Are type-2 biomarkers of any help in distinguishing chronic rhinosinusitis with nasal polyps from chronic rhinosinusitis without nasal polyps?

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Dear Editor,

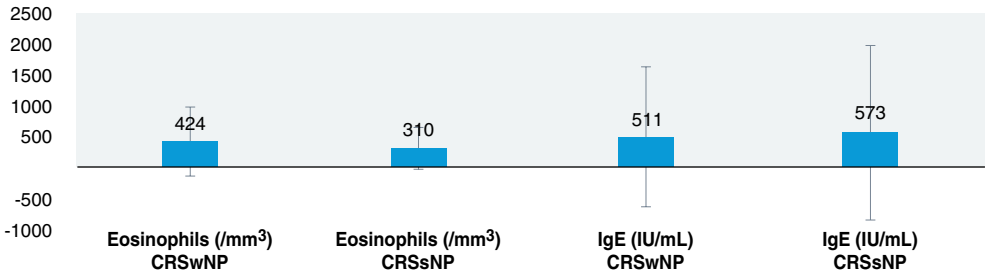
Chronic rhinosinusitis with nasal polyps (CSwNP) is a common chronic airway disease. Knowledge of CSwNP has progressed from an era where physicians collected information together with the patient using tools such as the endoscope, X-ray, and computed tomography (CT) scanner to the incorporation of methods of genotyping, phenotyping, and endotyping.[1] Genotypic classification is used to identify related monogenic conditions such as cystic fibrosis and ciliary dysmotility.[2,3] Phenotypic classifications use clinically observable characteristics such as endoscopic findings, the presence of comorbid or systemic illness, and timing of disease onset.[4] Endotypic classifications subdivide chronic rhinosinusitis (CRS) based on pathobiologic mechanisms, and for CRS this was based on histologic features such as the presence of neutrophilia, eosinophilia, fibrosis, glandular hypertrophy, and epithelial dysmorphosis.[1]

In western countries, approximately 80% of patients with CRSwNP exhibit a type 2 (T2) inflammatory endotype, which is characterized by increased levels of interleukin (IL) 4, IL-5, IL-13, and immunoglobulin E (IgE). Conversely, most patients with CRS without nasal polyps (CRSsNP) do not exhibit a T2 inflammatory endotype.[5,6] T2 inflammation is derived from the activation of antigen-specific T helper 2 (Th2) cells or group 2 innate lymphoid cells, and cytokines (IL-4, IL-5, and IL-13) likely act in concert with one another to drive the pathology of CRSwNP. In response to IL-4, B cells differentiate into IgE-producing plasma cells, which bind to the surface of mast cells and basophils via the high-affinity IgE receptor. IgE class switching is also caused by local mucosal inflammation induced by the presence of *Staphylococcus aureus* enterotoxins in the middle nasal meatus, a key region at the entrance to the sinuses.[5,7] IL-5 promotes the differentiation, migration, activation, and survival of eosinophils.[5] Current guidelines on the management of CRS recommend assessment of total immunoglobulin E levels and serum eosinophilia as biomarkers of T2 inflammation.[8,9]

We investigated the utility of T2 biomarkers in distiguising CRSwNP from CRSsNP. To this end, we conducted a retrospective study of patients with CRSwNP (n=137) and CRSsNP (n=23) on our database. Clinical data such as sex, age, serum eosinophilia, and total IgE levels were analyzed. Data were included after informed consent was obtained.

Ninety (56%) patients were women. Mean patient age was 63 years (18-89) in the CRSwNP group and 56 years (20-81) in the CRSsNP group. Serum eosinophilia ranged from 0 to 3.510 /mm^3 (mean = 423,5) in patients with CRSwNP and from 0 to 1.408 /mm^3 (mean = 310) in those with CRSsNP. In the CRSwNP group, mean total IgE level was 511 IU/mL (6-7.200); in the CRSsNP group, mean total IgE level was 573 IU/mL (4,5-5.190) (Figure 1).

Our data indicate that the use of T2 inflammation biomarkers as index tests is not effective in distinguishing



CSwNP: Chronic rhinosinusitis with nasal polyps.
CRSsNP: Chronic rhinosinusitis without nasal polyps.

Figure 1
Number of eosinophils and IgE levels (standard deviation)

patients with and without nasal polyps. However, it does not negate the clinical value of measuring T2 biomarkers in CRS phenotyping in times of precision medicine and availability of T2-driven biologics.

In conclusion, using T2 biomarkers to assess the presence or absence of nasal polyps lacks accuracy. Therefore, performing imaging tests such as nasal endoscopy and/or CT scan is extremely important.

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