Relationships between thickening of reticular basement membrane and the clinical features in children with asthma

Eun Soo Kim

Department of Medicine

The Graduate School, Yonsei University

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Directed by Professor Kyu-Earn Kim

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Eun Soo Kim

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This certifies that the Master's Thesis

of Eun Soo Kim is approved

Thesis Supervisor : Kyu-Earn Kim

Thesis Committee Member Jung Won Park

Thesis Committee Member Myung Hyun Sohn

The Graduate School

Yonsei University

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Written by Eun Soo Kim

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ABSTRACT

Relationships between thickening of reticular basement membrane and the clinical features in children with asthma

Eun Soo Kim

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The Graduate School, Yonsei University

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RATIONALE: Asthma is chronic inflammatory disease characterized by airway inflammation, bronchial hyperresponsiveness, airway obstruction. Although asthma induces partially reversible airway obstruction, in some patients, airflow obstruction can become irreversible. Such obstruction might be a consequence of airway remodeling. Remodeling comprises a number of structural changes, including epithelial detatchment, reticular basement membrane thickening, smooth muscle

hypertrophy, and new vessel formation. This study investigated whether reticular basement membrane thickening is already present in children with asthma.

METHODS: 18 children with asthma and 24 control subjects underwent flexible bronchoscopy with endobronchial biopsy. We used light microscopy to measure reticular basement thickness in plastic-embedded biopsy sections. We examined the relationship between reticular basement membrane thickening and age, sex, duration of asthma, asthma severity, FEV_1, FEV_1/FVC, $FEF_{25-75\%}$, methacholine PC_{20}, eosinophil count, or presence of atopy.

RESULTS: Reticular basement membrane thickness was greater in subjects with asthma (8.3 ± 1.4 ㎛) than in control subjects (6.8 ± 1.3 ㎛, p=0.0008). Multiple regression analysis revealed that sex, FEV_1/FVC, total IgE, or atopy (IgE for *Dermatophagoides pteronyssinus* > 0.34 kUA/L*)* were the significant predictive factors for reticular basement membrane thickness. There was no significant difference between reticular basement membrane thickness and age, duration of asthma, FEV_1, $FEF_{25-75\%}$, methacholine PC_{20}, eosinophil count, or asthma severity.

CONCLUSIONS: Reticular basement membrane thickening is already present in children with asthma. In addition, we find association between reticular basement membrane thickness and sex, FEV_1/FVC, total IgE, or presence of specific IgE to

Dermatophagoides pteronyssinus.

Key words: airway remodeling, reticular basement membrane thickening, endobronchial biopsy, children

Relationships between thickening of reticular basement membrane and the clinical features in children with asthma

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I. INTRODUCTION

Asthma is chronic inflammatory disease characterized by pulmonary inflammation, bronchial hyperresponsiveness, airway obstruction, and airway remodeling. In airway remodeling, structural airway changes include reticular basement membrane thickening, increased extracellular matrix protein deposition, increased smooth muscle mass, new vessel formation, and mucus gland hyperplasia. These changes lead to increased bronchial wall thickness, which in turn might affect the severity of

physiologic and clinical parameters in asthmatic subjects.[1] Thickening of the epithelial reticular basement membrane is pathognomonic of the adult asthma phenotype. In hematoxylin and eosin-stained tissue sections, the thickened layer has a hyaline appearance on light microscopy and, ultrastructurally, appears to consist of a plexiform arrangement of reticulin seen as fibrils in an amorphous matrix.[2] The thickened reticular layer is associated with deposition of immunoglobulins or collagen I and III, tenascin, and fibronectin.[2-5]

High-resolution computed tomography provides a high degree of anatomic details and can indirectly confirm airway remodeling in asthmatics, such as bronchial thickening, mucoid impaction, bronchial dilatation and bronchiectasis. de Blic et al showed that children with severe asthma have a significantly higher bronchial wall thickness on high-resolution computed tomography scan than control children.[6] They described that the bronchial wall thickness score significantly correlated with reticular basement membrane thickening and nitric oxide production by the airway wall. The correlation with the eosinophilic cationic protein level was just significant, whereas there was no correlation with FEV_1 or forced expiratory flow at 25% to 75% of forced vital capacity.

Reticular basement membrane thickening is known as very early marker of airway

remodeling. Several studies have suggested an association between theses changes and disease severity.[7,8] Few studies have evaluated the asthmatic airway in children.[2,6,9] Reticular basement membrane thickening has been described in children with asthma. Cokugras et al demonstrated qualitively the thickening and hyalinization of the basement membrane in nine patients (5-14 years).[9] Payne et al demonstrated reticular basement membrane thickening in 19 children (6-16 years) with difficult asthma.[2] They concluded that reticular basement membrane thickening was already present in children with difficult asthma and to similar extent to that seen in adults with asthma. de Blic et al performed endobronchial biopsy and bronchial alveolar lavage in 13 children with persistent symptoms and 15 with few or no symptoms.[10] They reported that reticular basement membrane thickening was similar in both groups, but the number of eosinophils and neutrophils in the epithelium was significantly higher in symptomatic children than in children with few symptoms.

Biopsy studies, evaluating small tissue fragments from the central airways, have demonstrated that elements of remodeling, in particular the thickening of the basement membrane, can occur even in patients with mild intermittent asthma.[11] Biopsy studies in young children and rhinitis patients seem to indicate that these alterations occur at an early stage in atopic individuals, even prior to the development

of symptomatic asthma.[12,13] Careful morphometric analysis indicates that in fetal asthma, the airway wall of both large and small airways is thickened, whereas in non-fetal asthma, the increased thickness is predominantly located in small airways.[14]

Here we investigated whether the reticular basement membrane thickening is already present in children with asthma. We also examine whether the reticular basement membrane thickening correlates with age, sex, duration of symptoms, FEV_1, FEV_1/FVC, $FEF_{25-75\%}$, methacholine PC_{20}, asthma severity, presence of atopy, and serum eosinophil count in a group of children with asthma. We used light microscopy and plastic-embedded sections to examine endobronchial biopsies from a group of children with asthma. The data were compared with those from biopsies obtained from a group of children without asthma undergoing flexible bronchoscopy for other clinical indications.

II. MATERIALS AND METHODS

1. Subjects

Forty-two children were prospectively included between August 2003 and March 2006. There were eighteen children with asthma. Asthma was diagnosed according to American Thoracic Society (ATS) criteria.[15] Atopy was defined as a positive skin test to more than one extract of the common local aeroallergens, and nonatopy was a negative skin test and serum IgE concentration smaller than 150 IU/ml.

Severity of asthma was defined as mild, moderate, or severe on the basis of the main symptoms of episodes of wheezing per year, episodic wheezing causing speech interruption, or nocturnal wakening.[16] Asthma was considered to be mild if 1 to 2 episodes of wheeze were reported in the past 12 months. Asthma was considered to be moderate if 3 to 12 wheezing episodes and not more than one occasion of nocturnal wakening per week (on average) caused by wheeze had been reported during the past 12 months. Severe asthma was defined as at least one of the following features: more than 12 episodes of wheeze, one or more episodes of acute asthma limiting speech, or more than one occasion of nocturnal wakening per week (on

average) throughout the past 12 months.[17]

At the time of the examination, all asthmatic subjects were clinically stable and had not experienced any respiratory infections for at least one month. Inhaled steroids were discontinued four weeks before bronchoscopy.[9] Before stopping steroid treatment the consent of the parents was obtained, and parents were informed about the probable complications of stopping steroid treatment. Each patient was followed very closely. We agreed to give bronchodilators such as salbutamol in cases of exacerbation of asthma but during the four weeks prior to bronchoscopy no exacerbations occurred. Endobronchial biopsy was also performed in 24 children without asthma undergoing bronchoscopy for persistent atelectasis (n=9), pulmonary tuberculosis (n=7), foreign body aspiration (n=4), and chronic cough that was unresponsible to bronchodilators, prolonged treatment with inhaled corticosteroids (n=4).

Performance of endobronchial biopsy for studying airway inflammation and remodeling was approved by the Severance Hospital Institutional Review Board committees. Written consent for participation was obtained from the parents and verbal assent from the children.

2. Bronchoscopy and endobronchial biopsies

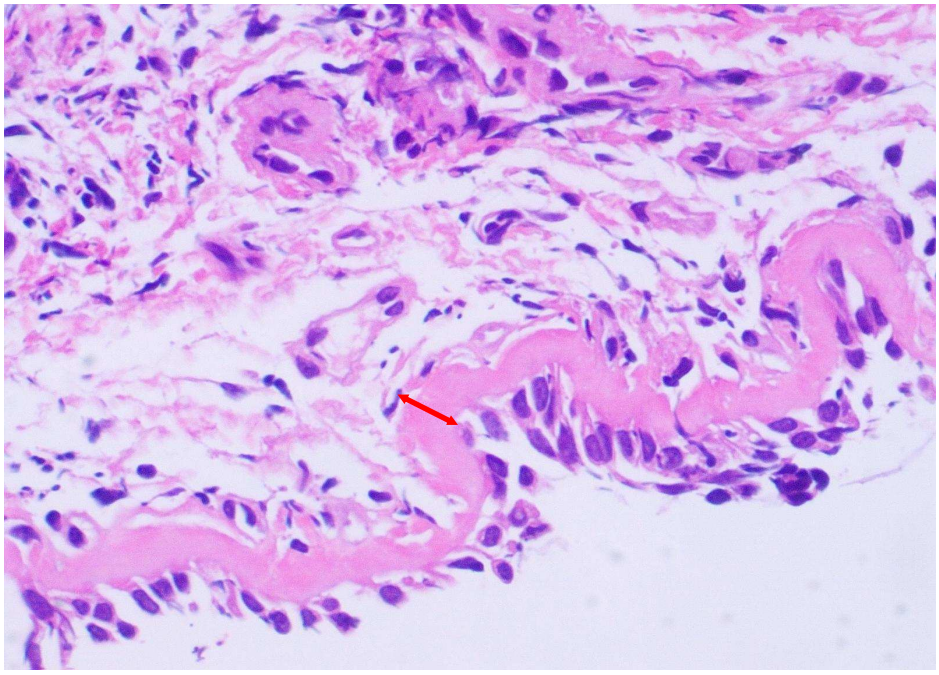
Flexible bronchoscopy was performed during light sedation (3C 30, Olympus, Tokyo, Japan). Bronchial biopsy samples were taken from third and fourth order bronchial divisions from either the left side or the right side by using cupped forceps. All children tolerated the procedure well and no complications occurred in the postprocedure period. There were no long term sequelae.

3. Tissue processing

Biopsy tissues were fixed in 10% formaldehyde and embedded in paraffin blocks before cutting. They were dissected 4 ㎛ thick and stained with hematoxylin and eosin staining. Sections were examined by light microscopy in random order by same observer, who was unaware of the origin of the sections. Intraobserver repeatability was assessed by measuring the same section five times. The within-biopsy variability for a single subject was assessed by measuring a single section from each of three biopsies from the same subject. The biopsies processed for measurement of reticular basement membrane thickness were generally of good quality and sufficient to allow

multiple measurements of reticular basement membrane in all subjects (Fig. 1, A-D).

A



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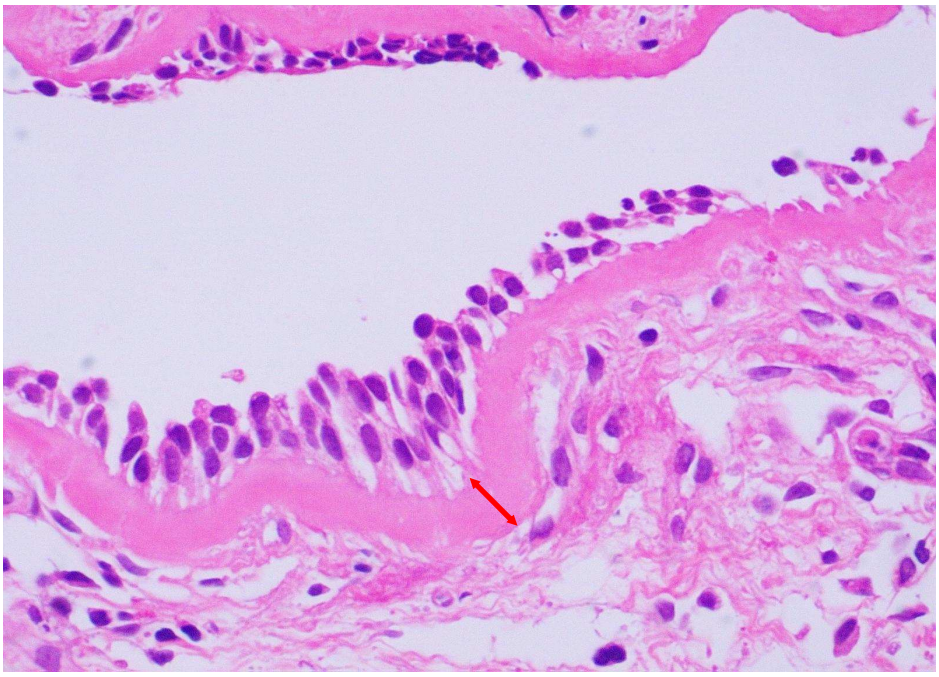

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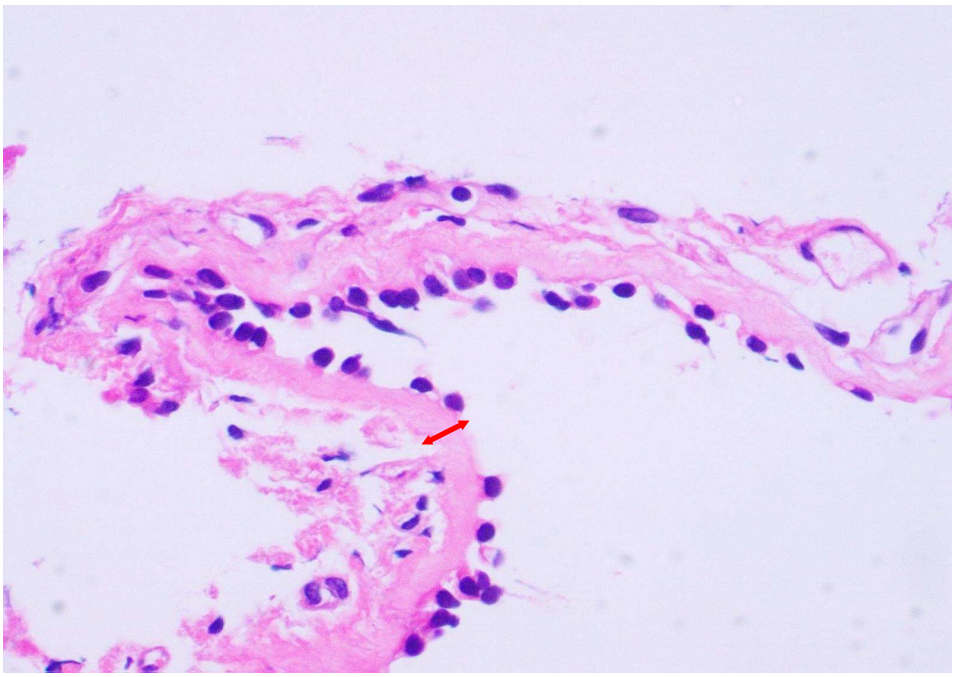

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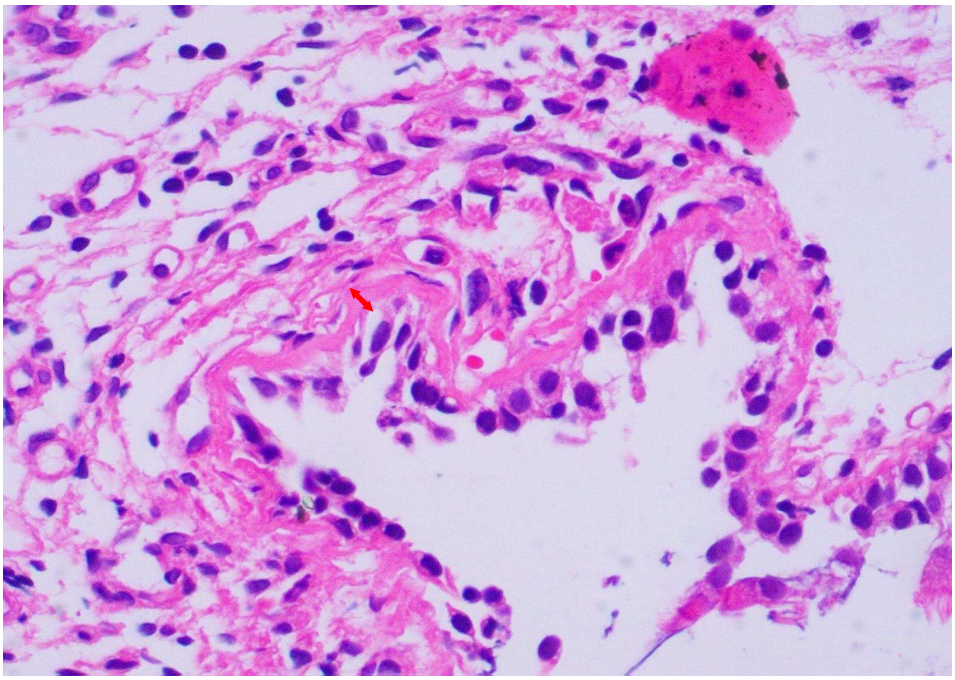

Fig. 1. Representative examples of bronchial biopsy specimens stained with hematoxylin and eosin staining from children with asthma (A and B) and control subjects (C and D) showing reticular basement membrane (arrows).

4. Methacholine challenge test

Methacholine challenge test was performed according to standardized procedure.[18] Each subject inhaled increasing concentrations of methacholine (0.075, 0.15, 0.31, 0.62, 1.25, 2.5, 5, 10, 25 mg/mL), nebulized by a dosimeter (Dosimeter MB3 Mefar, Brescia, Italy) until FEV_1 was reduced by 20% from postsaline solution value. Bronchial response to methacholine was expressed as the provocative concentration causing a 20% fall in FEV_1 (PC_{20} in mg/mL), and was calculated by linear interpolation between the two final points of the log-dose response curve.

5. Spirometric studies

Spirometry was performed the day before bronchoscopy, and before each

assessment of airway responsiveness. Flow volume curves obtained according to the ATS guidelines (VIASYS Healthcare Inc., Conshohocken, USA).[15]

6. Total IgE and specific IgE measurement

Total IgE and specific IgE were determined using the CAP system (Pharmacia-Upjohn, Uppsala, Sweden). Tests were performed according to the manufacturer's instructions. For specific IgE a CAP value of > 0.34 kUA/L was considered positive. Specific IgE to *Dermatophagoides pteronyssinus* was measured in asthmatics.

7. Statistical analysis

Data are expressed as mean and standard deviation. Differences of reticular basement membrane thickness between groups were assessed by a student's t-test. Differences of reticular basement membrane thickness according to asthma severity in children with asthma were analyzed by means of the nonparametric Kruskal-Wallis test. Multiple regression analysis was performed to assess the contributions of age, sex, duration of asthma, FEV_1, FEV_1/FVC, $FEF_{25-75\%}$, methacholine PC_{20}, eosinophil

count, and presence of atopy.

Probability values of less than 0.05 were considered to be statistically significant.

III. RESULTS

1. Patient characteristics

Biopsy specimens were taken from 5 subjects with mild, 11 subjects with moderate, and 2 subjects with severe asthma. The clinical characteristics of the patients are shown in Table 1. The mean age of the asthma group was 13 ± 1 years (range 11-15), with a male/female ratio of 11:7. The mean age of the control group was 12 ± 3 years (range 6-15), with a male/female ratio of 1:1. The children with asthma had atopy in 14 subjects, and the control group had atopy in 7 subjects. Duration of asthma were 4 ± 3 years. The mean ± SD FEV_1 percent predicted was 76 ± 12 in asthmatics, reflecting persistent airflow limitation despite maximal medical therapy, and 87 ± 11 in control groups, reflecting well preserved pulmonary function. Table 2 shows the each characteristic of children with asthma

Table 1. Characteristics of Subjects

	Asthmatics	Controls
Subjects	18	24
Age, yr	13±1	12±3
Sex ratio, M/F	11 / 7	12 / 12
With/without atopy	14 / 4	7 / 17
Duration of asthma, yr	4±3	NA
Severity (mild/moderate/severe)	5 / 11 / 2	NA
FEV_1, % predicted	76±12	87±11
PC_{20}, log mg/mL	0.55±1.50	NA
Total IgE, log IU/mL	6.13±1.42	5.82±0.75
Eosinophil count, log $\mu\ell^{-1}$	5.65±1.17	5.57±0.76
Der p - specific IgE, kUA/L	26.51±35.89	7.45±16.69

Data are represented as Mean±SD or absolute numbers.

NA : not applicable

Table 2. Characteristics of children with asthma

Subjects	Age (yr)	Sex	Duration of asthma (yr)	FEV_1 (% predicted)	FEV_1/FVC (%)
1	13	M	1	80	84
2	13	M	1	92	92
3	12	F	4	57	81
4	15	M	10	94	91
5	11	M	3	68	92
6	15	F	2	60	81
7	13	M	6	72	75
8	15	F	3	87	96
9	12	F	6	59	78
10	14	M	7	74	77
11	14	F	1	84	89
12	13	M	4	92	76
13	13	M	8	74	78
14	11	M	3	65	78
15	12	F	1	78	91
16	12	F	8	66	83
17	11	M	2	74	91
18	12	M	4	85	90

Subjects	$FEF_{25-75\%}$ (% predicted)	RBM thickness (mean, ㎛)	PC_{20}, log (mg/mL)	Total IgE, log (IU/mL)
1	80	8.3	1.46	7.17
2	81	7.4	-1.20	7.00
3	46	11.0	-1.35	6.41
4	103	9.1	1.82	6.61
5	83	7.2	1.96	4.71
6	51	8.3	-0.29	7.20
7	75	7.8	-1.17	6.54
8	86	9.2	2.07	7.64
9	56	6.8	-1.00	6.93
10	50	6.3	1.22	5.03
11	90	7.1	2.05	6.88
12	79	11.0	1.88	5.75
13	57	10.0	-2.30	7.83
14	78	8.2	-0.80	6.36
15	79	8.3	1.76	4.93
16	78	6.8	2.06	2.20
17	65	9.2	0.44	6.89
18	87	7.2	1.28	4.25

RBM = reticular basement membrane

Subjects	Eosinophil count, log ($\mu\ell^{-1}$)	*D.pteronyssinus* (kUA/L)	Severity
1	5.60	71.7	mild
2	4.70	62.5	mild
3	6.54	99.7	moderate
4	4.70	0.41	moderate
5	2.30	0	moderate
6	6.09	10.4	moderate
7	6.51	34.4	moderate
8	6.02	100	moderate
9	6.17	49.8	severe
10	6.09	42.1	moderate
11	4.09	0.63	mild
12	5.48	0.84	mild
13	6.52	0.58	mild
14	7.13	1.46	moderate
15	6.09	2.63	moderate
16	4.70	0	moderate
17	6.45	0	moderate
18	6.55	0	severe

2. Reticular basement membrane thickness in asthmatics and control subjects

The results of measurement of reticular basement membrane thickness are shown in Fig. 2. Reticular basement membrane thickness in the children with asthma was significantly greater than control subjects (mean ± SD 8.3 ± 1.4 ㎛ versus 6.8 ± 1.3 ㎛, p = 0.0008). This results have demonstrated that reticular basement thickness is present in children with asthma.

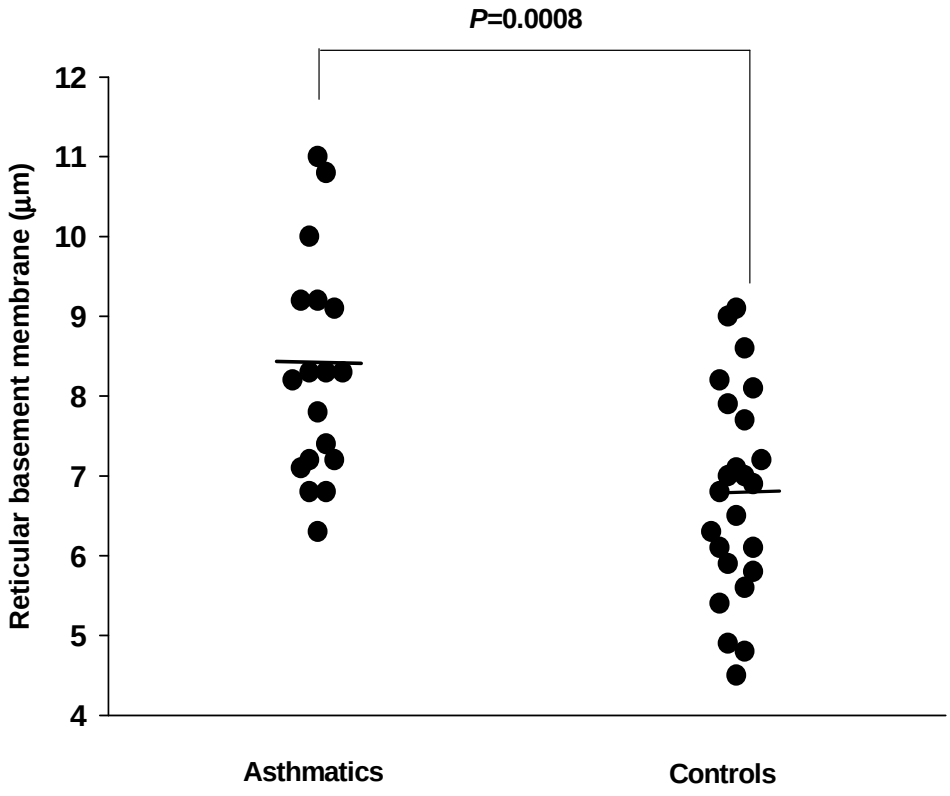

Fig. 2. Mean and individual values of reticular basement membrane thickness in asthmatics and control subjects. The mean is shown as a single black line. Each circle represents one individual.

3. Contributory factors to the reticular basement membrane thickness in asthmatics

In all asthmatic patients, a multiple regression analysis was performed considering reticular basement membrane thickness as the dependent variable, whilie age, sex, duration of symptoms, FEV_1, FEV_1/FVC, $FEF_{25-75\%}$, methacholine PC_{20}, total IgE, specific IgE to *Dermatophagoides pteronyssinus,* and serum eosinophil count were treated as independent variables. Analysis results indicated a significant contribution of sex, FEV_1/FVC, total IgE, and specific IgE to *Dermatophagoides pteronyssinus* to the reticular basement membrane thickness, but not age, duration of symptoms, FEV_1, $FEF_{25-75\%}$, methacholine PC_{20}, and serum eosinophil count.

Table 3. Regression coefficients and *p* values of reticular basement membrane thickness in asthmatics

	Beta	*p*-value
Reticular basement membrane thickness		
Age	-0.89	0.09
Sex	3.92	0.02
Duration of symptoms	0.27	0.07
FEV1, % predicted	-0.002	0.82
FEV1/FVC, %	-0.54	0.02
FEF25-75%, % predicted	0.03	0.08
PC20, log mg/mL	-0.35	0.10
Total IgE, log IU/ml	0.65	0.04
Eosinophil count, log μL-1	-0.45	0.09
Der p - specific IgE, kUA/L	0.04	0.04

Each parameter adjusted for the other clinical features.

4. Reticular basement membrane thickness in subjects with mild and moderate to severe asthma

There were no significant differences in reticular basement membrane thickness among the patients with mild and moderate to severe asthma: (mild asthmatics median 8.3 [range 7.1-11.0] versus moderate to severe asthmatics median 8.2 [range 7.2-11.0], p=0.26).

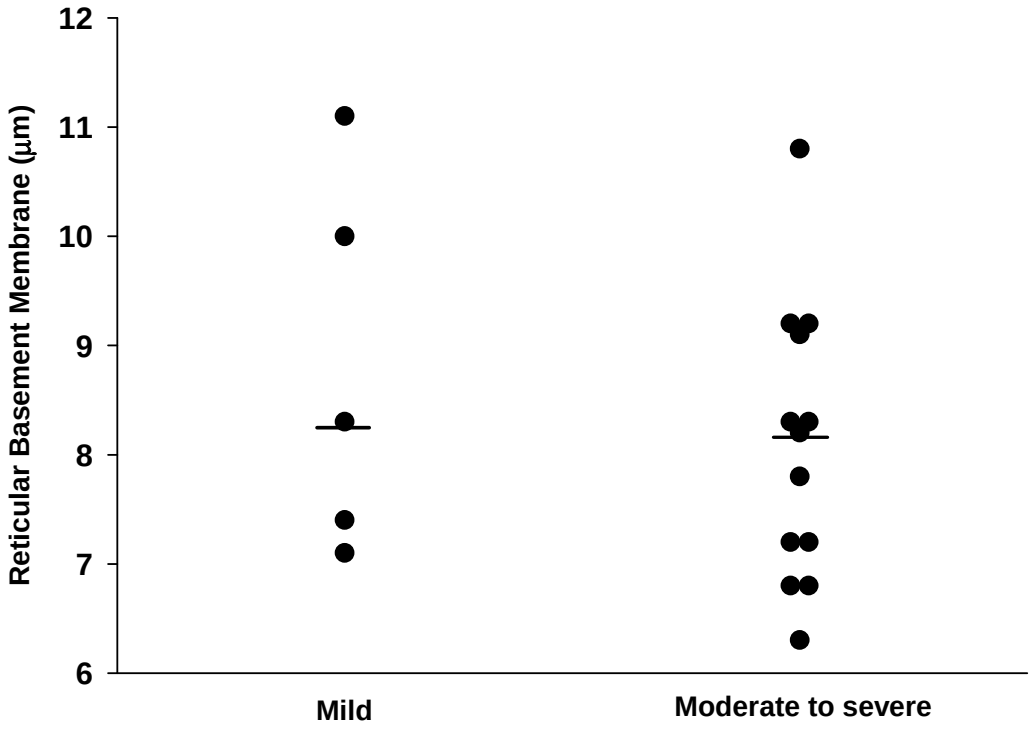

Fig. 3. Median and individual values of reticular basement membrane thickness in patients with mild and moderate to severe asthma. The median is shown as a single black line. Each circle represents one individual.

IV. DISCUSSION

The basement membrane of surface epithelium is composed of several layers: the basal lamina (referred to as the “true” basement membrane) and the lamina reticularis. The thickening of the lamina reticularis is a characteristic early typical feature of the asthmatic bronchus which is caused by deposition of reticulin. By light microscopy, this is homogeneous and hyaline appearance. Ultrastructurally, it appears to consist of a plexiform arrangement of the fibrils in an amorphous matrix. The basal lamina is of normal thickness in asthma, whereas the reticular layer is thickened associated with deposition of immunoglobulins and/or collagen I and III and fibronectin but not collagen types V and VII nor laminin. The additional reticulin is likely produced after activation of myofibroblasts leading to a so-called “fibrosis” of the airways.[19] The thickening has not been related to the severity, duration, or origins of asthma in some studies[5, 20] whereas a correlation with the severity of the disease has been observed in another one.[8] Chetta et al described that subepithelial layer thickness of those with severe asthma differed significantly from that of patients with moderate and mild asthma.[19] They also demonstrated that subepithelial layer thickness is related to the clinical and functional severity of asthma, such as FEV_1 and PC_{20}, but not to atopy or

length of asthmatic history. Payne et al described that reticular basement membrane thickening is already present in children with difficult asthma and to a similar extent to that seen in adults with asthma.[2] In addition, they found that no association with age, symptom duration, lung function, or concurrent airway inflammation.

We found that reticular basement thickening is already present in children with mild, moderate or severe asthma. Reticular basement membrane thickness in children with asthma was significantly greater than control subjects. Thus we confirmed that airway remodeling is a very distinctive and characteristic pathologic finding of bronchial asthma. And multiple regression analysis revealed that sex, FEV_1/FVC, total IgE, and specific IgE to *Dermatophagoides pteronyssinus* was important predicting factors for the reticular basement membrane thickness, while age, duration of asthma, FEV_1, $FEF_{25-75\%}$, methacholine PC_{20}, or total eosinophil count were not significant factors influencing this finding..

Our results are in agreement with previous data confirming that airway remodeling, due to reticular basement membrane thickness, clearly differentiates control from asthmatic subjects and should be considered as a peculiar characteristic of asthma.[8] But the control subjects without asthma was made up of children having a bronchoscopy for other clinical indications. So they cannot be regarded as healthy

control subjects. It is the limitation of our study, and it is also the limitation of study in children subjects. Because of ethical issues, and technical factors, information regarding airway in healthy children using invasive technique is restrictive. With appropriate ethical approval, future studies to obtain samples from children with healthy control subjects are likely to involve subjects who are intubated and undergoing a general anesthetic for another elective procedure.

In children with asthma, the lack of an association between reticular basement membrane thickness and symptom duration is in agreement with previous studies involving adults with asthma that were unable to demonstrate any such relationship.[2,21,22]

With regard to asthma severity, Chu et al. did not find any association between reticular basement membrane thickness and the clinical severity in adults.[23] Payne et al. did not find any association between reticular basement membrane thickness and the clinical severity in children.[2] But their study only included children with difficult asthma who were prescribed 1,600 μg/day. Severity of children with asthma in our study consist of mild, moderate, and severe. In agreement with previous studies, we did not find correlation between reticular basement membrane thickness and disease severity. The lack of an association between reticular basement membrane thickness

and symptom duration or severity and the similar degree of reticular basement membrane thickening raises the possibility that reticular basement membrane thickening, once established, varies very little within an individual. However, without follow-up biopsies, it cannot be determined whether reticular basement membrane thickness is maximal for any individuals.[2] The cross-sectional design of this study therefore does not allow accurate conclusions to be drawn about the precise relationship between reticular basement membrane thickness and symptom duration or disease severity. Further longitudinal studies involving infants and young children, with biopsies performed at a number of different time points, are needed.

Reticular basement membrane thickening and the eosinophilic inflammation are known as the characteristic of asthma in older children and adults.[24] But our study didn’t show any relationship between reticular basement membrane thickness and airway inflammatory markers such as total eosinophil count. This results was similar to those of previous study.[2] They measured exhaled nitric oxide, and there was no significant correlation between reticular basement membrane thickness and exhaled nitric oxide before or after prednisolone. Measurement of exhaled nitric oxide is an alternative approach to airway inflammation and structural changes. Airway inflammation is sustained by the relationships between eosinophilic infiltration and

exhaled nitric oxide.[25] Structural changes seem to be a consequence of the multiple intracellular and extracellular roles of nitric oxide.[26] Mahut et al demonstrated that nitric oxide output correlated with the reticular basement membrane thickness.[27] In future study, we will include the measurement of exhaled nitric oxide, and nitric oxide concentration in bronchial alveolar lavage fluid and induced sputum. We will describe the relationship between reticular basement membrane thickness and nitric oxide. And in future study, we will include the measurement of eosinophil count in bronchial alveolar lavage fluid and induced sputum.

We found relationship between reticular membrane thickness and the presence of atopy. Total IgE, and specific IgE to *Dermatophagoides pteronyssinus* were important predicting factors for the reticular basement membrane thickness. Allergens such as *Dermatophagoides pteronyssinus* impact atopic inflammation either by pomoting primary T helper cell type 2 (Th2) responses to allergens or by exacerbation of such inflammation in those already sensitized. So, presence of atopy can act as trigger of inflammation of asthmatic airway.

In regards to influence of sex, asthma is known more prevalent in males than in females at prepubertal period, but at postpubertal period, asthma is more prevalent in females than in males because obesity may increase prevalence overall and incidence

before menarche, and endocrine factors such as menstrual cycle are aggrevating causes of asthma.[28,29] In our study, age of children with asthma was in range of 11-15 years, so sex may contribute to reticular basement membrane thickness.

V. CONCLUSION

In conclusion, our results showed that reticular basement membrane thickness in children with asthma was significantly greater than control subjects (8.3±1.4 ㎛ vs 6.8±1.3 ㎛, p=0.0008). Moreover, analysis results indicated a significant contribution of sex, FEV_1/FVC, total IgE, and specific IgE to *Dermatophagoides pteronyssinus* to the reticular basement membrane thickness, but not age, duration of symptoms, FEV_1, $FEF_{25-75\%}$, methacholine PC_{20}, and serum eosinophil count. There was no significant difference between reticular basement membrane thickness and asthma severity.

It seems that reticular basement membrane thickness is a very early marker of airway remodeling that may precede the clinical manifestations of asthma. Following researches could be needed to better understand remodeling in asthma; finding the time that remodeling begins, finding progress of remodeling, whether remodeling is reversible or not, and finding useful and relevant markers of remodeling.

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ABSTRACT (in Korean)

천식 환아에서 기도 기저막 비후와 천식관련 인자간의 연관성

(지도교수 김규언)

연세대학교 대학원 의학과

김은수

목적: 천식은 기도 염증과 과민성, 기도 폐쇄를 특징으로 하는 만성 염증성 질환이다. 천식이 부분적으로는 가역적인 기도 폐쇄를 일으키지만, 궁극적으로 비가역적인 폐쇄를 일으키는 기도 개형을 발생 시키게 된다. 기도 개형이 일어난 기도는 여러 구조적 변화를 동반하게 되는데 상피세포층의 탈락, 기저막의 비후, 기도 평활근의 증식, 신생 혈관의 증가 등의 소견을 보인다. 본 연구에서는 소아 천식환자의 기저막의 두께를 측정하여 기도 기저막 비후가 소아 천식에 미치는 영향을 알아보고자 하였다.

방법: 기관지 내시경을 통해 조직검사를 시행한 18 명의 천식 환아와 24 명의 대조군을 대상으로 하였다. 기도 기저막의 두께를 측정하였고, 기저막의 두께와 연령, 성별, 천식 발병기간, 천식의 중등도, FEV_1, FEV_1/FVC, $FEF_{25-75\%}$, 메타콜린 PC_{20} 및 호산구 수, 혈청 총 IgE, 집먼지 진드기 (*Dermatophagoides pteronyssinus*) 에 대한 특이 IgE 와의 상관관계를 분석하였다.

결과: 천식 환아에서의 기저막의 두께는 8.3±1.4 ㎛로 6.8±1.3 ㎛인 대조군에 비해 기도 기저막이 의미있게 비후되어 있었다 (p=0.0008). 다중 회귀 분석을 시행해 보았을 때 성별, FEV_1/FVC, 혈청 총 IgE, 집먼지 진드기에 대한 특이 IgE 가 기도 기저막 비후를 예견할 수 있는 인자로 나타났다. 기도 기저막 비후와 연령, 천식 발병기간, FEV_1, $FEF_{25-75\%}$, 메타콜린 PC_{20} 및 호산구 수, 천식의 중등도 간에는 유의한 상관관계를 보이지 않았다.

결론: 소아 천식 환아들은 대조군에 비해 의의있게 기도 기저막의 비후가 관찰되었으며, 성별, FEV_1/FVC, 혈청 총 IgE, 집먼지 진드기에 대한 특이 IgE 와 관련을 보였다.

핵심되는 말: 기도 개형, 기저막 비후, 기관지 내시경, 소아