

Correspondence

Nonatopic persistent asthma in children, a missed phenotype of asthma?

To the Editor:

We read with great interest the study by Fitzpatrick et al,¹ showing how, in preschool children with persistent asthma, the type 2 inflammation biomarkers (ie, aeroallergen sensitization and/or increased blood eosinophilic counts) are strong predictors of a positive therapeutic response to daily inhaled corticosteroid treatment. To our knowledge, Fitzpatrick et al's study is the first to extrapolate and clearly identify a particular phenotype of persistent eosinophilic asthma, without pneumoallergen sensitization. Global Initiative for Asthma 2016 guidelines define it as "intrinsic asthma," a rare phenotype affecting only adulthood; the PRACTALL consensus report is the only children guideline that mentions persistent asthma in children without relevant allergic sensitization as "unresolved asthma." We had previously called this specific phenotype of nonallergic eosinophilic asthma in children² NAPA (nonatopic persistent asthma). It is now well known that some eosinophilic nonallergic sensitization-dependent bronchial inflammation is controlled by type 2 innate lymphoid cells that are induced as a result of direct stimulation by exogenous agents such as viruses and bacteria.³ Turato et al⁴ analyzed bronchial biopsies obtained in children with multitrigger wheeze (median age, 5 years; range, 2-10 years), and found that airway pathology typical of asthma (thickened basement membrane, increased number of eosinophils, and cytokine expression) is identical in nonatopic and atopic wheezing children.

In our reference center for pediatric asthma, we defined persistent (multitrigger) asthma, without aeroallergen sensitization, blood eosinophil counts of 400/mL or greater and/or nasal eosinophilia 10% and/or exhaled nitric oxide level of more than 25 ppb as NAPA.⁵ NAPA represented about 8% of cases of persistent asthma (55 of 685) seen in our recent clinical record. In our experience, we observed noticeable differences in the clinical features of NAPA compared with allergic persistent asthma (APA):

patients with NAPA lack atopic familiarity and early onset atopic dermatitis; furthermore, NAPA is clinically more severe, requiring hospital admission in 50% versus 10% of patients with APA ($P < .001$). However, daily low-dose inhaled corticosteroid induces a rapid and good remission of asthma in almost all children.

As we previously stated,² it is surprising that NAPA in children has not yet been recognized as a separate clinical phenotype in specific medical literature and in guidelines for pediatric asthma. This implies that the NAPA best treatment schedule and natural history are still unknown. In our clinical practice, about 40% of patients recovered after 5 years; a 2-year-old patient completely recovered after 10 months. This evidence suggests that NAPA, despite a more severe clinical onset, could have a milder and non-life-long prognosis than APA.

Giorgio Longo, MD^a
Ester Conversano, MD^a
Elisa Panontin, MD^a
Giovanna Ventura, MD^b
Alessandro Ventura, MD^{a,b}

From ^athe University of Trieste and ^bthe Institute for Maternal and Child Health, IRCCS "Burlo Garofolo," Trieste, Italy. E-mail: giorgio.longo@burlo.trieste.it.

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