

Clinical Communications

A retrospective analysis of bronchiectasis in patients with aspirin-exacerbated respiratory disease

Yih-Chieh S. Chen, MD^{a,b}, Jillian C. Bensko, PA-C^a,
Tanya M. Laidlaw, MD^{a,b}, and Kathleen M. Buchheit, MD^{a,b}

Clinical Implications

- This study provides evidence for the presence of bronchiectasis and describes risk factors for bronchiectasis in patients with aspirin-exacerbated respiratory disease. Patients with aspirin-exacerbated respiratory disease and poorly controlled respiratory symptoms should be evaluated for comorbid bronchiectasis.

Bronchiectasis is an acquired chronic airway disease characterized by dilatation and destruction of the bronchial wall. Radiologic findings of airway dilation, bronchial wall thickening, mucopurulent plugs, and air trapping confirm the diagnosis. Patients classically present with productive cough, dyspnea, and recurrent respiratory infections.

Risk factors for bronchiectasis include airway obstruction, cystic fibrosis, immune deficiency, recurrent pulmonary infections, cigarette smoking, allergic bronchopulmonary aspergillosis (ABPA), atopy, and other systemic inflammatory diseases.¹⁻³ Bronchiectasis is associated with severe asthma and is believed to be a contributor to asthma severity. Coman et al⁴ reported that bronchiectasis may be identified by chest computed tomography (CT) in up to 47% of patients with severe asthma, and that patients with severe asthma and bronchiectasis were more likely (odds ratio, 2.24) to have hypersensitivity to nonsteroidal anti-inflammatory drugs. However, the relationship between bronchiectasis and aspirin-exacerbated respiratory disease (AERD), the triad of adult-onset asthma, chronic rhinosinusitis with nasal polyps (CRSwNP), and pathognomonic respiratory reactions to nonsteroidal anti-inflammatory drugs that inhibit cyclooxygenase 1, is not known.

Bronchiectasis is also associated with chronic rhinosinusitis (CRS). In a Spanish cohort, 80% of the patients with bronchiectasis were also diagnosed with CRS, and 26% were diagnosed with CRSwNP.⁵ In a US cohort, CRS was present in 45% of patients with bronchiectasis, and the presence of both CRS and bronchiectasis was associated with higher rates of asthma, allergic rhinitis, gastroesophageal reflux disease, and antibody deficiency compared with patients with bronchiectasis alone.⁶ A recent systematic review of 8 studies found that CRS was present in 62% and CRSwNP was present in 29% of patients with bronchiectasis.⁷ Furthermore, comorbid CRSwNP and bronchiectasis is associated with lower quality-of-life measures compared with bronchiectasis alone.⁸ Therefore, patients with AERD have 2 possible correlates to bronchiectasis development—asthma and CRSwNP.

We conducted a nested case-control study via retrospective chart review of a cohort of 742 patients with physician-diagnosed AERD seen at Partners HealthCare (Brigham and Women's Hospital, Massachusetts General Hospital, Massachusetts Eye and Ear Infirmary). The study was approved by the Partners HealthCare Institutional Review Board. Electronic charts (Epic Systems, Verona, Wis) were reviewed for the presence of the agreed-upon terms: "bronchiectasis," "CT chest," "CAT scan," "CT," and "CAT." Of the 742 patients with AERD, we identified 149 patients with chest CT imaging. The chest CT imaging reports for the 149 patients were reviewed for the presence of bronchiectasis as based on the radiologist's clinical read. Demographic information, clinical characteristics, imaging characteristics, AERD history, and laboratory data were extracted from the Partners HealthCare electronic medical record using a previously studied query tool.⁹ We compared markers of disease severity and known risk factors for bronchiectasis between patients with AERD with bronchiectasis on chest CT (cases) and patients with AERD without bronchiectasis on chest CT (controls), including lung function, respiratory disease treatment, duration of disease, and comorbidities relevant to the development of bronchiectasis. Data were analyzed using student *t* test and χ^2 test with GraphPad Prism software v7.0a (GraphPad, La Jolla, Calif).

Of the 149 patients with AERD and prior chest CT, 57 (38%) had bronchiectasis. There was no significant difference between the sex or race distribution of the control group versus the bronchiectasis group (Table I). Patients who did not report their race were excluded from this statistical analysis. However, the patients with bronchiectasis had a significantly higher mean age at the time of chart review compared with control patients without bronchiectasis. Among the bronchiectasis cohort, 82% had middle- or lower-lobe bronchiectasis, whereas 18% had upper-lobe bronchiectasis. The presence of bronchiectasis was associated with a longer duration of AERD ($P = .004$) and lower FEV₁% predicted at the time point closest to the CT imaging ($P = .01$) (Table I). In addition, the bronchiectasis group had higher rates of ABPA ($P = .001$), aspiration ($P = .03$), mycobacterial infection ($P = .001$), and pneumonia ($P = .02$). There was no difference in smoking history, diagnosis of autoimmune disease, gastroesophageal reflux disease, or absolute eosinophil count (Table II). There was a trend toward higher rates of physician-diagnosed atopy in the bronchiectasis cohort, but specific allergen sensitization data were not available for many subjects to determine whether this was specific to fungal sensitization. There were also more patients in the bronchiectasis cohort with immunoglobulin or immunoglobulin subclass deficiencies. However, because of the retrospective nature of the review, we could not establish whether this was a primary immune defect or whether it reflected increased oral corticosteroid exposure in the bronchiectasis cohort. In the bronchiectasis group, the diagnosis of asthma and nasal polyps almost always preceded the diagnosis of bronchiectasis by an average of 23 and 20 years, respectively. Only 3 patients were diagnosed with asthma 1 to 2 years after the diagnosis of bronchiectasis. However, there was no significant difference in the age of asthma

TABLE I. Demographic characteristics and markers of AERD severity of the control vs bronchiectasis cohort

Characteristic	Control (N = 92)	Bronchiectasis (N = 57)	P value
Age (y), mean $\pm$ SEM	60 $\pm$ 15	65 $\pm$ 1.8	.03*
Sex % Female (N)	67% (62)	53% (30)	.07†
Race % white (N/total)	83% (75/90)	83% (33/40)	.90†
Mean FEV ₁ % predicted $\pm$ SEM	76.4 $\pm$ 2.3	67.1 $\pm$ 2.7	.01*
Mean duration of AERD (y) $\pm$ SD	18.5 $\pm$ 1.4	26.5 $\pm$ 2.5	.004*
Mean lifetime number of sinus surgeries $\pm$ SEM	2.4 $\pm$ 0.3	2.8 $\pm$ 0.4	.50*
Median age of asthma diagnosis (y) $\pm$ SEM	36 $\pm$ 2	35 $\pm$ 3	.60*
Absolute eosinophil count (K/ μ L) $\pm$ SEM	0.48 $\pm$ 0.6	0.6 $\pm$ 0.7	.27*

Bold indicates statistical significance ($P < .05$).

*Unpaired, 2-tailed t test.

† χ^2 test.

TABLE II. Risk factors for development of bronchiectasis in patients with AERD with and without bronchiectasis

Characteristic	Control (N = 92)	Bronchiectasis (N = 57)	P value*
Smoking history, n (%)	32 (35)	23 (40)	.49
GERD, n (%)	52 (57)	37 (65)	.28
ABPA: physician diagnosed, n (%)	0 (0)	6 (11)	.001
Aspiration, n (%)	6 (7)	9 (16)	.03
Mycobacterial infections, n (%)	1 (1)	8 (14)	.001
Pneumonia, n (%)	50 (54)	41 (75)	.02
Atopy: physician diagnosed, n (%)	36 (39)	30 (53)	.05
Autoimmune disease, n (%)	11 (12)	12 (21)	.08

GERD, Gastroesophageal reflux disease.

Bold indicates statistical significance ($P < .05$).

* χ^2 test.

diagnosis or lifetime number of sinus surgeries between the patients with and without bronchiectasis.

Our study is the first to explore a relationship between AERD and bronchiectasis. Comorbid AERD and bronchiectasis was associated with a longer duration of AERD, which is not unexpected given that asthma and CRSwNP are known independent risk factors for bronchiectasis⁴⁻⁸ and are both present in patients with AERD. Compared with patients without bronchiectasis, patients with both AERD and bronchiectasis had reduced lung function and an increased rate of concomitant lung disease such as aspiration, ABPA, and pneumonia. Presence of these characteristics in patients with AERD, or poorly controlled asthma not responsive to standard-of-care therapies, should prompt consideration of coexisting bronchiectasis and need for CT imaging, because patients with bronchiectasis may require more aggressive respiratory management.

Our limited retrospective data are insufficient to determine the prevalence of bronchiectasis in patients with AERD or to explain the mechanism by which patients with AERD develop bronchiectasis. However, on the basis of our cohort, we would estimate the prevalence of bronchiectasis in patients with AERD to be between 8% and 38% (57 of 742 to 57 of 149 in those with CT scans). The range of estimated prevalence parallels the reported prevalence of bronchiectasis in patients with severe asthma,⁴ suggesting that bronchiectasis in our AERD cohort is attributable to asthma severity and is not specifically related to the unique AERD phenotype. In addition, the retrospective nature of the study did not allow for complete objective characterization of atopy, ABPA, and functional immune status. Prospective studies controlling for asthma severity are needed to

further understand the relationship between AERD and the development of bronchiectasis.

^aBrigham and Women's Hospital, Division of Allergy and Clinical Immunology, Jeff and Penny Vinik Center for Allergic Diseases Research, Boston, Mass

^bHarvard Medical School, Boston, Mass

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Corresponding author: Kathleen M. Buchheit, MD, Brigham and Women's Hospital, 60 Fenwood Rd, Building of Transformative Medicine, Rm 5002H, Boston, MA 02115. E-mail: kbuchheit@bwh.harvard.edu.

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