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Letter to the Editor

Functional Defects in B Lymphocytes in Asthmatic Patients With IgG Subclass Deficiency

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Asthma is a common comorbidity in patients with immunoglobulin G subclass deficiency (IGGSCD).[1,2] Patients with asthma and IGGSCD often have recurrent respiratory infections, which contribute to asthma exacerbation and severity and lung function decline.[3,4] In this study, we investigated functional defects in B lymphocytes in adult asthmatic patients with IGGSCD and analyzed them in relation to clinical parameters.

A total of 44 patients were enrolled in this study; 17 were asthmatic patients with IGGSCD, and the remainder were those without IGGSCD. Among the patients with IGGSCD, immunoglobulin (Ig) G3 subclass deficiency was the most common type (15/17, 88.2%). The male to female ratio was 16:28, and the median age was 52.5 years (interquartile range [IQR], 44.0–60.8 years). The median percentage of the forced expiratory volume in one second (FEV1) of the asthmatic patients with IGGSCD and those without IGGSCD was 80.8% (65.3–98.7) and 87.3% (72.9–100.0), respectively (**Supplementary Table S1**). To assess B lymphocyte function, a [^{3}H]-thymidine incorporation assay and flow cytometry to measure CD23 expression on peripheral blood mononuclear cells were performed after the stimulation with anti-CD40/interleukin (IL)-4 according to the protocols of a previous study.[5,6] This study was approved by Institutional Review Board of Ajou University Medical Center (AJOUIRB-KSP-2020-158), and all study patients provided informed consent.

When cell proliferation was compared according to the presence or absence of IGGSCD, the fold change in [^{3}H] thymidine-incorporated cells was significantly lower in asthmatic patients with IGGSCD than in those without (median, 2.45 [IQR, 1.30–3.78] vs. 3.69 [1.97–7.52], $P = 0.054$; **Figure A**). $CD23^+CD3^-CD19^+$ cells (%) were significantly lower in asthmatic patients with IGGSCD than in those without (median, 41.10 [IQR, 8.16–69.20] vs. 65.20 [56.20–72.00], $P = 0.026$; **Figure B**). We further analyzed them according to the severity of asthma (severe asthma *vs.* non-severe asthma), which was defined according to the American Thoracic Society/European Respiratory Society guidelines.[7] The patients with severe asthma (SA) (22/44, 50%) showed a significantly decreased fold change in [^{3}H] thymidine-incorporated cells and the percentage of $CD23^+CD3^-CD19^+$ cells compared to those with non-severe asthma (NSA) (median, 2.32 [IQR, 1.28–4.21] vs. 3.81 [2.62–8.42] for proliferation assay and 53.9% [23.04–65.75] vs. 68.80 [56.70–73.65] for $CD23^+CD3^-CD19^+$ cells, $P = 0.008$, and $P = 0.011$, respectively; **Figure C and D**). Among the patients with IGGSCD, B lymphocytes from the patients with SA were less proliferated and less expressed

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Disclosure

There are no financial or other issues that might lead to conflict of interest.

CD23 antigen than those with NSA ($P = 0.364$ and $P = 0.050$, respectively; **Figure E and F**). In all asthmatic patients, $CD23^+CD3^-CD19^+$ cells (%) correlated with lung function parameters such as FEV1% and FEV1/forced vital capacity (FVC) ($r = 0.387$, $P = 0.011$ for FEV1%, and $r = 0.392$, $P = 0.010$ for FEV1/FVC, respectively; **Figure G and H**). The patients with SA showed a strong positive correlation between $CD23^+CD3^-CD19^+$ cells (%) and FEV1% ($r = 0.521$, $P = 0.015$, data was not shown). However, no correlation was noted in the subgroup of patients with/without IGGSCD.

This study demonstrated that B lymphocyte proliferation and activation were significantly decreased in asthmatic patients with IGGSCD compared to those without. Furthermore, B-cell proliferation and activation were lower in patients with SA than in those with NSA. In addition, there was a significant association between the percentage of CD23 expression

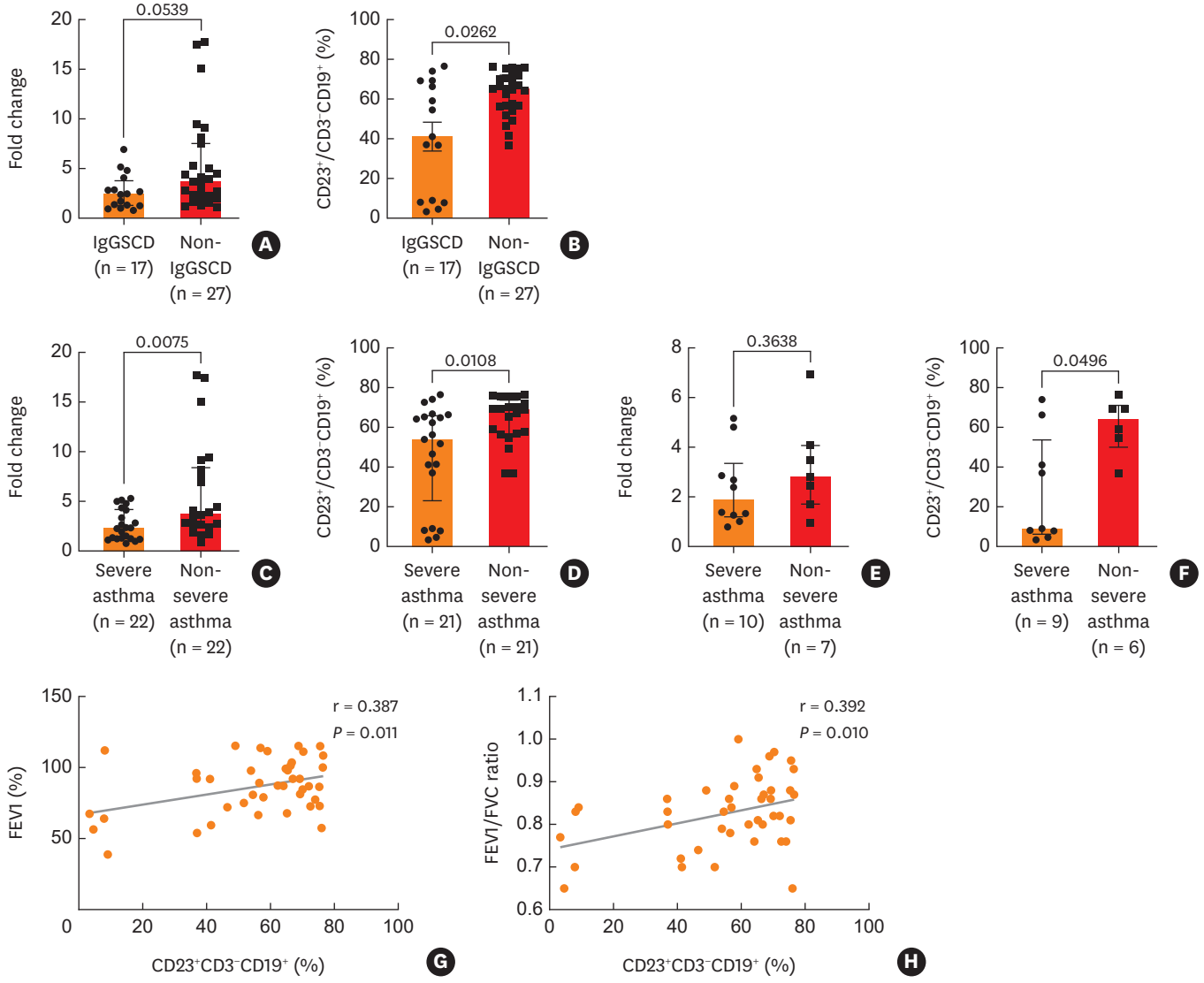

Figure. Comparisons of cell proliferation (A, C, E) and the percentage of CD23 expression (B, D, F) of B lymphocytes under anti-CD40/IL-4 stimulation according to the presence of IGGSCD and asthma severity. Correlation of CD23 expression in B lymphocytes with FEV1 (%) or FEV1/FVC (G, H) in all subjects. Cell proliferation data (A, C, E) are presented as a fold increase in [^{3}H]-thymidine incorporation, and the percentages of CD23 expression (B, D, F) are presented as median and interquartile ranges.
IL, interleukin; IGGSCD, immunoglobulin G subclass deficiency; FEV1, forced expiratory volume in one second; FVC, forced vital capacity.

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in response to anti-CD40/IL-4 stimulation and lung function parameters, suggesting that functional defects in B lymphocytes were involved in the pathogenesis of IGGSCD and related to the severity of asthma. However, these require further validation in a larger cohort. In conclusion, functional defects in B lymphocytes exist in asthmatic patients with IGGSCD in which CD23 expression is associated with clinical outcomes.

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SUPPLEMENTARY MATERIAL

Supplementary Table S1

Baseline characteristics of the study subjects

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