CLINICAL VIGNETTE

Do Food Allergies Cause Chronic Rhinosinusitis with Nasal Polyposis?

Lorraine Anderson, MD and Samantha Swain, MD

A 39-year-old female with asthma and chronic rhinosinusitis presented to Allergy Immunology for re-evaluation. She was diagnosed with asthma in her twenties, which was well-controlled until age thirty when frequent exacerbations began, accompanied by anosmia and severe nasal congestion. Despite high-dose inhaled corticosteroids, Montelukast, and two courses of oral systemic corticosteroids (OCS), she needed nebulized albuterol twice daily and an albuterol inhaler every four hours. Due to poorly controlled asthma despite maximal therapy, she was referred to an otolaryngologist and diagnosed with chronic rhinosinusitis with nasal polyposis (CRSwNP). After endoscopic sinus surgery, she regained asthma control and return of her sense of smell. However, over seven months, she developed persistent shortness of breath, wheezing and cough, despite Fluticasone Salmeterol 500mcg /50mcg, Montelukast, nebulized albuterol and three courses of OCS. She observed that alcohol and fermented drinks worsened her nasal congestion within minutes of ingestion and sought food allergy evaluation.

Upon further questioning, she denied symptoms of IgE-mediated food hypersensitivity, including immediate urticaria, mouth/throat itching, tongue/throat angioedema, shortness of breath or nausea/vomiting/diarrhea, beginning within five minutes to two hours post ingestion with any food item. She also denied symptoms of non-IgE mediated food hypersensitivity, including dysphagia, food impaction, recurrent chest pain after eating, persistent refractory heartburn, abdominal pain or vomiting occurring one to three hours post ingestion. She complies with daily saline rinses and intranasal corticosteroid spray (INCS) but had no follow-up evaluation with otolaryngology. She denied allergy to NSAIDs, was a non-smoker and reported occasional alcohol use. Physical exam was significant for bilateral nasal polyposis, end-expiratory wheezing, and nasal voice quality. Computed Tomography (CT) chest imaging showed "*Moderate diffuse bronchial wall thickening with mucous plugging and extensive gas trapping compatible with severe large/small airway disease.*" CT sinus imaging showed *"Prior endoscopic sinus surgery with diffuse opacification of all paranasal sinuses "* Laboratory data revealed an absolute eosinophil count of 410-900 cells/µL, negative environmental allergy skin test and a total IgE of 558 kIU/L.

This patient with asthma, non-allergic rhinitis, CRSwNP, and sinus surgery suffers from recurring nasal polyps causing asthma exacerbations, anosmia, and severe nasal congestion. Symptoms worsen after consuming alcohol and she is worried about possible food allergy.

Discussion

CRSwNP is a predominantly type 2 inflammatory condition of the paranasal sinuses characterized by progressive bilateral polyp growth of the nasal mucosa and frequent disease flares. Nasal polyps, translucent and gelatinous inflammatory masses ranging from yellowish gray to white, form in predisposed individuals' nasal cavities or paranasal sinuses. These are generally benign and typically occur bilaterally. Type 2 inflammation is characterized by tissue infiltration of eosinophils, mast cells, type 2 innate lymphoid cells, T-helper type 2 cells, and basophils. These immune cells produce type 2 proinflammatory mediators (IL4, IL5, IL13 and IgE), which stimulate the ongoing sinus inflammatory response. Eosinophils, the predominant inflammatory cell in nasal polyposis, suggest an allergic predisposition contributes to nasal polyp formation. Clinically, the disease presents as facial pain/pressure, anosmia, nasal congestion, and anterior/posterior nasal discharge. Chronic rhinosinusitis (CRS) is defined by clinical symptoms lasting twelve weeks or longer and CT sinus or nasal endoscopic findings indicating significant bilateral mucosal thickening. CRS is divided into CRSwNP, including aspirin-exacerbated respiratory disease (AERD), CRS without nasal polyps (CRSsNP) and Allergic Fungal rhinosinusitis (AFRS). CRS is a complex inflammatory disorder, not a simple infectious process, anatomic problem, or allergic process. However, bacterial colonization or infection, noninvasive fungal colonization or infection, and environmental allergies may contribute to CRS fostering nasal polyp development and a chronic inflammatory process. 50-80% of patients with CRS have environmental allergies and test positive for perennial allergens including house dust mites, fungal spores, animal dander, and cockroaches. Without immunodeficiency, primary ciliary dyskinesia, cystic fibrosis, odontogenic disease, and other underlying disorders, CRSwNP or CRSsNP is not a primary infectious disorder.[1] "CRSwNP affects 1-3% of the population, and comorbid asthma (50-65%) and allergic rhinitis (50-84%) are common."[2] While CRS is a predominantly type 2 inflammatory process, various triggers (allergens, pollutants, viruses, bacteria, and toxins) can activate type 2 inflammation. Thus, while CRS is not primary infectious it is associated with a rich bacterial microbiome. The combination of "inflammation driven by microinvasive disease, the secondary inflammatory process in response to bacterially derived pathogen-associated

molecular patterns and bacterial toxins contribute to the persistence and severity of disease" and exists in addition to any comorbid allergic disease (asthma, allergic rhinitis).[3] As such, treatment of CRS is not focused on a pathogenic infection but rather involves addressing the underlying type 2 inflammation. The type 2 pathway, linked with CRSwNP, allergic rhinitis, asthma, eosinophilic esophagitis, and other type 2 diseases, is extensively studied. Recognizing this inflammatory endotype has implications for targeted therapies.

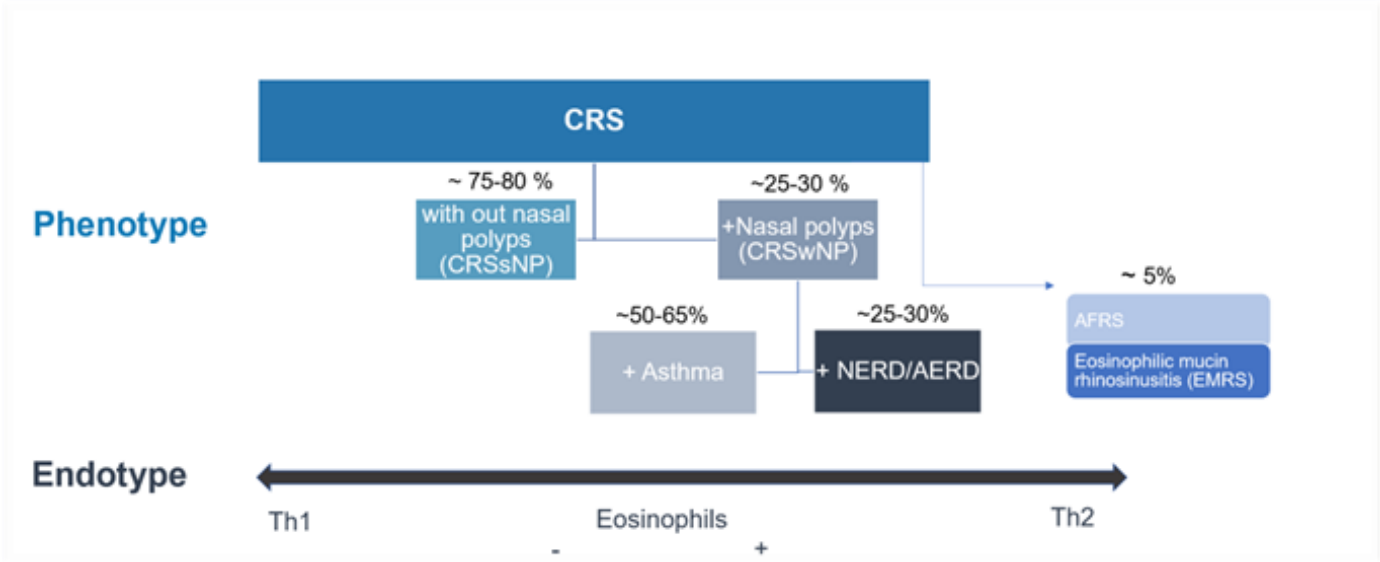
CRSwNP treatments include nasal saline rinse to improve sinus mucociliary function and intranasal steroids (sprays, high-volume irrigation, stent, drops and exhalation delivery). INCS are first-line therapy for CRSwNP due to their ability to improve nasal congestion, sense of smell, and decrease the need for OCS and endoscopic sinus surgery. However, if the standard treatment fails and the disease flares, treatment options include OCS or endoscopic sinus surgery.[2] Unfortunately, many patients have rapid recurrence of nasal polyposis. They must undergo multiple revision surgeries or utilize biologic therapies that target type 2 markers IL-4 and IL-13 (dupilumab), IL-5 (mepolizumab), IgE (omalizumab), and thus polyp recurrence.

The cause of type 2 inflammation in CRS is unknown, but research indicates that CRSwNP is not caused by environmental or food allergies. Despite some studies showing high food sensitization in CRS patients through skin prick, intradermal (not evidence-based for diagnosing IgE-mediated food allergies), or serum-specific IgE testing, these are not linked to the disease's cause. While pilot and retrospective studies have shown a high prevalence of food sensitization in CRS patients, they have not found any significant difference in "the prevalence, type of food, number of food sensitizations and the severity between CRSwNP and CRSsNP."[4] A 2021 prospective case-control study of food-specific IgE and IgG antibodies in patients with CRSwNP showed "food allergy does not have an important role in CRSwNP etiopathogenesis, whether it is IgG or IgE mediated"[5] The specificity of both prick testing and serum specific IgE testing to foods is <50%. The negative predictive value of a food allergy skin test is >95% and highly accurate in confirming the absence of IgE-mediated food allergy. Similarly, using a cutoff of 0.35kU/L in serum-specific IgE food allergy testing has a high sensitivity but a poor specificity to diagnose IgE-mediated food allergy. In the absence of appropriate symptoms suggestive of IgE-mediated food allergy, performing food allergy skin tests or blood tests have limited specificity for predicting clinical allergy and are associated with a high rate of false positives due to homologous protein cross-reactivity. The gold standard for diagnosing a food allergy is oral food challenge with >95% positive and negative predictive values. Patients often worry that specific foods exacerbate or cause nasal polyps. However, research clarifies that food allergies and sensitivities do not cause nasal polyps, nor do they contribute to nose-specific symptoms. Medical literature distinctly separates CRSwNP from food allergies as a cause. The Rhinitis 2020 practice parameter update notes, "Food allergy testing is not recommended in the routine evaluation of rhinitis"[6] Per the practice parameters, "there is no indication to test for food allergens when evaluating patients presenting with rhinitis symptoms. Furthermore, no published studies of oral food challenges produce isolated rhinitis symptoms."[6]

We explained to our patient that her lack of food allergy signs and symptoms makes this diagnosis unlikely, and evidence does not support testing for IgE-mediated food allergies. However, her rhinitis worsening with alcohol may be due to other potential diagnoses. Vasomotor rhinitis, a subtype of non-allergic rhinitis, results in heightened neurogenic activity and causes symptoms due to "nociceptive neurons with heightened sensitivity to stimuli such as temperature change, airborne irritants, foods (especially hot and spicy), alcoholic beverages, cool, dry air and exercise."[6] Food-induced rhinitis can cause rhinitis after ingestion (especially hot and spicy) due to a "neurogenic reflex of the noncholinergic, non-adrenergic system."[6] Similarly, alcohol-induced rhinitis causes rhinitis due to vasodilator effects and alcohol hyperresponsiveness. It is seen in "up to 14% of healthy individuals, 33% of asthmatics, and 75% of patients with AERD and correlates with the severity of the nasal inflammatory response, being greater in patients who have AERD or CRSwNP (with or without asthma) than in patients with allergic rhinitis or CRSsNP."[6] This is not due to allergic hypersensitivity or alcohol allergy. Interestingly, any alcoholic beverage can cause rhinitis in CRS patients who have reported wine may be worse than other alcoholic beverages. We informed the patient that she had alcohol-induced rhinitis, and her constellation of symptoms suggests that her nasal polyps have recurred. She was given a short course of OCS, advised to follow up with her otolaryngologist and return to Allergy Clinic for treatment with a biologic to prevent polyp recurrence. Most CRSwNP patients prefer avoiding medication, yet there is no natural cure. Online, various diets are suggested for CRS types, causing confusion. However, food allergies do not relate to CRS, and dietary changes are not a proven alternative to standard care. A balanced diet, regular exercise, adequate rest, and healthy weight management generally benefit chronic illnesses.

This case demonstrates that food-related symptoms do not equate to IgE-mediated food allergies. Clinicians should recognize alcohol-induced rhinitis as a call for further diagnostic tests like nasal endoscopy, CT sinus, spirometry and referrals to otolaryngologists and allergy/immunology specialists, rather than a sign of food allergy.

Figure 1. Classification of CRS



Adapted from Lee et. al. 2021

REFERENCES

1. **Lee K, Tai J, Lee SH, Kim TH**. Advances in the Knowledge of the Underlying Airway Remodeling Mechanisms in Chronic Rhinosinusitis Based on the Endotypes: A Review. *Int J Mol Sci*. 2021 Jan 18;22(2): 910. doi: 10.3390/ijms22020910. PMID: 33477617; PMCID: PMC7831322.
2. **Oykhman P, Paramo FA, Bousquet J, Kennedy DW, Brignardello-Petersen R, Chu DK**. Comparative efficacy and safety of monoclonal antibodies and aspirin desensitization for chronic rhinosinusitis with nasal polyposis: A systematic review and network meta-analysis. *J Allergy Clin Immunol*. 2022 Apr;149(4):1286-1295. doi: 10.1016/j.jaci.2021.09.009. Epub 2021 Sep 17. PMID: 34543652.
3. **Borish L, Baroody FM, Kim MS, Lieberman JA, Peters A, Stevens WW, Bernstein JA**. Yardstick for the medical management of chronic rhinosinusitis. *Ann Allergy Asthma Immunol*. 2022 Feb;128(2):118-128. doi: 10.1016/j.anai.2021.10.014. Epub 2021 Oct 20. PMID: 34687874.
4. **Al-Qudah M**. Food Sensitization in Medically Resistant Chronic Rhinosinusitis with or without Nasal Polyposis. *Int Arch Allergy Immunol*. 2016;169(1):40-4. doi: 10.1159/000443737. Epub 2016 Mar 9. PMID: 26954667.
5. **Veloso-Teles R, Cerejeira R, Rodrigues D, Roque-Farinha R, von Buchwald C**. Food-Specific IgE and IgG Antibodies in Patients With Chronic Rhinosinusitis With Nasal Polyps: A Case-Control Study. *Ear Nose Throat J*. 2021 Mar;100(3):177-184. doi: 10.1177/0145561319867668. Epub 2019 Sep 23. PMID: 31547710.
6. **Dykewicz MS, Wallace DV, Amrol DJ, Baroody FM, Bernstein JA, Craig TJ, Dinakar C, Ellis AK, Finegold I, Golden DBK, Greenhawt MJ, Hagan JB, Horner CC, Khan DA, Lang DM, Larenas-Linnemann DES, Lieberman JA, Meltzer EO, Oppenheimer JJ, Rank MA, Shaker MS, Shaw JL, Steven GC, Stukus DR, Wang J; Chief Editor(s):; Dykewicz MS, Wallace DV; Joint Task Force on Practice Parameters:; Dinakar C, Ellis AK, Golden DBK, Greenhawt MJ, Horner CC, Khan DA, Lang DM, Lieberman JA, Oppenheimer JJ, Rank MA, Shaker MS, Stukus DR, Wang J; Workgroup Contributors:; Dykewicz MS, Wallace DV, Amrol DJ, Baroody FM, Bernstein JA, Craig TJ, Finegold I, Hagan JB, Larenas-Linnemann DES, Meltzer EO, Shaw JL, Steven GC**. Rhinitis 2020: A practice parameter update. *J Allergy Clin Immunol*. 2020 Oct;146(4):721-767. doi: 10.1016/j.jaci.2020.07.007. Epub 2020 Jul 22. PMID: 32707227.