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Progressive Development of Bronchial Asthma From Allergic Rhinitis in a Patient Sensitized to Artemisia SPP. Pollen; A Case Report

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The association between allergic rhinitis and bronchial asthma, that is, whether it is a seqential process or independent diseases, has not been established. We confirmed that a 25 year-old woman with allergic rhinitis sensitized to Artemisia spp. pollens and house dust mites developed bronchial asthma during a 2 year follow-up period. Severe broncho-constriction was noted after inhalation of methacholine, and the bronchoprovocation test with extract of Korean Artemisia spp. pollen showed early bronchoconstriction. Total IgE and specific IgE antibodies to Artemisia absinthium increased, compared to the initial levels. It is suggested that some patients with allergic rhinitis progress to bronchial ashtma.

Key Words: Allergic rhinitis, bronchial asthma, Korean Artemisia spp. pollen

The occurence of bronchial asthma as a result of natural exposure to pollen was first recognized by Blackley (1873). More recently, most studies (Cockroft *et al.* 1977; Cartier *et al.* 1982; Boulet *et al.* 1980; Sotomayor *et al.* 1984) agree that allergen exposure significantly increases bronchial responsiveness to histamine or methacholine in sensitized subjects, but a few studies (Rosenthal *et al.* 1979; Bleecker *et al.* 1982) disagree.

Several investigators (Austen and Orange 1975; Cookson *et al.* 1985) suggested that appreciable numbers of subjects with allergic rhinitis demonstrated physiologic evidence of peripheral airway obstruction which occurs in response to a cholinergic agent. Some allergic rhinitis patients develop bronchial asthma after a lag period, but it is not known how many patients with allergic rhinitis who have had non-specific bronchial hyper-reactivity develop frank bronchial asthma (Townley *et al.* 1975).

This report confirmed the occurence of bronchial asthma in a patient with allergic rhinitis sensitized to Artemisia spp.pollen and noted the change in reponsiveness to methacholine and the level of total and specific IgE antibodies.

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MATERIALS AND METHOD

Korean Artemisia spp.pollen extracts

Artemisia spp. and ragweed (Ambrosia spp.) pollens were collected during their seasons. They were defatted with ethylether, dried and extracted with modified Coca's solution (NaCl 9gm, phenol crystal 4 gm, $NaHCO_3$ 2.5 gm in 1000 ml of distilled water, Phillips 1967) in 1;10 w/v at room temperature for 72 hours. The supernatant was dialysed against an adequate amount of 0.4% phenol-0.9% saline and mixed with an equal amount of sterile glycerine (Korean Artemisia spp.pollen extract for skin test, 1:20 w/v). This was mixed with an equal amount of 0.4% phenolized saline (1;20 w/v) and used for the bronchoprovocation test.

METHODS

Allergy skin test

Skin prick tests with Korean pollen extracts, Bencard and Torii's pollen extracts were performed simultaneously. The results were read 15 minutes after the prick and the wheal and erythema size were

presented as maximum diameter and vertical length at the mid-portion of maximum length.

Methacholine bronchial challenge test

Non-specific bronchial reactivity was determined by the previously described standard method (Chai et al. 1975). Aerosols of saline followed by doubled concentrations of methacholine (0.075 to 25.0 mg/ml) were inhaled. The FEV1 was measured 5 mins after each inhalation and continued until the forced expiratory volume (FEV1) had fallen by 20% (calculated from the post-saline value). The methacholine PC20 value was obtained from the dose response curve.

Bronchoprovocation tests with allergens

Bronchoprovocation test were performed, using aqueous extracts of Korean Artemisia spp.pollen and house dust (1;10 w/v, Torii company). The FEV1 and maximun mid-expiratory flow (MMEF) were measured with a spirometer before inhalation and 10 mins after inhalation. The test solutions were delivered by a Vapornefrine nebulizer aero- air source and the patients were asked to breath the nebulized aerosol 5 times until one's vital capacity was achieved. A 0.4% phenolized saline solution was inhaled for a baseline value and serial increments in antigen concentraion (1;500, 1;100, 1;50, 1:20) were given at 10 min interval until a 20% or greater decrease in FEV1 from the baseline value was recorded. The FEV1 was measured at hourly intervals for 7 hours after the challenge.

Case Summary

A 25 year-old female patient presented at Severance hospital in Oct., 1985 with a chief complaint of watery rhinorrhea and sneezing for 3 years. Her symptoms were aggravated from late summer through autumn (the end of August through October). Past history revealed that she had experienced severe urticaria after eating fish several years ago. On her first visit, the patient seemed to be in a healthy state. Breathing sounds were clear without wheezing and her heart beats were regular.

The total IgE level by PRIST was 769.42 IU/ml and total eosinophil count was 133/mm3. The sputum and nasal smears showed less than 1% of eosinophils. Skin prick tests to ragweed (9×28/52×71), wormwood (2.5×5/26×36), sagebrush (Torii company, 22.5×9/57×34), house dust (2×2.5/20×23), Dermatophagoides farinae (3×2/23×25), and Dermatophagoides pteronyssinus (2×2.5/28×28) were positive (Table 1). IgE-RAST showed all negative responses with the exception of RAST to Artemisia absinthium (W5-RAST class 2, 5.41%). There was no change in pulmonary function test after methacholine

Table 1. The results of skin prick test and RAST according to initil and follow-up tests

Allergens	Skin prick test (Wheal/erythema in mm)		RAST class (Scores)	
	Oct., '85	Aug., '87	Oct., '85	Aug., '87
Ragweed	9 ×28/52×71	2 ×2 /23×14	0	ND
Korean ragweed	ND[a]	–[b]	NA[c]	NA
Wormwood	2.5× 5/26×36	27 ×9.5/68×43	2 (5.41%)	2 (6.88%)
Sagebrush (Torri)	22.5× 9/57×34	17 ×7 /44×35	NA	NA
Korean Artemisia spp.	ND	10 ×8 /45×37	NA	NA
Marguerite	–	4 ×2.5/46×40	ND	ND
Dandelion	–	2 ×2.5/36×20	ND	ND
House dust	2 ×2.5/20×23	2 ×2.5/36×28	O	ND
D. pteronyssinus	2 ×2.5/28×28	2 ×3 /27×28	O	ND
D. farinae	3 ×2 /23×25	2 ×2 /22×22	O	ND
0.1% histamine[d]	2 ×2 /22×20	4 ×3 /36×31		

a) ND: Not done

b) – : Negative

c) NA: Not available, because the allergens used for skin test in this study were collected by authors from Korean plants, paper disc coated with same allergens were not available.

d) 0.1% histamine: Used for positive control (+++)

inhalation.

Two years later (the end of Aug., 1987), she returned to our hospital with complaints of dyspnea and coughing, especially at night. She had experienced intermittent shortness of breath for 1 year (since Sep., 1986) and these symptoms became aggravated 15 days prior to the second visit. On physical examination, coarse breathing sounds with expiratory wheezing were audible on the whole lung field.

Total IgE level by PRIST was 972.3 IU/ml and total eosinophil count was 830/mm3.Skin prick tests (Table 1) were positive to ragweed (2×2/23×14), wormwood (27×9.5/68×43), sagebrush (Torii company, 17×7/44×35), Korean Artemisia spp. extracts (10×8/45×37), marguerite (4×2.5/46×40), dandeolion (2.5×2/36×20), W5-RAST performed simultaneously with the initial serum showed a class 2 response (6.8%). The methacholine bronchial challenge test showed more than 20% decrease in FEV1 and FEF_{25-75} after inhalation of 2.5 mg/ml of methacholine (PC20; 1.75 mg/ml, Fig.1). The bronchoprovocation test with Korean Artemisia spp extracts showed severe bronchoconstriction after inhalation of 1;20 w/v solution (Fig. 2) and then, she also complained of dyspnea and coughing and expiratory wheezing sounds were audible in both lung fields. There was no change in the pulmonary function test in a bronchoprovocation test with house dust (Torii company, 1;10 w/v, used for immunotherapy).

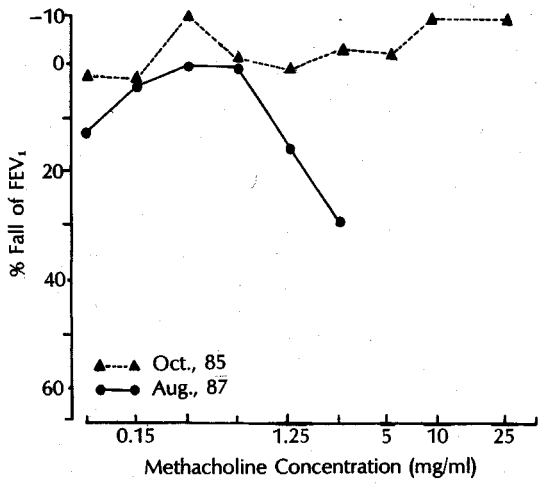

Fig. 1. The results of methacholine bronchial challenge test. The initial test (▲——▲) was performed in Oct., 1985 and follow-up test (●——●) was in Aug., 1987

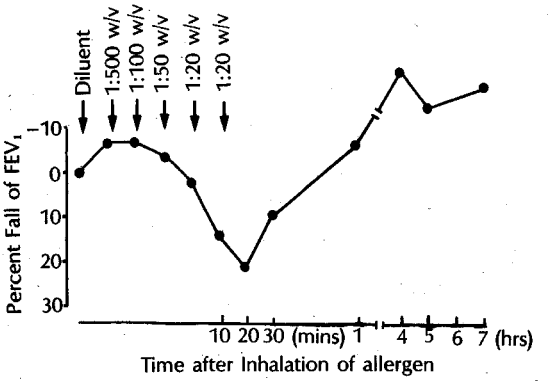

Fig. 2. The bronchoprovocation test with Korean Artemisia spp. pollen extracts showed early bronchoconstriction. Diluent: 0.4% Phenolized saline.

DISCUSSION

In Korea, there are two discrete pollen seasons, involving tree pollens (March through May) and weed pollens (the end of Aug. through Sep.) (Min *et al.* 1984; Hong *et al.* 1986). The results of skin prick tests with Korean pollen extracts (Kim *et al.* 1987) revealed that the incidence of sensitization to Artemisia spp. was the highest, 14.2% and to ragweed, the next, 10.4%. Ahn *et al.* (1987) presented six cases of atopic bronchial asthma induced by Korean Artemisia spp. extracts. Therefore, the weed pollens such as sagebrush and ragweed are considered to be as important respiratory allergens in Korea (Hong *et al.* 1981).

Allergic rhinitis and atopic bronchial asthma are major respiratory allergic diseases. Half of the bronchial asthma patients were also found to have allergic rhinitis and half of the patients with allegic rhinitis showed significant bronchoconstriction in the methcholine bronchial challerge test. Subjects with allergic rhinitis who have lower respiratory symptoms suggestive of asthma are more likely to have hyperreactive airways than are subjects with allergic rhinitis alone (Cockcroft *et al.* 1977). Townley *et al.* (1979) revealed that 50-60% of patients with allergic rhinitis exhibited a positive reponse in the methacholine challenge test and other investigators (Grossman and Putnam 1975; Doggett *et al.* 1976; Morgan and Hall 1976) also noted that appreciable numbers of them showed similar results. In Korea, 69% of them reponded to the methacholine challenge test (% decrease

of FEV1>15%, Park *et al.* 1981; Oh *et al.*1986).

The mechanism for the development of non-specific bronchial hyper-reactivity in sensitized patients is not clear. Cockroft *et al.* (1986) noted that exposure to allergens in sensitized and susceptible (atopic) persons altered bronchial responsiveness. There are several reports of progressive decline in bronchial hyper-reactivity or a reversal of bronchial hyper-reactivity with avoidance of allergens (Altounyan 1970; Plattes-Millis *et al.* 1982; Platts-Millis *et al.* 1985). It is possible that concentrated allergens cause a immediate local reaction, followed by a delayed reaction. Allergen induced late reactions can be associated with an increase in bronchial reponsiveness to histamine (Cockcroft *et al.* 1977; Cartier *et al.* 1982). Possible pathogenic mechanisms for the exaggerated smooth muscle constriction in bronchial reactivity include a decrease in baseline airway caliber, and increased responsiveness of the smooth muscle or an increase in the accessibility of the stimulus to the target cells (Boushey *et al.* 1980). Also damage to the airway epithelium might play the most important role in causing airway hyper-reactivity (Nadel 1973). However, which atopic patients will eventually develop atopic asthma is not known. The risk of developing asthma was found to be significantly increased in those individuals with previous allergic rhinitis (seasonal or non-seasonal) without regard to skin test results (Smith 1971; Broder *et al.* 1974) and was also increased in positive skin test individuals (Hogy and Settipane 1976).The risk frequency in developing a new asthma in allergic rhinitis subjects was reported as 6.0% by Hagy and Settipane (1976), 2.9% by Smith (1971) and 1.5% by Broder *et al.* (1974), compared to 0.2% in non-allergic subjects by Broder *et al.* (1974) and 1.3% by Hagy *et al.* (1976). Townly *et al.* (1975) noted that patients with allergic rhinitis and atopic eczema, as well as other members of asthmatic families are more likely to develop asthma. Two cases of allergic rhinitis with non-specific bronchial hyper-reactivity which subseqently developed into frank bronchial asthma were reported by Townley *et al.* (1975), and there was a report of subjects whose bronchial reactivity increased when they developed their first attack of wheezing, chest tightness and dyspnea (Townley *et al.* 1965).

As expected, once the airway tract becomes hyper-reactive, airway obstruction is easily provoked by allergic challerge or various stimuli. Bronchial reactivity is known to be enhanced by respiratory viral infections, cigarette smoke, ozone, nitrogen dioxide and specific antigens in normal and asthmatic subjects (Cockroft *et al.* 1977; Holtzman *et al.* 1979: Hargreave *et al.* 1981; Sotomayor *et al.* 1984; Barbato *et al.* 1987; Madonini *et al.*1987). Bronchial hyper-reactivity increases together with IgE titer during pollen exposure and decrease with avoidance. Positive bronchial challenge can be found in patients if they possess sufficient allergen-specific IgE antibodies (Boulet *et al.* 1982; Platts-Millis *et al.* 1982).

In this case, during her first visit, the patient complained of nasal symptoms only and did not show non-specific bronchial hyper-reactivity. Positive skin prick tests to wormwood and ragweed were noted but the skin reactivity to wormwood was weaker than that of ragweed. The bound radioactivity on W5-RAST was 5.41%. Asthmatic symptoms developed one year later, and two years later, at her second visit, increased bronchial responsiveness to a cholinergic agent (methacholine) was noted and severe bronchoconstriction was induced after inhalation of the extracts of Korean Artemisia spp pollens. Skin reactivity to wormwood increased markedly, to ragweed decreased and to Korean Artemisia spp. extracts, a strong response was also evident. The total IgE level and bound radioactivity on W5-RAST (6.88%) increased, compared to the initial levels.

In conclusion, increase bronchial responsiveness is an important feature of bronchial asthma patients and could be used in diagnosing the presense of asthma and may help in assessing its prediction in patients with allergic rhinitis. It is suggested that regular evaulation of the presense of bronchial hyper-reactivity in patients with allergic rhinitis could assist in the decision of whether or not more aggressive treatment is required.

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