

In Reply: Central compartment atopic disease: the missing link in the allergy and CRSwNP saga

I read with great interest the letter by Dr DelGaudio regarding the relationship between allergy and what is proposed as a distinct phenotype of chronic rhinosinusitis with nasal polyps (CRSwNP). It is agreed upon that the relationship between these disease entities is difficult to describe in linear terms and that there are certain subcategories (and endotypes) within the CRSwNP phenotype in which allergy may be an underlying or amplifying factor, and others where it is not. It also makes sense that central anatomic subsites of the nose, notably the turbinates, are more likely to be exposed to the ambient air stream and would thus be more affected by allergic stimuli. It remains questionable, however, whether the central compartment inflammatory picture DelGaudio describes is indeed the “definitive” link between allergy and CRSwNP. There are several reasons to call this into question.

Although the clinical presentation can be described broadly as central compartment inflammatory disease, the primary feature related to this work is polyps involving the middle turbinate. Clearly, this is a manifestation of nasal inflammatory disease, but it remains undetermined whether this entity reflects true polyposis vs bulbous mucosal hypertrophy of the middle turbinate head. In fact, DelGaudio and coauthors (White et al) entitled their initial article on the subject as “Polypoid changes of the middle turbinate as an indicator of atopic disease,” which is a distinctly different entity than is CRSwNP in the classic sense.¹ This point perhaps invokes the question of what exactly constitutes a true sinonasal polyp. A simplistic definition would designate this entity as a nononcologic swelling in the sinonasal cavity, but more granular analysis demonstrates substantial histopathologic differences between typical polyps observed in diffuse CRSwNP and ethmoid tissue from the same patients, suggesting a distinct inflammatory pattern.² Unfortunately, White et al did not report histopathologic features, and the endoscopic photos shown appear more consistent with bulbous hypertrophy of the middle turbinate rather than true polyposis.¹ Therefore, it remains unclear whether their observations even reflect a disease entity that would fall into the spectrum of phenotypes encompassed by CRSwNP.

Another issue revolves around why more patients with allergic rhinitis do not develop nasal polyps, either central compartment disease involving the middle turbinate or classic diffuse CRSwNP. The prevalence of polyps in allergic patients has been estimated at <5%, and in fact as little as 0.5%.³ Furthermore, other studies have demonstrated that the presence of polyps is most closely related to carrying an asthma diagnosis, a finding that was independent of atopic status.⁴ Although DelGaudio may posit that central compartment disease reflects a unique and distinct subset of allergic patients, the current body of evidence does not support that this represents a “link to” (implying a transition toward) classic forms of CRSwNP.

DelGaudio's report does accurately describe the computational fluid dynamics of parabolic airflow, and why this would be related to allergen deposition, but this still does not account for why polyps are almost never seen involving the inferior turbinate, whereas pale edema and hypertrophy—both indicative of allergic disease—are commonly seen. Some authors have proposed fundamental immunohistochemical differences (eg, in vascular cell adhesion molecules and leukotriene receptors) between inferior and middle turbinate tissues.⁵ Although this suggests that different nasal subsites are immunologically unique and may thus be more prone to polyp development, the observations also indicate that a myriad of factors besides atopy account for the anatomic distribution inflammation that may be observed.

Finally, DelGaudio also offers local allergic rhinitis as an explanation for the lower-than-expected prevalence of asthma in their series. Although this phenomenon is certainly accepted, it should also be noted that even classic forms of nasal polyposis are associated with local production of immunoglobulin E (IgE) and most other immunoglobulin isotopes, 90% of which were thought to be produced locally.⁶ It is also questionable whether antibody production is antigen-specific, vs autoreactive, or a superantigen response.⁷ Overall, these findings demonstrate that IgE-mediated inflammation and local antibody production are not features unique to central compartment disease, and many are seen even in classic CRSwNP. Although this does introduce the question of whether central compartment disease is indeed the beginning of a continuum to more classic CRSwNP, this has not been observed clinically and leaves the question unanswered of how antigens would gain access to naive mucosa of the endoluminal spaces of the surrounding sinuses.

In conclusion, it is difficult to doubt that aeroallergens inhaled through the nasal cavity induce local IgE-mediated responses in susceptible individuals. Furthermore, this may

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involve the middle turbinate and other central compartment structures besides the inferior turbinates, possibly as a function of unique airflow dynamics in certain patients. Thus, the currently available data also make it difficult to conclude that this phenomenon is the so-called “missing

link“ between allergy and CRSwNP, rather than simply a more diffuse presentation of allergic rhinitis.

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