Non-eosinophilic asthma in nonsteroidal anti-inflammatory drug exacerbated respiratory disease

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November 29, 2022

Abstract

Background: The cellular inflammatory pattern of nonsteroidal anti-inflammatory drug–exacerbated respiratory disease (N-ERD) is heterogeneous. However, data on the heterogeneity of non-eosinophilic asthma (NEA) with aspirin hypersensitivity are scanty. By examination of N-ERD patients based on clinical data and eicosanoid biomarkers we aimed to identify NEA endotypes potentially guiding clinical management. **Methods**: Induced sputum was collected from 133 patients with N-ERD. Sixty six patients (49.6%) with NEA were included in the hierarchical cluster analysis based on clinical and laboratory data. The quality of clustering was evaluated using internal cluster validation with different indices and a practical decision tree was proposed to simplify stratification of patients. **Results**: The most frequent NEA pattern was paucigranulocytic (PGA; 75.8%), remaining was neutrophilic asthma (NA; 24.2%). Four clusters were identified. Cluster #3 included the highest number of NEA patients (37.9%) with severe asthma and PGA pattern (96.0%). Cluster #1 (24.2%) included severe only asthma, with a higher prevalence of NA (50%). Cluster #2 (25.8%) comprised well-controlled mild or severe asthma (PGA; 76.5%). Cluster #4 contained only 12.1% patients with well-controlled moderate asthma (PGA;62.5%). Sputum prostaglandin D_2 levels distinguished cluster #1 from the remaining clusters with an area under the curve of 0.94. **Conclusions**: Among identified four NEA subtypes, clusters #3 and #1 represented N-ERD patients with severe asthma but a different inflammatory signatures. All the clusters were discriminated by sputum PGD_2 levels, asthma severity, and age of patients. The heterogeneity of non-eosinophilic N-ERD suggests a need for novel targeted interventions.

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