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学位論文の題名	<p>A preliminary study of novel asthma phenotyping by the predominant site of eosinophilic airway inflammation: Use of dual-phased sputum induction (好酸球性気道炎症の主座による新たな喘息表現型に対する予備的研究 : 喀出時間で分けた誘発喀痰での検討)</p> <p>Nagoya Medical Journal (accepted for publication)</p>
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Abstract

Small airways dysfunction has been associated with poor asthma control, and a new concept “small airway asthma phenotype” has been proposed. However, pathophysiology of this phenotype, as compared with asthmatics predominated by large airways disease, is poorly known. Fractional analysis of early- and late-phase induced sputum samples can differentially evaluate large and small airways inflammation. (Holz O et al. Clin Exp Allergy. 1998, Gershman NH et al. J Allergy Clin Immunol. 1999, Ohbayashi H et al. Arerugi. 2008) Asthmatic patients (classic or cough-variant asthmatics) inhaled 3% hypertonic saline for 30 minutes, and coughed up sputum, which were separately collected during the former and the latter 15 minutes and examined for cell differentials. Among 119 asthmatics who underwent sputum induction between November 2013 and October 2014, 47 patients successfully produced both early-phase and later-phase samples. Twelve patients who had no eosinophils in both samples were excluded, and the remaining 35 patients were classified into “larger airway-eosinophil-predominant” group (early-phase eosinophils% > late-phase eosinophils%; n=22) and “smaller airway-eosinophil-predominant” group (early-phase eosinophils% < late-phase eosinophils%; n=13) for comparison. The smaller airway-eosinophil-predominant group significantly differed from the larger airway- eosinophil-predominant group for impulse oscillometry indices

(frequency resonance [Fres; 12.6 ± 3.7 vs. 10.4 ± 2.8 Hz, $p=0.032$] and low-frequency reactance area [AX; 0.39 ± 0.34 vs. 0.25 ± 0.22 kPa/L, $p=0.015$]), alveolar nitric-oxide levels (11.0 [8.1 – 31.5] vs. 3.6 [3.5 – 13.3] ppb, $p=0.047$), and the prevalence of cough-variant asthmatics (8% vs. 45% , $p=0.02$). Spirometry indices, airway responsiveness, asthma control or exacerbation frequency were similar between the two groups. Our sputum-based novel phenotyping reflects larger/smaller airways pathophysiology represented by IOS and nitric-oxide levels. Cough symptom in asthmatic patients may arise predominantly from larger airways inflammation.