CLINICAL VIGNETTE

A Case of Samter's Syndrome

William Reid, M.D., and Shivani Patel, M.D.

Case Report

A 53-year-old female with reported medical history of asthma was admitted with shortness of breath and thought to be due to asthma attack. She used a budesonide/formoterol inhaler daily, and short-term inhalers for exacerbations a few times per year. She had been hospitalized once prior for asthma but never intubated. The patient was in her usual state of health on the morning of admission when she boarded a flight heading from Tucson toward Israel. She was concerned about developing a blood clot on the long journey, so she took 325mg of aspirin right before take-off. Shortly thereafter, she noticed difficulty breathing, described as trouble getting air in. Symptoms persisted throughout a scheduled stopover in Los Angeles, and the patient became concerned that she would not be able to tolerate the second leg of the flight. She presented to the Emergency Department for further evaluation. She denied chest pain, palpitations, dizziness, visual change, audible wheeze, fevers, chills, sick contacts, weight gain, orthopnea, paroxysmal nocturnal dyspnea, tobacco use, or IV drug use.

On arrival to the ER her vital signs were stable with temperature 36°C, blood pressure 128/68, heart rate 88, respiratory rate 22, and oxygen saturation 93% on room air. Exam was significant for diffuse inspiratory wheezes throughout both lungs. She had no stridor, neck mass, thyromegaly, jugular venous distention, or peripheral edema. Cardiac and oral exams were normal. Labs were noteworthy for an elevated D-dimer of 1254, for which she underwent CTA of the chest that was negative for pulmonary embolism. A chest X-ray was unremarkable. She received nebulized albuterol and oral prednisone 60mg with some improvement in breathing but no return to baseline status. She was admitted overnight for observation.

Further questioning on hospital day 2 revealed a distant history of nasal polyps. In conjunction with her known asthma, the diagnosis of an aspirin allergy was entertained, and the patient was treated with oral diphenhydramine, loratidine, and montelukast. Her shortness of breath and wheezing resolved, and she was discharged on montelukast with instructions to follow-up with an Allergist when she returns home. She subsequently saw an Otolaryngologist and underwent nasal polyp removal, followed by an aspirin-desensitization protocol. On telephone interview one year later, the patient reports doing well without any further asthma attacks while on daily aspirin and montelukast therapy.

Discussion

Aspirin-exacerbated respiratory disease (AERD), also referred to as aspirin-induced asthma (AIA) or Samter's syndrome, consists of asthma, chronic rhinosinusitis with nasal polyposis (CRS with NP), and sensitivity to aspirin or other COX-1 inhibitors. This pattern is known as Samter's Triad, for German-American Immunologist Dr. Max Samter who publicized the association between asthma and nasal polyps in the 1960s.[1,2] The classic reaction combines acute bronchospasm with profuse rhinorrhea, conjunctival injection, periorbital edema, and sometimes flushing of the head and neck.[3] The reaction is classified as a Type 1 pseudoallergic reaction as it is not IgE-mediated, but rather it is an abnormal response to buildup of leukotriene byproducts from inhibition of the COX-1 pathway.[4] Leukotrienes are potent bronchoconstrictors and increase vascular permeability, thereby precipitating airway spasm, eosinophil migration, mucus production, and airway edema.[5] Provocative aspirin challenge is the gold standard for diagnosis of AERD, involves administering 30-150mg ASA, and assessing for a decrease in FEV1 of more than 20% and/or a prominent naso-ocular reaction.[6] Reactions usually occur within 3 hours of ingesting COX-1 inhibiting compounds.[7]

A multi-pronged approach is required to mitigate the major symptoms of AERD. Asthma management includes standard therapies with the addition of a leukotriene-receptor antagonist (LTRA). More data exist for montelukast than zafirlukast in this regard. One 4-week randomized trial of 80 patients with AERD showed 54% fewer exacerbations in patients treated with montelukast compared to placebo.[8] For patients who fail to improve with a LTRA, consideration can be given to the 5-lipoxygenase inhibitor zileuton, which prevents formation of leukotrienes. Unfortunately, zileuton is a twice daily medication that requires hepatic monitoring since 3-5% of patients will have elevations in liver function tests to greater than 3 times the upper limit of normal.[9] To date, simultaneous use of both LTMA and zileuton has not been studied. Management of chronic rhinosinusitis usually involves corticosteroid administration to reduce edema and allow aeration and drainage of sinus tracts.[10] Nasal polyposis

that does not shrink in response to oral glucocorticoids may require referral to an Otolaryngologist for surgical debulking,[11] as was the case with our patient.

Preventing further exacerbations of disease requires either discontinuation of all COX-1 compounds or desensitization with continuous ASA therapy.[10] Patients with AERD should be instructed to avoid all COX-1 inhibitors. Alternative options for treatment of pain in these patients include COX-2 inhibitors or acetaminophen. It is important to note that up to 34% of aspirin-sensitive asthmatics will also have cross-reactivity to high doses (greater than 1 gram) of acetaminophen. These reactions are usually mild, however, with an easily-reversed bronchospasm occurring in only 22% of the cases.[12] In patients with refractory symptoms or atherosclerotic heart disease and need for aspirin therapy, aspirin desensitization in consultation with an Allergist can be considered. Desensitization protocols require gradual uptitration of aspirin over several days, then continuous use of 650mg twice daily for maintenance.[13] Repeat desensitization is needed if aspirin therapy is stopped for longer than 48 hours.[10] Patients tend to report improvement in smell and nasal blockade following desensitization therapy.[14] The mechanism of action is incompletely understood, but it appears to involve reduced leukotriene expression via a decrease in interleukin-4.[15] Symptomatic treatment, surgery, removal of offending agents, and ASA desensitization therapy are all effective methods of managing AERD.

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