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Atopy and the Development of Chronic Rhinosinusitis in Children with Allergic Rhinitis

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Short Summary

The role of allergic rhinitis (AR) in the development of chronic rhinosinusitis (CRS) in children remains unknown. This study demonstrates the degree of atopy, as reflected by the number of aeroallergen sensitivities or the presence of atopic comorbidities, is not associated with progression to CRS in the pediatric age group.

Keywords

allergic rhinitis; hypersensitivity; respiratory hypersensitivity; sinusitis; pediatrics; asthma; food hypersensitivity

To the Editor

Allergic rhinitis (AR) has been previously associated with chronic rhinosinusitis (CRS) by virtue of similar inflammatory profiles and increased prevalence of AR in patients with CRS^{1,2}. Logistical issues such as requisite follow-up time and cohort sizes render impractical longitudinal studies of pediatric patients to detect the impact of AR on the development of CRS. In adults, the study of associations with CRS development in patients with AR has, however, been feasible and provided some insight^{3,4}. From the common clinical presentations of AR and CRS, it is reasonable to hypothesize that in children with AR, atopic characteristics—reflected by the number of atopic comorbidities or aeroallergen sensitivities—may be associated with CRS development.

We studied two cohorts of children with AR in order to identify specific characteristics potentially associated with CRS development. We identified these pediatric cohorts by screening the records of 19,186 children diagnosed with AR over a ten year period through formal clinic evaluation and skin testing in our institution's division of allergy and immunology (described in this article's Online Repository). One cohort (N=117), referred to as the AR cohort, is defined by at least nine years of allergy or otolaryngology follow-up subsequent to the diagnosis of AR without a diagnosis of CRS. This AR cohort is assumed

to reflect children with AR who do not develop CRS. The other cohort (N=37), referred to as the AR-CRS cohort, consists of children diagnosed with CRS after a minimum of one year of allergy or otolaryngology follow-up subsequent to initial diagnosis of AR and is assumed to reflect children with AR who later develop CRS. Patients in both cohorts were closely monitored with an average of 1.4 clinic visits (SD: 0.7) per year for patients in the AR cohort and 3.5 clinic visits (SD: 1.9) per year for patients in the AR-CRS cohort over the follow-up period. Clinical, demographic and atopic characteristics of these children were obtained and analyzed with descriptive statistics (described in this article's Online Repository) (Table 1).

Although children in the AR cohort (mean: 5.4 years; SD: 3.7 years) initially presented at a younger age ($P=0.047$) compared to children in the AR-CRS cohort (mean: 6.9 years; SD: 3.7 years), the children in the AR cohort (mean: 14.9 years, SD: 3.8 years) were generally older ($P<0.001$) than children in the AR-CRS cohort (mean: 11.0 years, SD: 3.6 years) at the time of the last office visit. This is attributable to the follow-up duration criteria utilized to identify the two cohorts. There were otherwise no statistically significant differences in the prevalence of asthma, eczema, or serum total IgE levels (Table 1). Children in the AR cohort had a greater prevalence of food allergies ($P=0.008$). While no specific aeroallergen sensitivity is more prevalent in either cohort (although a trend existed towards greater dog allergy in the AR cohort), children in the AR cohort had more aeroallergen sensitivities overall ($P < 0.001$) (Table 1). A history of smoke exposure from in-home parental tobacco use was more prevalent in the AR-CRS cohort ($P=0.029$) (Table 1).

We assessed the children's demographic characteristics, atopic comorbidities and aeroallergen sensitivities for association with the development of CRS by both univariate and multivariate logistic regression analyses (described in this article's Online Repository) (Table 2). On univariate analysis, exposure to tobacco smoke was positively associated with progression to CRS (OR=3.96 [95% CI: 1.50–10.48]). This is consistent with previous work showing tobacco smoke both induces biofilm formation⁵ and adversely impacts nasociliary clearance⁶. In contrast, increasing age, the presence of concurrent asthma, food allergy and aeroallergen sensitivities were negatively associated with CRS development (Table 2).

Multivariate analysis revealed only age (OR=0.71 [95% CI: 0.57–0.89]) and food allergy (OR=0.06 [95% CI: 0.01–0.29]) to be negatively associated with CRS development in children with AR (Table 2). The detected negative association between increasing age and CRS development may simply reflect an artifact of the inclusion criteria used to identify each cohort. Alternatively, this negative association may suggest that pediatric CRS more likely to occurs earlier in childhood. To date, no data supports this latter conclusion, while the former explanation is supported by the finding that food allergy was the only statistically significant characteristic associated with CRS development by multivariate Cox proportional hazards regression (HR=0.26 [95% CI: 0.10–0.66], $P=0.004$) (described in this article's Online Repository).

In adults, Th1 and Th2 patterns of inflammation have been associated with CRS without polyps and with polyps, respectively^{1,7}. Such immunologic profiling in pediatric CRS has not been performed as extensively, although one recent study of sinonasal mucosa from pediatric CRS patients has not revealed any particular immunologic differentiation pattern⁸. By comparison, the immunologic profiles of food allergy may vary from classic IgE-mediated to cell-mediated delayed hypersensitivity⁹. The negative association between food allergy and the development of CRS may reflect some as yet uncharacterized, fundamental difference in the immunologic mechanisms underlying pediatric CRS and food allergy. This poses an interesting topic for future directed research.

In children with AR, the surprising absence of a positive association between the number of aeroallergen sensitivities or the presence of atopic comorbidities with the subsequent development of CRS suggests that the severity of atopy alone may not be positively predictive of CRS development. The detected negative association between the presence of food allergy in children with AR and subsequent development of CRS is suggestive but not necessarily indicative that AR children who develop CRS are less atopic. However, lack of positive association between atopic measures and development of CRS may suggest a greater role for infectious rather than inflammatory etiologies in the pathogenesis of pediatric CRS. Just as the pathophysiology of pediatric CRS remains largely uncharacterized, clearly so does its relationship with AR. The results of this study may also assure the parents and clinicians of atopic children that, while routine follow-up surveillance should be practiced, atopy alone may not fully predict an increased risk for CRS development. Other factors should be considered from a monitoring standpoint for this debilitating disease.

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References

1. Van Crombruggen K, Zhang N, Gevaert P, Tomassen P, Bachert C. Pathogenesis of chronic rhinosinusitis: Inflammation. *J Allergy Clin Immunol*. 2011; 128(4):728–732. [PubMed: 21868076]
2. Ryan MW, Brooks EG. Rhinosinusitis and comorbidities. *Curr Allergy Asthma Rep*. 2010; 10(3): 188–193. [PubMed: 20424995]
3. Sedaghat AR, Gray ST, Wilke CO, Caradonna DS. Risk factors for development of chronic rhinosinusitis in patients with allergic rhinitis. *Int Forum Allergy Rhinol*. 2012; 2(5):370–375. [PubMed: 22648994]
4. Sedaghat AR, Gray ST, Chambers KJ, Wilke CO, Caradonna DS. Sinonasal anatomic variants and asthma are associated with faster development of chronic rhinosinusitis in patients with allergic rhinitis. *Int Forum Allergy Rhinol*. 2013
5. Goldstein-Daruech N, Cope EK, Zhao KQ, et al. Tobacco smoke mediated induction of sinonasal microbial biofilms. *PLoS One*. 2011; 6(1):e15700. [PubMed: 21253587]
6. Wang LF, White DR, Andreoli SM, Mulligan RM, Discolo CM, Schlosser RJ. Cigarette smoke inhibits dynamic ciliary beat frequency in pediatric adenoid explants. *Otolaryngol Head Neck Surg*. 2012; 146(4):659–663. [PubMed: 22237301]
7. Van Zele T, Claeys S, Gevaert P, et al. Differentiation of chronic sinus diseases by measurement of inflammatory mediators. *Allergy*. 2006; 61(11):1280–1289. [PubMed: 17002703]
8. Wu X, Ghimbovski S, Aujla PK, Rose MC, Pena MT. Expression profiling of inflammatory mediators in pediatric sinus mucosa. *Arch Otolaryngol Head Neck Surg*. 2009; 135(1):65–72. [PubMed: 19153309]
9. Sampson HA. Update on food allergy. *J Allergy Clin Immunol*. 2004; 113(5):805–19. quiz 820. [PubMed: 15131561]

Table 1

Clinical and Demographic Characteristics

	AR Cohort (N = 117)	AR-CRS Cohort (N = 37)	P-value
Demographics			
Age ¹ (yrs)	14.9	11.0	< 0.001
Gender (%male)	72.6%	62.2%	0.65
Tobacco smoke exposure (%)	8.5%	27.0%	0.03
Comorbidities			
Asthma (%)	82.9%	64.9%	0.47
Eczema (%)	56.4%	51.4%	0.87
Food allergy (%)	72.6%	27.0%	0.008
Aeroallergen Sensitivities			
Log ₁₀ [total serum IgE] (SD) ²	2.6 (0.7)	2.3 (0.7)	0.08
Molds (%)	62.4%	37.8%	0.19
Any indoor (%)	86.3%	83.8%	1.00
Dust mites	73.5%	64.9%	0.77
Cats	62.4%	59.5%	1.00
Dogs	53.8%	24.3%	0.052
Mouse	22.2%	8.1%	0.14
Cockroach	27.4%	21.6%	0.68
Any outdoor (%)	67.5%	48.6%	0.35
Trees	60.7%	37.8%	0.19
Grasses	33.3%	24.3%	0.56
Weeds	44.4%	35.1%	0.60
Number of sensitivities (SD)	4.8 (2.4)	3.1 (2.2)	< 0.001

¹ Age at the final follow-up visit

² Total serum IgE levels were in units of U/mL. Comparisons were made on log10 transformed total serum IgE levels for both cohorts.

Table 2Association of Atopic Characteristics with Progression to CRS^{1,2}

	Univariate Odds Ratio	Univariate P-value	Multivariate Odds Ratio ³	Multivariate P-value
Demographics				
Age ⁴	0.69 (0.59 – 0.81)	< 0.001	0.71 (0.57 – 0.89)	0.002
Tobacco smoke exposure	3.96 (1.50 – 10.48)	0.006	—	
Comorbidities				
Asthma	0.38 (0.17 – 0.87)	0.022	—	
Food allergy	0.12 (0.05 – 0.26)	< 0.001	0.06 (0.01 – 0.29)	0.001
Aeroallergen Sensitivities				
Number of sensitivities	0.74 (0.62 – 0.88)	0.001	—	
Dust mites	0.36 (0.16 – 0.86)	0.020	—	
Dogs	0.20 (0.08 – 0.47)	< 0.001	—	
Mouse	0.25 (0.07 – 0.89)	0.03	—	
Any outdoor	0.46 (0.21 – 0.97)	0.041	—	
Trees	0.27 (0.12 – 0.60)	0.001	—	

¹ Odds ratios with 95%CI are shown only for variables meeting statistical significance on univariate association. Variables not meeting statistical significance on univariate analysis (and therefore not shown) are: gender, history of eczema, total serum IgE, presence of any indoor allergy, and allergies to molds, cat, cockroach, grasses and weeds.

² Aeroallergen sensitivities were unavailable for 12 children in the AR cohort who had allergy testing performed at another institution; these 12 children were excluded from analyses involving aeroallergen data. Thus univariate analysis of aeroallergen sensitivities as well as multivariate analysis included 105 of the 117 patients from the AR cohort but all 37 patients in the AR-CRS cohort

³ Odds ratios for predictor variables included in the multivariate analysis that are not statistically different from 1.0 are represented as —

⁴ Age at the final follow-up visit