specific biomarker was recently highlighted by Cahill and Laidlaw.[11] Identifying those patients with AERD and

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concomitant alcohol-related symptoms could link these conditions and aid in the search for a specific biomarker. In the interim, physicians should be cognizant that symptoms of alcohol-induced respiratory reactions could be an indication for AERD screening.

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