

RESEARCH NOTE

Similarities between allergen sensitivity patterns of central compartment atopic disease and allergic rhinitis

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INTRODUCTION

Chronic rhinosinusitis (CRS) is an inflammatory condition of the nose and paranasal sinuses that persists for greater than 12 weeks.¹ CRS has traditionally been categorized based on the presence (CRSwNP) or absence (CRSSNP) of nasal polyps. CRSwNP can be further subcategorized into endotypes including aspirin-exacerbated respiratory disease (AERD), allergic fungal rhinosinusitis (AFRS), and, recently, central compartment atopic disease (CCAD) has been proposed as a novel endotype.²

There is a complex relationship between allergic rhinitis (AR) and CRS³; one potential link may be CCAD. CCAD is an inflammatory nasal condition characterized by polypoid changes localized to the posterior-superior nasal septum, and middle and superior turbinates, which are all central nasal structures of ethmoid origin.⁴ It has been hypothesized to have an allergic etiology, with inhaled allergens presumably stimulating an immunoglobulin E (IgE)-mediated response within this central sinonasal compartment.⁵

Although the association of CCAD with allergy has been supported by the literature, there have been no studies exploring the specific allergens to which patients with CCAD are susceptible. We compared results of allergy skin testing among AR, CCAD, and CRS subtypes to determine

specific allergens associated with these conditions and any relationships between their allergen sensitivity profiles.

PATIENTS AND METHODS

A retrospective chart review was conducted of all patients who underwent aeroallergen skin testing performed in the Otolaryngology-Allergy Clinic at the Hospital of the University of Pennsylvania from July 2016 to December 2018. Patients were organized into categories based on diagnosis of CRSwNP, CRSSNP, and AR without CRS. Patients with a diagnosis of CRSwNP were further categorized into the subtypes AERD, AFRS, CCAD, and CRSwNP not otherwise specified (NOS). Patients were classified as CCAD if nasal polyps were visualized on endoscopy and if radiologic evidence of polypoid change was localized to the posterior-superior nasal septum, middle turbinate, and/or superior turbinate in the absence of lateral paranasal sinus involvement.

The data collected included demographic data and results of allergy skin testing. Cutaneous testing for immediate hypersensitivity to common regional aeroallergens was performed. All negative cutaneous prick-puncture tests were confirmed with intradermal testing. Appropriate histamine and saline positive and negative controls

TABLE 1 Clinical parameters of study subjects: demographic information and allergen sensitivities for study cohorts

Parameters	CCAD (<i>n</i> = 24)	CRSsNP (<i>n</i> = 159)	AFRS (<i>n</i> = 18)	AERD (<i>n</i> = 15)	CRSwNP NOS(<i>n</i> = 125)	AR (<i>n</i> = 174)
Age (years), mean ± SD	43.1 ± 15.7	45.6 ± 16.9	42.0 ± 15.8	46.0 ± 13.2	47.7 ± 15.3	40.8 ± 15.3
Sex, <i>n</i> (%)						
Males	12 (50.0)	58 (36.5)	9 (50.0)	8 (53.3)	64 (51.2)	67 (39.5)
Females	12 (50.0)	101 (63.5)	9 (50.0)	7 (46.7)	61 (48.8)	107 (61.5)
Allergen sensitivities, <i>n</i> (%)						
Trees	14 (58.3)	66 (41.5)	14 (77.8)	9 (60.0)	61 (48.8)	96 (55.1)
Grasses	14 (58.3)	56 (35.2)	11 (61.1)	5 (33.3)	48 (38.4)	81 (46.5)
Weeds	16 (66.7)	53 (33.3)	12 (66.7)	3 (20.0)	53 (42.4)	79 (45.4)
Cat	14 (58.3)	46 (28.9)	12 (66.7)	6 (40.0)	47 (37.6)	90 (51.7)
Dog	14 (58.3)	50 (31.4)	11 (61.1)	3 (20.0)	52 (41.6)	93 (53.4)
Feather	7 (29.2)	20 (12.6)	2 (11.1)	0 (0.0)	21 (16.8)	49 (28.2)
Other animals	6 (25.0)	8 (5.0)	8 (44.4)	2 (13.3)	14 (11.2)	30 (17.2)
Cockroach	5 (20.8)	34 (21.4)	7 (38.9)	1 (6.7)	21 (16.8)	57 (32.7)
Outdoor molds	9 (37.5)	34 (21.4)	14 (77.8)	3 (20.0)	44 (35.2)	51 (29.3)
Indoor molds	7 (29.2)	66 (41.5)	15 (83.3)	4 (26.7)	67 (53.6)	77 (44.2)
Minor molds	12 (50.0)	50 (50.0)	16 (88.9)	3 (20.0)	49 (39.2)	77 (44.2)
Dust mites	15 (62.5)	69 (43.4)	12 (66.7)	7 (46.7)	55 (44.0)	121 (69.5)

Abbreviations: AERD, aspirin-exacerbated respiratory disease; AFRS, allergic fungal rhinosinusitis; AR, allergic rhinitis; CCAD, central compartment atopic disease; CRSsNP, chronic rhinosinusitis without nasal polyposis; CRSwNP NOS, chronic rhinosinusitis with nasal polyposis not otherwise specified; SD, standard deviation.

respectively were performed. Allergen categories included trees, grasses, weeds, cat, dog, feather, other animals, cockroach, outdoor molds, indoor molds, minor molds, and dust mites.

The percentage of CCAD patients positive for each allergen was calculated. The allergen sensitivities were then compared among diagnostic categories. An odds ratio (OR) and chi-square analysis was utilized to compare sensitivity to each allergen between the CCAD cohort and CRS subtypes or AR group. Statistical significance was set to $p < 0.05$.

RESULTS

A total of 515 patients met inclusion criteria for our study (Table 1). A total of 341 patients were diagnosed with CRS and 174 diagnosed with AR. CRS patients were subdivided into CRSwNP ($n = 182$) and CRSsNP ($n = 159$). CRSwNP patients were further subdivided into AERD ($n = 15$), AFRS ($n = 18$), CCAD ($n = 24$), and CRSwNP NOS ($n = 125$).

CCAD patients had the highest qualitative sensitization to weeds, followed by dust mites. There was no statistically significant difference in the inhalant allergen sensitization profiles of patients with AR and CCAD, except for a higher prevalence of weed allergy in the CCAD group,

which barely reached statistical significance. (OR = 2.41, $p = 0.049$) (Table 2a).

When compared to patients with CRSsNP, patients with CCAD showed a greater sensitivity to most allergens; sensitivity to grasses, weeds, cat, dog, feather, and other animal was significantly higher in CCAD patients (Table 2b). A similar pattern was seen when patients with CCAD were compared to those with AERD (Table 2c). Patients with AFRS generally showed greater sensitivity to most allergens compared to those with CCAD; sensitivity to molds was significantly greater in the AFRS cohort, as expected (Table 2d). Finally, patients with CCAD showed a greater sensitivity to most allergens compared to CRSwNP NOS; sensitivity to indoor molds was significantly greater in CRSwNP NOS and sensitivity to weeds was significantly greater in CCAD (Table 2e).

DISCUSSION

CCAD is a distinct, recently identified subtype of CRSwNP that is characterized by inhalant allergy creating an inflammatory response in the central compartment of the sinonasal mucosa. Although many studies have identified a strong relationship between CCAD and allergy, there is no literature identifying the specific allergens to which CCAD patients are sensitive. Our study aimed to identify

TABLE 2 Results of allergy skin testing in CCAD compared to other subtypes of CRS and AR

Category	Odds ratio	95% CI	<i>p</i>
(a) CCAD versus AR			
Trees	1.14	0.48–2.70	0.77
Grass	1.61	0.68–3.82	0.279
Weeds	2.41	0.98–5.91	0.049
Cat	1.31	0.55–3.10	0.543
Dog	1.22	0.51–2.89	0.653
Feather	1.05	0.41–2.69	0.918
Other animals	1.6	0.59–4.37	0.356
Cockroach	0.54	0.19–1.52	0.238
Outdoor molds	1.45	0.60–3.52	0.413
Indoor molds	0.52	0.20–1.31	0.161
Minor molds	1.26	0.54–2.96	0.596
Dust mite mix	0.73	0.30–1.77	0.486
(b) CCAD versus CRSsNP			
Trees	1.97	0.83–4.71	0.121
Grass	2.58	1.07–6.17	0.03
Weeds	4	1.61–9.94	0.002
Cat	3.44	1.43–8.30	0.004
Dog	3.05	1.27–7.34	0.01
Feather	2.86	1.06–7.76	0.033
Other animals	6.29	1.96–20.19	0.001
Cockroach	0.97	0.34–2.78	0.951
Outdoor molds	2.21	0.89–5.48	0.083
Indoor molds	0.58	0.23–1.48	0.25
Minor molds	2.18	0.98–5.19	0.073
Dust mite mix	2.17	0.90–5.26	0.08
(c) CCAD versus AERD			
Trees	0.93	0.25–3.47	0.918
Grass	2.8	0.73–10.75	0.129
Weeds	8	1.74–36.70	0.005
Cat	2.1	0.56–7.81	0.265
Dog	5.6	1.25–25.17	0.019
Feather	N/A	N/A	0.021
Other animals	2.17	0.38–12.49	0.38
Cockroach	3.68	0.39–35.14	0.233
Outdoor molds	2.4	0.53–10.88	0.249
Indoor molds	1.13	0.27–4.80	0.866
Minor molds	4	0.90–17.87	0.061
Dust mite mix	1.9	0.51–7.05	0.322
(d) CCAD versus AFRS			
Trees	0.4	0.10–1.58	0.186
Grass	0.89	0.26–3.10	0.856
Weeds	1	0.27–3.66	1
Cat	0.7	0.20–2.50	0.582

(Continues)

TABLE 2 (Continued)

Category	Odds ratio	95% CI	<i>p</i>
Dog	0.89	0.26–3.10	0.856
Feather	3.29	0.59–18.27	0.158
Other animals	0.42	0.11–1.55	0.186
Cockroach	0.41	0.11–1.62	0.2
Outdoor molds	0.17	0.04–0.68	0.009
Indoor molds	0.08	0.02–0.38	0.001
Minor molds	0.13	0.02–0.67	0.008
Dust mite mix	0.69	0.18–2.63	0.591
(e) CCAD versus CRSwNP NOS			
Trees	1.47	0.61–3.56	0.392
Grass	2.25	0.92–5.46	0.07
Weeds	2.72	1.08–6.82	0.029
Cat	2.32	0.96–5.65	0.058
Dog	1.97	0.81–4.77	0.131
Feather	2.04	0.75–5.53	0.155
Other animals	2.64	0.90–7.77	0.069
Cockroach	1.3	0.44–3.88	0.633
Outdoor molds	1.1	0.45–2.73	0.829
Indoor molds	0.36	0.14–0.92	0.028
Minor molds	1.55	0.65–3.73	0.424
Dust mite mix	2.12	0.86–5.21	0.096

Notes: Values in bold represent a significant value ($p < 0.05$). (a) Odds ratio analysis of categorical allergen sensitivities of CCAD compared to AR. (b) Odds ratio analysis of categorical allergen sensitivities of CCAD compared to CRSsNP. (c) Odds ratio analysis of categorical allergen sensitivities of CCAD compared to AERD. (d) Odds ratio analysis of categorical allergen sensitivities of CCAD compared to AFRS. (e) Odds ratio analysis of categorical allergen sensitivities of CCAD compared to CRSwNP NOS.

Abbreviations: AERD, aspirin-exacerbated respiratory disease; AFRS, allergic fungal rhinosinusitis; AR, allergic rhinitis; CCAD, central compartment atopic disease; CI, confidence interval; CRS, chronic rhinosinusitis; CRSsNP, chronic rhinosinusitis without nasal polyposis; CRSwNP NOS, chronic rhinosinusitis with nasal polyposis not otherwise specified; NA, not applicable.

the allergen sensitivity profile in a cohort of CCAD patients and compare these findings to patients with AR, CRSsNP, AFRS, AERD, and CRSwNP NOS.

Allergen sensitivity profiles of CCAD and AR were strikingly similar in our retrospective review. The only significant difference seen was the CCAD cohort having a marginally greater prevalence of a weed allergy ($p = 0.049$). This single significant difference was the fewest out of all the comparison categories, and the remainder of the allergen categories showed ORs ranging from 0.52 to 1.61. These results support the potential role of inhalant allergy and AR in the pathophysiology of CCAD, differentiating this condition from other subtypes of CRS. Of the 24 patients placed in the CCAD cohort, all but one (96.0%) were found to have some aeroallergen hypersensitivity. The high

degree of atopy within this population supports existing literature associating allergy with polypoid changes localized to the central compartment.

Our findings show a high degree of similarity between allergen sensitivities in CCAD and AR, which could indicate an overlap in these pathologies. The homogeneity of these cohorts implies that CCAD could be a progression of poorly controlled AR. This topic should be the focus of future studies exploring the pathophysiology of CCAD.

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