Patients with chronic rhinosinusitis and serum IgE greater than 1,000 ng/mL have a higher prevalence of allergic bronchopulmonary aspergillosis (ABPA) and nonsteroidal anti-inflammatory drugs exacerbated respiratory disease

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Chronic rhinosinusitis (CRS) is defined as a mucosal inflammation associated with tissue remodeling that persists for ≥ 12 weeks.[1] There are different phenotypes and endotypes of CRS patients. According to EPOS,[1] phenotypes are organisms distinguishable from others by clinical features, such as having or not having polyposis, while endotypes are features within an individual, such as elevated serum IgE. Elevated serum IgE is a T2 response marker of the nonsteroidal anti-inflammatory drug-exacerbated respiratory disease (N-ERD) phenotype, as well as other diseases, such as hyper-IgE syndrome and allergic bronchopulmonary aspergillosis (ABPA).

When eosinophilic nasal polyps are related to asthma or respiratory reactions to aspirin or other nonsteroidal anti-inflammatory drugs, the patient may present N-ERD. The prevalence of N-ERD varies from 1.8% to 44%.[2] Ingesting aspirin or other COX-1 inhibitors triggers upper and lower airway symptoms. Patients with N-ERD are more likely to have severe disease and rapid recurrence of nasal polyps, and their cases are difficult to manage.[3]

Another disease associated with type 2 immunity is ABPA, which is described as an allergic pulmonary condition caused by hypersensitivity to *Aspergillus allergens*, commonly *A. fumigatus*.[4] Symptoms are characterized by difficult-to-treat asthma, hemoptysis, cough, fever, weight loss, and potential death. The community prevalence of ABPA as a complication of asthma is about 5%,[5] while the prevalence of ABPA in patients with severe acute asthma admitted to an intensive care unit can be as high as 39%.[5] In 2019 Patel & Greenberger[6] established a set of minimal essential criteria for ABPA: asthma, immediate cutaneous reactivity to *A. Fumigatus*, and total serum IgE > 1000 ng/mL, plus one of the following: elevated specific IgE or IgG-A. Fumigatus or central bronchiectasis in the absence of distal bronchiectasis. The immune response leads to airway remodeling, inflammation, bronchiectasis, and fibrosis.

Our evidence was collected from a sample of adult patients diagnosed with CRS, but not cystic fibrosis, whose IgE serum was measured and who were followed up in a university hospital. Patients with IgE > 1000 ng/mL underwent diagnostic investigation for ABPA, including: prick test reactivity to *A. fumigatus*, specific IgE *A. fumigatus* measurement, spirometry with a bronchodilator test, anamnesis for asthma diagnosis, and chest computed tomography. To diagnose N-ERD, patients underwent anamnesis and, if needed, an oral aspirin challenge test.[3]

Out of a group of 135 patients diagnosed with CRS whose serum IgE was measured, 13 had IgE > 1000 ng/mL and followed the algorithm (Figure 1). Those with ABPA (3 men and 1 woman) were > 45 years of age at the time of diagnosis. Pulmonary symptoms included cough, wheezing, and purulent sputum. In 2 cases, asthma was confirmed with a pulmonary function test and bronchodilator challenge, with the results ranging from moderate to severe obstructive lung disease. The diagnosis of the other 2 patients was based on clinical history. *A. fumigatus*-specific IgE was measured at admission, with results ranging from 0.35 to 15 µg/mL (median = 4.95). Bilateral bronchiectasis was diagnosed in lung computed tomography in all 4 patients.

The age range of those diagnosed with N-ERD (3 women and 1 man) was 47 to 68 (median = 58) years. Clinical symptoms included nasal manifestations of CRS, with asthma-related nasal polyps, in addition to respiratory symptoms induced by aspirin or other nonsteroidal anti-inflammatory drugs. A pulmonary function test and bronchodilator challenge showed obstructive lung disease in 3 patients. An oral celecoxib challenge test was needed to confirm diagnosis in 1 patient.

Of the 135 patients in the sample, 3% were diagnosed with ABPA. We could find no articles in English or Portuguese describing the prevalence of ABPA in patients with CRS, indicating that it is not suspected, and thus not

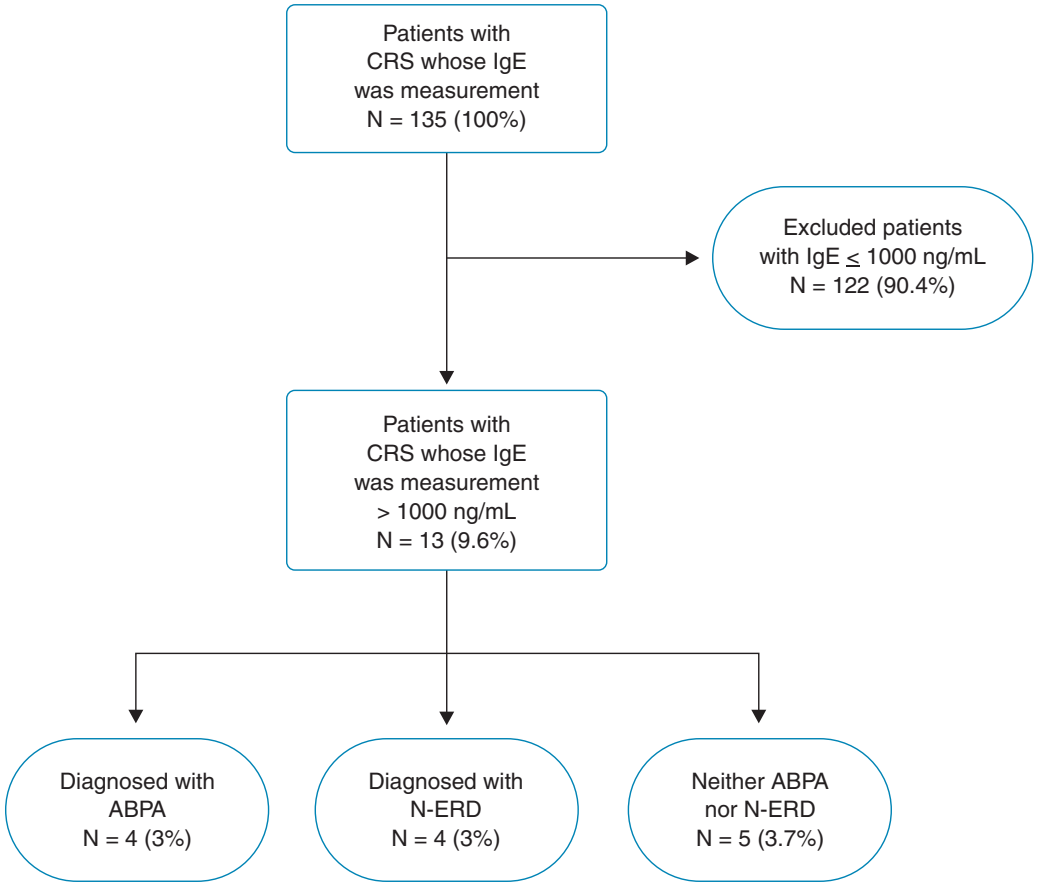

Figure 1
Flowchart of the diagnostic evaluation of patients with chronic rhinosinusitis and serum IgE >1000 ng/mL
ABPA: allergic bronchopulmonary aspergillosis; CRS: chronic rhinosinusitis; IgE: immunoglobulin E; N-ERD: nonsteroidal anti-inflammatory drug-exacerbated respiratory disease.

investigated, among these patients. Of the 13 patients with CRS and IgE > 1000 ng/mL, 30.8% were diagnosed with ABPA. Requesting an affordable blood test and IgE measurement could lead to an active search for ABPA and early treatment, preventing potentially fatal pulmonary lesions.

Since the overall prevalence of N-ERD in this CRS clinic was 10%, the prevalence of N-ERD was 3 times higher in patients with IgE > 1000 ng/mL. This illustrates the importance of an active investigation for the disease, since this diagnosis influences treatment and prognosis.

As a result of the analysis, considering that 61.6% of the patients with IgE > 1000 ng/mL were diagnosed with 1 of the 2 comorbidities, we encourage the measurement of IgE in all patients diagnosed with CRS, as well as careful investigation for ABPA and N-ERD.

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Priscila Novaes Ferraiolo[1]
Nathalia Fernanda da Silva[1]
Marise da Penha Costa Marques[1]
Sergio Duarte Dortas-Junior[2]
Cláudia Maria Valete[1,3]
Fabiana Chagas da Cruz[1]

1. Serviço de Otorrinolaringologia, Hospital Universitário Clementino Fraga Filho (HUCFF-UFRJ) - Rio de Janeiro, RJ, Brasil.
2. Serviço de Imunologia, Hospital Universitário Clementino Fraga Filho (HUCFF-UFRJ) - Rio de Janeiro, RJ, Brasil.
3. Fundação Oswaldo Cruz, Instituto Nacional de Infectologia Evandro Chagas, Laboratório de Pesquisa Clínica e Vigilância em Leishmanioses - Rio de Janeiro, RJ, Brazil.