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Blood Mononuclear Cell Subsets in Patients with Chronic Obstructive Pulmonary Disease

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=국문초록=

흡연은 혈청 IgE치를 높이며 또한 IgE는 환기장애와 관련이 있다. 한편 흡연은 혈액 T세포 분획에 변화를 초래한다. 이러한 소견들은 흡연자에서 발생하는 기도 폐쇄의 발생기전에 T세포를 매개로 하는 면역학적 이상이 관여할지도 모른다는 것을 시사한다. 이러한 가설을 증명하기 위하여 18명의 정상인과 18명의 만성폐쇄성폐질환 환자에서 혈액 단핵구 분획과 혈청 면역글로블린을 측정하였다.

정상 대조군과 만성폐쇄성폐질환 환자 사이에 백혈구 수 및 감별계산 그리고 T 세포 분획에는 차이가 없었고 호중구만 환자군에서 높았다. 만성폐쇄성폐질환 환자를 폐확산능치가 낮은 10명과 정상인 8명의 두 군으로 나누어 분석하여 보니 폐확산능치가 정상인 환자들은 정상대조군과 확산능이 낮은 환자군보다 유의하게 높은 $CD8^+$T세포와 낮은 $CD4^+/CD8^+$비를 보였다. FEV_1/FVC는 폐확산능 정상 환자군에서만 $CD4^+/CD8^+$비와 유의한 상관관계를 보였다. 혈청 IgG, IgM 그리고 IgE치는 세군에서 유사하였고, IgA치만 확산능 정상 환자군에서 높았다.

이러한 소견들은 확산능 정상 만성폐쇄성폐질환 환자의 기도폐쇄 발생기전에 T세포 매개성 면역조절 이상이 관여할 것을 시사하며 기도폐쇄는 IgE 생산과 무관한 것으로 사료되었다.

The role of cigarette smoking in the etiology of chronic obstructive pulmonary disease (COPD) has been well established, yet the pathogenetic mechanisms by which smoking leads to chronic airflow limitation are not fully understood. Only 15 to 20 percent of smokers develop clinically manifest COPD and differences in the prevalence of obstructive airways disease among ethnic groups or races have been observed[1], indicating the existence of differences in the individual susceptibility to COPD among smokers. Understanding of the host characteristics that inflence this susceptibility would be of great importance in

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the elucidation of the pathogenesis of this disorder.

Of interest is the finding that serum IgE levels are higher in smokers than nonsmokers irrespective of their atopic status[2]. Elevated serum IgE is related to low FEV_1 along with symptomatic asthma or chronic bronchitis, suggesting a clinical correlation between the elevation of serum IgE and the development of symptomatic lung disease[3]

On the other hand, studies on analysis of T lymphocyte in the peripheral blood have shown significant changes in the T cell subsets in smokers[4,5,6,7,8]. In view of the importance of immunoregulatory T cell functions in the regulation of IgE synthesis[9], it could be possible that smoking-induced alterations in the balance of T cell-mediated helper and suppressor activity could influence regulation of IgE synthesis in smokers.

It is conceivable then that T cell mediated immunologic abnormalities might be involved in the pathogenesis of COPD through IgE synthesis regulation in susceptible smokers. In order to test this hypothesis, we measured peripheral blood mononuclear cell subsets and serum immunoglobulins in the patients with airflow limitation (patients with COPD) and the normal control.

Because chronic airflow limitation may be caused by either emphysema or the small airways disease[10,11], comparative analysis was done beween the patients with low diffusing capacity for carbon monoxide (COPD/low DLco) and COPD patients with normal DLco (COPD/normal DLco). To our knowledge, this is the first report which compared the blood T cell subsets in these two subgroups of patients with COPD.

Methods

Study population

The study population consisted of eighteen normal controls without airflow limitation, 18 smokers with airflow limitation (patients with COPD). All subjects were male. Nine of the 18 normal controls were smokers. Our preliminary study (data not shown) showed that 18 smokers without airflow limitation did not differ from 18 nonsmokers in their spirometric data and blood T cell subset. Also as our goal was to test whether any difference exists beween subjects with and without airflow limitation, we selected the normal controls from both nonsmoker and smoker groups. No subject was under corticosteroid or immunosuppressive treatment, or had other serious illness or acute viral syndrome during the two months prior to the test. No subjects had tuberculosis, parasite infestation such as clonorchis sinensis and hepatitis B surface antigenemia, which are prevalent in Korea. The normal controls with normal chest roentgenogram and spirometry were selected from a population who has undergone annual health check-up. The patients with COPD had a history of dyspnea and/or sputum production for various duration in their medical history and airflow limitation on spirometry (FEV_1/FVC was less than 70 percent and FEV_1 was less than 80 percent of predicted normal). Their airflow limitation was irreversible based on negative immediate bronchodilator response and stable pulmonary function for several months under observation. Positive immediate bronchodilator response required two of 3 following criteria : an increase of 15 percent or greater in the forced expiratory volume in one second (FEV_1) or the forced vital capacity

(FVC), or an increase of 25 percent or greater in mean forced expiratory flow during the middle half of the FVC ($FEF_{25-75\%}$).

Pulmonary function study

Spirometric measurements were made using a spirometer (System 2100 computerized pulmonary function laboratory, Sensor Medics Corp., Yorba Linda, U.S.A.) in all subjects. All values are expressed as percent predicted using the formula of Morris[12]. The lung volume subdivisions were measured in a body plethysmograph (System 2800 automated pressure/flow plethysmograph, Sensor Medics Corp.) in patients with COPD and expressed as percent predicted using the prediction formula of Goldman and Becklake[13]. Single-breath diffusing capacity for carbon monoxide (DLco and DL/VA)(System 2100 computerized pulmonary function laboratory, Sensor medics Corp.) were also expressed as percent predicted using the formula of Burrows and colleagues[14] in patients with COPD. We adopted these prediction formulas for Caucasians as those for Koreans are not fully available.

Analysis of mononuclear cell subsets

Peripheral venous blood was drawn from all subjects. Aliquots were subjected to the laboratory for complete blood count (CBC) and differential white blood cell (WBC) count. Peripheral blood mononuclear cells (PBMCs) were separated from heparinized venous blood by centrifugation on Ficoll-Hypaque (Pharmacia, Uppsala, Sweden) within 24 hours.

Expression of the mononuclear cell surface markers CD3, CD19, CD4, CD8, CD14, and HLA−DR was detected using specific fluorescein isothiocyanate (FITC) or phyconery thrin (PE) conjugated mouse monoclonal antibodies (Becton Dickinson Immunocytometry System, Mountain View, U.S.A.). For staining these markers, aliquots of 100 μl of cells of PBMC suspension ($1X10^6$/ml) were incubated for 45 minutes at 4℃ with monoclonal antibodies. FITC - IgG1 and PE-IgG2 murine isotype control reagents were used to evaluate the nonspecific binding. Two color analysis was performed on FACScan (Becton Dickison, Mountain View, U.S.A.) equipped with argonlaser tuned to 488 nm and data analysis was done using CONSORT™ 30 Data Management System. After gating live lymphocytes or monocytes on the basis of forward and right angle light scatter, 10,000 cells were evaluated for each determination. Fluorescence-positive cells were quantified as percent of lymphocytes in the range of fluorescence intensity channels above a predefined threshold channel.

Measurement of serum immunoglobulins

Serum IgG, IgA and IgM were measured in 12 normal controls and 16 patients with COPD using immunogolbulin reagents(Beckman Instruments, Inc., Galway, Ireland) by rate nephelometry (Beckman Specific Protein Analyzer, Beckman Instruments, Inc., Fullerton, U.S.A). IgE were measured by enzyme immunoassay method (Enzygnost IgE micro., Behring, Marbug, Germany).

Statistical analysis

The rusults are repored as the mean ± SD. All statistical analysis were done on a personal computer using SAS-PC statistical analysis sofware (SAS Institute Inc., Cary, U.S.A.). Comparison of means among groups was performed using nonparametric analysis of variance (Kruskal-Wallis test). When this was signficant, each pairing was examined by means of a nonparametric unpaired two-tailed t-test (Wilcoxon rank sum test). Correlation coefficients (γ_s) were obtained using Spearman's rank method to assess the relationships between the indicator of airflow obstruction and the T cell subsets. P values of less than 0.05 were considered significant.

Results

Subjects

The mean (±SD) age of the normal controls and patients with COPD were 62.6±5.8 and 66.4 ± 7.3 years, respectively, showing no statistical difference between the two groups. The mean smoking history was 14.0±16.5 pack-years for the normal controls and 38.2±10.5 pack-years for the patients with COPD.

Pulmonary function tests

Normal controls were originally designed to have normal spirometry values. Patients with COPD had severe airflow limitation (FVC 59.2±13.4%, FEV_1 44.8±14.9%, FEV_1/FVC 51.8±8.1% and $FEF_{25-75\%}$ 25.2±9.7%), hyperinflation(total lung capacity [TLC] 138.8±27.3% and functional residual capacity [FRC] 161.1±43.5%), air trapping(residual volume [RV] 220.4±57.7%) and decreased diffusing capacity for carbon monoxide (DLco 72.5±26.8% and DL/VA 76.1±28.3%).

Subclassification of patients with COPD

Because patients with airflow limitation might not be a homogeneous group[10,11] and their pathogenesis could be different, patients with COPD were divided into two groups on the basis of their results of diffusing capacity for carbon monoxide[15]. Cases with diffusing capacity for carbon monoxide less than 80 percent of predicted normal value were grouped as patients with low DLco (COPD/low DLco) and cases with diffusing capacity equal to or more thon 80 percent were grouped as patients with normal DLco (COPD/normal DLco). Ten cases of COPD/low DLco (mean age, 67.4±4.5 years) and 8 cases of COPD/normal DLco (65.1±9.6 years) were subclassified out of 18 patients with COPD. All cases of COPD/low DLco had a charcteristic radiologic appearances suggestive of emphysema. The mean smoking history was 34.8±8.7 and 42.5±10.9 pack-years ($p>0.05$) for COPD/low DLco and COPD/normal DLco, respectively. Characteristics and pulmonary function of the three study groups are shown in Table 1. COPD/low DLco had severe air flow limitation, hyperinflation, air trapping and decreased diffusing capacity for carbon monoxide. COPD/normal DLco also had severe airflow limitation, hyperinflation and air trapping, but normal diffusing capacity for carbon monoxide. COPD/low DLco had a higher FRC ($p<0.05$) and RV ($p<0.05$) compared to COPD/normal DLco.

Peripheral leucocyte count and mononuclear cell subsets in patients with COPD

There were no differences between normal controls and patients with COPD in their WBC count, differential count and the proportion and absolute count of mononuclear cell subsets, except the absolute count of neutrophils was higher in patients with COPD than the normal controls ($P<0.05$).

Peripheral leucocyte count and mononuclear cell subsets in COPD/low DLco and COPD/normal DLco

No significant differences were found in WBC count and differential cell count among the normal controls, COPD/low DLco and COPD/normal DLco (Table 2). When compared with the normal controls or COPD/low DLco, COPD/normal DLco had a higher proportion of CD8+cells ($P<0.005$ vs. normal controls and $P<0.008$ vs. COPD/low DLco, respectively) (Fig.1) and a lower CD4+/CD8+ratio ($P<0.006$ and $P<0.02$, respectively (Fig. 2). Also, COPD/normal DLco had a higher absolute CD8+cell count than did COPD/low DLco ($P<0.04$).

Table 1. Clinical features of patients with COPD

Variabie	Control (n=18)	Patients with COPD		p Value
		Low DLco (n=10)	Normal DLco (n=8)	
Age, yrs	62.6± 5.8	67.4± 4.5	65.1± 9.6	NS
Smoking, Pack-yrs	14.3±16.5	34.8± 8.7	42.5±10.9	0.0005*
FVC, % pred	95.4±14.8	56.9±13.4	62.1±12.8	0.0001*
FEV_1, % pred	104.4±15.7	46.1±16.5	48.9±11.6	0.0001*
FEV/FVC, %	78.8± 5.3	49.6± 9.1	54.6± 5.3	0.0001*
$FEF_{25-75\%}$, % pred	100.5±24.9	22.6±10.8	28.5± 6.7	0.0001*
TLC, % pred		148.3±21.7	126.0±27.2	NS
FRC, % pred		182.1±32.6	132.3±38.5	0.034+
RV, % pred		248.3±50.0	181.1±44.0	0.024+
DLco, % pred		55.4±19.7	97.6±12.4	0.003+
DL/VA, % pred		58.5±23.0	99.8±10.9	0.006+

Values are presented as mean and SD. COPD : chronic obstructive pulmonary disease ; Controls : normal controls ; DLco : pulmonary diffusing capacity for carbon monoxide ; FVC : forced vital capacity ; FEV_1 : forced expiratory volume in one second ; $FEF_{25-75\%}$: forced expiratory flow during the middle half of the FVC ; TLC : total lung capacity ; FRC : functional residual capacity ; RV : residual volume ; VA : alveolar volume ; NS : not significant.
* : Statistical significance among the groups by Kruskal−Wallis test.
+ : Statistical significance vs COPD with low DLco by Wilcoxon rank sum test.

Correlation between FEV_1/FVC and T cell subsets

FEV_1/FVC was significantly correlated with CD4+/CD8+ratio in COPD/normal DLco (γ_s=0.785, $P<0.05$), but not in the normal controls (γ_s=0.102, $P>0.05$) or COPD/low DLco (γ_s=0.444, $P>0.05$) (Fig. 3).

Serum immunglobulin levels

No significant differences were observed in the serum IgG, IgM and IgE levels between the twelve normal controls and 16 patients with COPD, as well as among 12 normal controls, 8 COPD/low DLco and 8 COPD/normal DLco, while the serum IgA level was significantly higher in COPD/normal DLco (305.3± 91.8 mg/dL) than in normal controls (186.0±47.6 mg /dL)($P<0.03$). No significant correlation between the serum IgE level and the CD4+/CD8+ ratio or FEV_1/FVC was present in any group of patients with COPD.

Discussio

Although we did not find any differences in the serum IgE level and the peripheral blood T lymphocyte subsets between the normal controls and patients with COPD, we detected an alteration in the blood T lymphocyte subsets in the COPD/normal DLco compared with the normal controls or the COPD/low DLco in that they had a high proportion of CD8+cells and a low CD4+/CD8+ratio. In addition, a significant correlation was found between FEV_1/FVC, an indicator of airflow limitation, and CD4+/CD8+ratio, which reflects the balance of immunoregulatory T cells, in COPD/normal DLco group.

The relationship between cigarette smoking and

Table 2. Leucocyte mononuclear cell profile in blood of patients with COPD

Variable	Controls (n=18)	Patients with COPD		p Value
		Low DLco (n=10)	Normal DLco (n=8)	
WBC,$10^3/mm^3$	6.50±0.36	7.37±2.77	7.43±1.91	NS*
Neut.,$10^3/mm^3$	4.07±2.74	5.11±2.82	4.87±2.11	NS*
Neut., %	59.7±9.6	67.1±8.8	63.0±12.2	NS*
Lym.,$10^3/mm^3$	1.91±0.50	1.74±0.53	2.01±0.38	NS*
Lym., %	32.1±7.3	25.6±7.4	28.7±8.4	NS*
Eso./mm^3	206.7±362.0	191.2±135.7	229.2±223.8	NS*
Eso., %	3.0±4.0	2.9±2.3	3.7±4.0	NS*
CD3+cell/mm^3	1,061.2±286.8	904.5±310.8	1,163.8±310.0	NS*
CD3+cell, %	56.4±8.6	51.9±7.4	57.8±10.6	NS*
CD4+cell/mm^3	393.1±154.0	325.1±164.9	349.8±128.1	NS*
CD4+cell, %	36.5±6.4	35.0±6.6	29.5±7.	NS*
CD8+cell/mm^3	316.5±101.1	258.5±113.8	455.5±155.2	0.031^{+}
CD8+cell, %	29.8±5.4	28.0±5.2	37.7±4.3	0.003^{++}
CD4+/CD8+	1.27±0.36	1.29±0.30	0.79±0.22	0.005^{++}
CD19+cell/mm^3	130.4±88.4	114.3±90.4	94.0±34.3	NS*
CD19+cell,%	6.7±3.8	6.6±5.0	4.7±1.5	NS*
CD14+cell/mm^3	51.3±39.4	62.3±31.7	66.7±47.4	NS*
CD14+cell, %	17.4±6.6	21.3±6.4	23.2±11.2	NS*
HLA-DR+cell/mm^3	611.4±237.7	607.5±247.7	709.0±269.0	NS*
HLA-DR+cell, %	27.9±8.6	30.2±11.8	31.3±11.0	NS*

Values are presented as mean and SD. COPD : chronic obstructive pulmonary disease ; Controls : normal controls ; DLco : pulmonary diffusing capacity for carbon monoxide ; WBC : white blood cell count ; Neut. : neutrophil, lym. : lymphocyte ; Eos. : eosinophil ; NS : not significant.

* : Statistical significance among the groups by Kruskal-Wallis test.

+ : Statistical significance between COPD with normal DLco and COPD with low DLco by Wilcoxon rank sum test

++ : Statistical significance vs controls or COPD with low DLco by Wilcoxon rank sum test

chronic airflow limitation is well established, but not all smokers are affected with the condition. The majority of smokers continue smoking with little deterioration in their lung function, and it is not clear why certain smokers develop airflow limitation while others do not. What determines this difference among smokers? Certain factors, such as the genetically determined alpha$_1$-antitrypsin phenotype (Pi type), as well as many risk factors such as age, gender, race and allergy also have been suggested to be related to the development of airflow limitation.

Orie and colleagues[16] have suggested that persons with atopy or increased levels of nonspecific bronchial responsiveness (or both) may constitute a group at

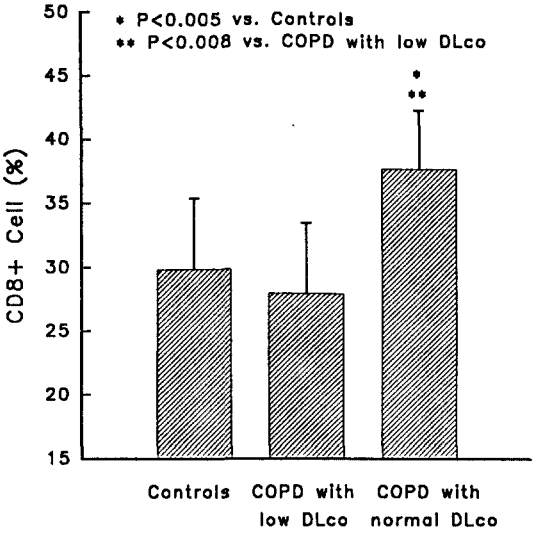

Fig.1. Mean (±SD) proportion of CD8+cells in the peripheral blood of the normal controls, COPD/low DLco and COPD/normal DLco. COPD/normal DLco had a significantly higher CD8+cells than did normal controls ($P<0.005$) or COPD/low DLco ($P<0.008$).

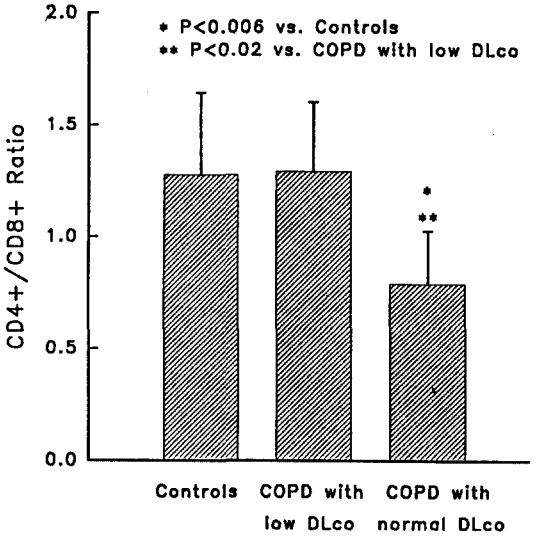

Fig.2. Mean (±SD) CD4+/CD8+ratio in the peripheral blood of the normal controls, COPD /low DLco and COPD/normal DLco. COPD/ normal DLco had a significantly lower CD4+ /CD8+ratio than did normal controls ($P<0.006$) or COPD/low DLco ($P<0.02$).

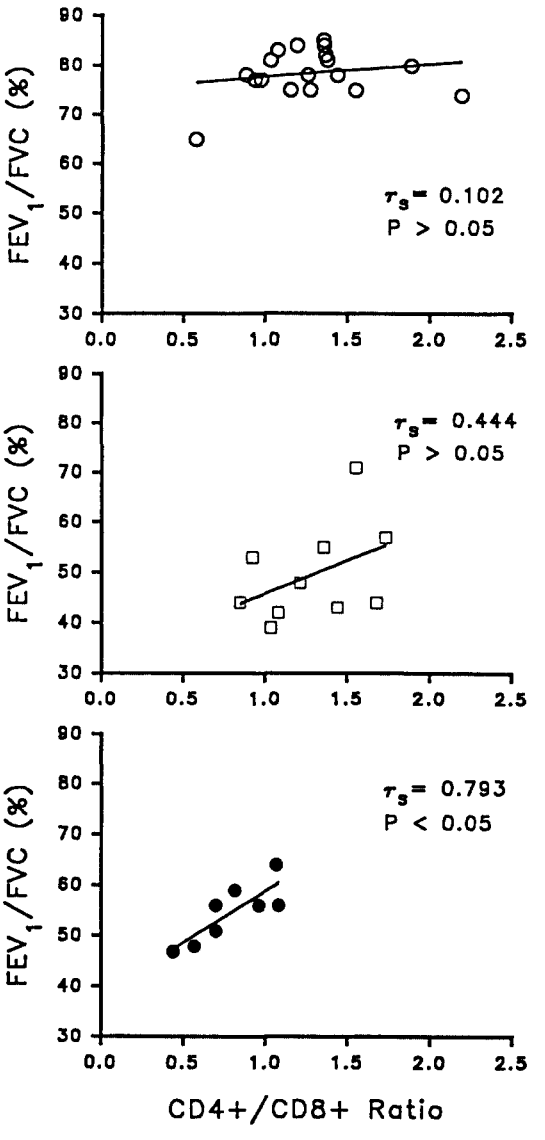

Fig.3. Relationship between FEV_1/FVC and CD4+ /CD8+ratio in normal controls (open circles), COPD/low DLco (open squares) and COPD/normal DLco (solid circles). Correlation coefficient by Spearman's rank correlation was significant in COPD/normal DLco ($\gamma_s=0.793$, $P<0.05$), but not in normal controls ($\gamma_s=0.102$, $P>0.05$) or COPD/low DLco ($\gamma_s=0.444$, $P>0.05$)

risk for the occurrence of COPD. Recent studies on smokers with COPD also indicate heightened airway responsiveness to histamine in the majority of such patients[17]. Allergy, manifested either by positive skin test reactions to aeroallergens or by a high IgE level, was reported to be a major predictor of increased bronchial responsiveness[18].

There is evidence that smoking may increase allergy skin test reactivity and serum IgE[2]. On the other hand, analysis of T lymphocyte subsets in the peripheral blood indicates increases in the total T cells and CD4+T cell populations in light and moderate smokers, and a relative decrease in CD4+cell and increases in both percentage and total numbers of the CD8+T cells in heavy smokers[4,5]. Other studies also have shown changes in blood T cell subsets in smokers[6,7,8] In view of the evidences that T cells are involved in the regulation of IgE synthesis[9], above findings suggest the possibility that T cell mediated immunologic abnormalities may play a role in the pathogenesis of airflow limitation in smokers. In order to investigate this, our data were analyzed according to the presence or absence of airflow limitation in the subjects. Our finding shows that no significant differences in the blood T cell subsets and serum immunoglobulin levels between normal controls and the patients with COPD.

It is thought that chronic airflow limitation may be caused by either emphysema or irreversible obstructive changes in the peripheral airways[10,11]. Whether these two pathologic processes are pathogenetically related or represent two separate responses to a common exposure has been remained a subject of investigation[10]. Recently we[19] have shown that smokers develop different patterns of lung destruction, some with pure or predominant centrilobular emphysema and others with pure or predominant panlobular emphysema and that in centrilobular emphysema, flow limitation is primarily a function of the small airways abnormalities, whereas in panlobular emphysema flow limitation is always accompanied by loss of elastic recoil pressure of the lung. This suggested to us that different pathogenetic mechanisms would be at play in these two types of emphysema. It has also been reported that smokers with centrilobular emphysema are more reactive to methacholine than patients with panlobular emphysema and this increased reactivity was correlated with the amount of pathological abnormalities in the small airways in centrilobular emphysema, but not in panlobular emphysema[20]. These results prompted us to separate the smokers with airflow limitation in this study into two groups of COPD/low and COPD/normal DLco based on their diffusing capacity for carbon monoxide. The high degree of airflow limitation (FEV_1 48.9±11.6% and FEV_1/FVC 54.6±5.3%) found in the normal DLco group with no history or evidence of asthma may indicate the presence of a large amount of peripheral small airways disease without sufficient degree of emphysema that would decrease the surface area for diffusion[15]. If we assume that small airways disease would temporally precede centrilobular emphysema as previously suggested[21,22], our COPD/normal DLco could correspond to small airways disease stage, which occurs prior to the fully developed stage of centrilobular emphysema. In contrast, our smokers with airflow limitation who had very low diffusing capacity for carbon monoxide (DLco 58.5±23.0%), high residual volume (248.3±50.0%)[15] and high total lung capacity (148.3±21.7%)[23] would correspond to predominant emphysema, probably panlobular.

The COPD/low DLco and COPD/normal DLco in this study had similar mean age, smoking history and degree of airflow limitation. However, the proportion

of blood CD8+cells was significantly high and CD4+/CD8+ratio was significantly low in COPD/normal DLco relative to the normal controls or COPD/low DLco. When the patients were analyzed as a single group, no difference from the normal controls in T cell subsets was apparent, while upon dividing them into COPD/low DLco or COPD/normal DLco groups, differences in T cell subsets became apparent. This suggests that different pathogenetic mechanisms, possibly involving T cells, are at play in COPD.

The cellular makeup of inflammation of bronchioles in centrilobular emphysematous lungs may be variable, but lymphocytes seem to predominate[21,24]. While the airway mucosa of patients with chronic bronchitis has been shown to contain T lymphocytes and cigarette smoking alone was not found to influence the scores of intraepithelial T lymphocytes, smokers who had both chronic bronchitis and airflow limitation displayed increased numbers of CD3+, CD4+ and CD8+ lymphocytes[25].

In the present study, the cause and effect relationship between abnormality in blood T cell subsets and small airways disease is not known. The changes seen in the peripheral circulation may reflect either a "spill-over" from the bronchioles or an influence of the bronchiolar microenvironment on circulating T lymphocytes. In some probably genetically determined and immunologically susceptible smokers, tobacco pigment deposited around the bronchioles seems to trigger a chronic inflammatory lymphocytic infiltration in the small airways. This is accompanied by changes in the proportion and the ratio of lymphocytes in the blood which may reflect changes in the lungs.

What does the large proportion of blood CD8+ cell and the low CD4+/CD8+ ratio in COPD/normal DLco mean? A study on lymphocytic infiltration of central airway epithelium has shown that constant predominance of CD8+ over CD4+ intraepithelial cells in nonsmokers, smokers and smokers with airflow limitation. Infiltration of CD8+ T cells on alveolar epithelium in cryptogenic fibrosing alveolitis has been reported[26]. Also it was found that the predominant cells present in the inflammatory infiltrates of bronchiectasis were immunologically active T lymphocytes and that CD8+ cells outnumbered CD4+ cells, suggesting that a cell mediated immune response being one component of the bronchial inflammation[27]. An increase of bronchoalveolar lavage fluid CD8+ cells has been shown in patients with chronic bronchitis[28] and young, healthy smokers compared to never smokers[29]

In COPD/normal DLco, pathological studies in the small airways would be necessary for elucidation of the meaning of the high proportion of CD8+ cells and low CD4+/CD8+ratio in the peripheral blood. However, while the mechanism of its pathogenesis is unknown, the present findings suggest that at least T cell mediated immunoregulatory abnormalities might be involved in the pathogenesis of airflow limitation in COPD/normal DLco. The significance of the change in this study is further supported by the correlation between FEV_1/FVC and the CD4+/CD8+ ratio. As shown in figure 3, the degree of airflow limitation was significantly correlated with the abnormality in the ratio of T cell subsets and airflow decreased with the decrease of CD4+/CD8+ ratio in COPD/normal DLco.

Unexpectedly, the IgE levels were not increased in any of our groups, and not related to the change in T cell subsets. While serum IgA level was high in COPD/normal DLco relative to the normal controls, the meaning of this finding is not known.

The CD4+/CD8+ ratio in Korean controls was

very low compared with that of Caucasian[6] (1.27±0.36 vs 2.26±1.04). However, similar values (1.213±0.597) have been reported in a Chinese population[30] and immunologic differences between whites and blacks have been reported[7], suggesting the existence of racial differences.

In conclusion, we have found that the proportion of peripheral blood CD8+ cells and the CD4+/CD8+ ratio in COPD/normal DLco are significantly different from those in normal controls or COPD/low DLco and the degree of airflow limitation is significantly correlated with the CD4+/CD8+ ratio in COPD/normal DLco, but not in COPD/low DLco. This suggest that T cell mediated immunoregulatory abnormalities might be involved in the pathogenesis of airflow limitation of COPD/normal DLco in suscptible Korean smokers. However, no correlation was observed between the IgE levels and the blood lymphocyte abnormalities among these groups. In order to confirm these findings further studies in a larger number of cases and in different races with simultaneous pathologic analysis of small airways would be needed.

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