

Allergen-specific IgE Antibody Serologic Assays in Patients with Autoimmune Pancreatitis

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Abstract

Objective To clarify the allergic manifestations in patients with autoimmune pancreatitis (AIP).

Methods We assessed 67 AIP patients, before they received steroid therapy, for a past history of allergic disease, the peripheral eosinophil count (n=62) and the serum IgE level (n=53). Allergen-specific IgE antibody serologic assays were performed in 15 patients.

Results A positive past history and/or the presence of active allergic disease were found in 24 AIP patients (36%), including 15 patients with acute allergic rhinitis and eight patients with bronchial asthma. Peripheral eosinophilia and elevation of the serum IgE level were detected in 16% (10/62) and 60% (32/53) of the patients, respectively. Allergen-specific IgE antibody serologic assays were positive in 13 patients (87%). There were no differences between the assay-positive and -negative patients regarding the clinical profiles.

Conclusion In conclusion, 87% of the 15 AIP patients tested had positive allergen-specific IgE antibody serologic assays. Allergic mechanisms may be related to the occurrence of AIP.

Key words: autoimmune pancreatitis, IgE

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Introduction

Autoimmune pancreatitis (AIP) is characterized radiologically by enlargement of the pancreas and narrowing of the main pancreatic duct, serologically by elevation of the serum gammaglobulin, IgG or IgG4 levels and the presence of autoantibodies and histologically by abundant infiltration of IgG4-positive plasma cells and lymphocytes with dense fibrosis of the pancreas and is frequently associated with sclerosis of other organs and steroid responsiveness (1, 2). Based on its systemic manifestations, AIP is currently recognized to be a pancreatic lesion of an IgG4-related disease (3, 4). Based on its serological findings and steroid responsiveness, an autoimmune etiology is presumed to be the pathogenic mechanism of AIP; however, the target antigens for AIP have not yet been identified.

Recently, evidence of allergic manifestations in AIP pa-

tients has been accumulating. In our previous study, 20 of 45 (44%) AIP patients had a history of allergic disease (5). Sah et al. also reported that allergic disorders were detected in 12 of 78 (15%) AIP patients (6). Most allergic manifestations, including bronchial asthma, acute allergic rhinitis, hay fever and atopic dermatitis, are caused by type 1 hypersensitivity reactions. Detecting the presence of an allergen-specific IgE antibody is most important for diagnosing type 1 hypersensitivity reactions. In our previous study, elevated serum IgE levels were detected in 12 of 45 (34%) AIP patients (5), and Hirano et al. reported that the serum IgE levels were elevated in 36 of 42 (86%) AIP patients (7). However, the significance of these findings is unclear. To clarify the associated allergic manifestations, we performed allergen-specific IgE antibody serologic assays in AIP patients.

Materials and Methods

The subjects of this study included 67 type 1 AIP patients (54 men and 13 women, median age: 64 years) who were diagnosed according to the international consensus diagnostic criteria for AIP (2), enlargement of the pancreas and narrowing of the main pancreatic duct (n=67), elevation of the serum IgG4 level (n=52), the presence of histologically proven lymphoplasmacytic sclerosing pancreatitis (n=13) and responsiveness to steroid therapy (n=50). A positive past history and the extent of morbidity from allergic diseases, including bronchial asthma, acute allergic rhinitis, hay fever and atopic dermatitis, were ascertained using a review of the patients' clinical records and definitive clinician diagnoses. The serum IgG4 (<135 mg/dL) and IgE (<250 IU/mL) levels and peripheral eosinophil count (<600 cells/mm³) (8) were determined in 67, 53 and 62 patients, respectively. Allergen-specific IgE antibody serologic assays were performed in 15 patients [radioallergosorbent test (RAST), n=7 and multiple antigen simultaneous test (MAST), n=8] before administering steroid therapy in a prospective manner beginning in 2008. Levels of IgE greater than 0.34 UA/mL according to RAST and a result of more than class 1 according to MAST were considered positive findings. The assay-positive and -negative AIP patients were compared with regard to various clinical features, such as allergic disease, symptoms, other organ involvement and serological findings. The two groups were compared using the chi-square and Fisher's exact tests.

Results

Active allergic disease and/or a past history of allergic disease were found in 24 (36%) AIP patients, as follows: hay fever with acute allergic rhinitis, 15 patients (22%); bronchial asthma, 8 patients (12%); drug allergy, 4 patients (6%); atopic dermatitis, 2 patients (3%); and mackerel allergy, house dust allergy and hamster allergy, 1 patient each (1.5%). Peripheral eosinophilia and elevation of the serum IgE level were detected in 16% (10/62) and 60% (32/53) of the patients, respectively. Six (19%) of 31 patients with elevation of the serum IgE level had eosinophilia, while three (14%) of 21 patients without an elevated IgE level had eosinophilia (p=0.92).

Allergen-specific IgE antibody serologic assays were positive in 13 of the 15 (87%) patients tested (RAST, 6 of 7 and MAST, 7 of 8). The causative agents were cedar (n=8), Japanese cypress (n=4), ticks (n=3), shrimp (n=3), crab (n=3), orchard grass (n=3), house dust (n=2), moths (n=2), *Ambrosia artemisiifolia* (n=2), *Candida* (n=2), wheat (n=2), *Aspergillus* (n=2), guinea pig (n=1), mugwort (n=1), peanut (n=1), buckwheat (n=1), sweet vernal grass (n=1), timothy (n=1), *Betula platyphylla* (n=1) and *Penicillium* (n=1). Among 15 patients tested with allergen-specific IgE antibody serologic assays, seven had allergic diseases [hay fever

Table. Differences in Clinical and Serological Features between Allergen-specific IgE Antibody Serologic Assay-positive and -negative AIP Patients

	Assay-positive (n=13)	Assay-negative (n=2)	p values
Age (average, years)	62.5	74.5	0.67
Male/female	7/6	1/1	
Steroid responsiveness	13/13	2/2	
Recurrence of AIP	0	0	
Allergic disease	6	1	0.50
Obstructive jaundice	3	0	0.44
Acute pancreatitis	1	0	0.68
Other organ involvement	9	2	0.95
Elevation of serum IgG	7	0	0.50
Elevation of serum IgG4	9	1	0.78
Elevation of serum IgE	8	1	0.64
Eosinophilia	5	0	0.78

(n=4), bronchial asthma (3), drug allergy (1) and mackerel allergy (1)]. All seven patients were positive for allergen-specific IgE antibody assays.

There were no significant differences between the assay-positive and -negative patient groups in age, gender, steroid responsiveness, recurrence of AIP, allergic disease, obstructive jaundice, acute pancreatitis, other organ involvement, elevation of the serum IgG, IgG4 or IgE levels or eosinophilia (Table).

Discussion

Recently, evidence of allergic manifestations in AIP patients has been accumulating. It has been reported that, in the setting of AIP, allergic diseases are observed in 15% (12/78) (6), 17% (7/42) (7), 41% (10/24) (9) and 44% (20/45) (5) of patients, peripheral blood eosinophilia is observed in 8% (1/13) (9), 11% (5/45) (5) and 28% (22/78) (6) of patients, elevation of the serum IgE levels is observed in 34% (12/35) (5) and 86% (36/42) (7) of patients and marked eosinophil infiltration in the pancreas is detected in 67% (12/18) (6) and 88% (21/24) of patients (9). It has been demonstrated that the Th2 and regulatory cytokine expressions are upregulated in the affected tissues of AIP patients and that regulatory T-cells are involved in the in-situ production of IL-10 and TGF- β , which is followed by an IgG4 class switch and fibroplasia (10). The immune reactions that are predominantly mediated by Th2 and regulatory T-cells are closely involved in the pathogenesis of allergic disorders, such as bronchial asthma and atopic dermatitis (11).

In this study, allergic disease, peripheral eosinophilia and elevation of the serum IgE level were detected in 36%, 16% and 60% of AIP patients, respectively. The major allergic manifestation was allergic rhinitis (63%) followed by bronchial asthma (33%) in our series, while allergic rhinitis (43%) and bronchial asthma (43%) were observed in another Japanese series (7). However, bronchial asthma is predominant in the USA, with reported rates ranging from 75% (9/12) (6) to 80% (8/10) (9). Such differences may be attrib-

utable to racial or geographic factors.

Allergen-specific IgE antibody serologic assays are one of the tools used for precise allergy testing (12-14). In this study, 87% of 15 AIP patients were positive for an allergen-specific IgE antibody, and the causative antigens were various. We were unable to find any data pertaining to positive rates of allergen-specific IgE antibody serologic assays in the Japanese general population; however, we speculate that the positive rate observed in this study is higher than that seen in the general population. Ito et al. reported three AIP patients in whom bronchial asthma preceded AIP; the asthma symptoms worsened at the onset of AIP and were accompanied by high serum IgE levels and positivity on allergen-specific IgE antibody serologic assays (15).

There were no significant differences between the assay-positive and -negative patients regarding clinical characteristics, possibly because the number of assay-negative patients was too small (n=2). However, Sah et al. reported that, in their study, there were no differences in the clinical profiles of AIP patients with and without peripheral eosinophilia (6), and Hirano et al. reported that there were no differences in the clinical profiles of AIP patients with and without elevation of the serum IgE levels (7). Peripheral eosinophilia and the serum IgE levels do not seem to reflect the disease activity.

This study revealed a higher level of allergen-specific IgE antibody serologic assay positivity than the incidence (36%) of clinical allergic disease found among the AIP patients enrolled. The reasons for this discrepancy are unknown; however, it has been reported that, in symptomatic self-selected populations, a positive test result significantly increases the probability that the patient is allergic, while the use of multiple allergen tests to screen unselected populations results in an unacceptable number of false-positive and false-negative results (12).

The small sample size of patients in whom assays were performed is the greatest limitation of this study. A second limitation is that other allergy tests, such as skin tests, were not performed. However, to our knowledge, this is the first report of the use of allergen-specific IgE antibody serologic assays in AIP patients. Further studies are therefore warranted to clarify the relationship between allergic phenomena and AIP.

In conclusion, the results of allergen-specific IgE antibody serologic assays were positive in 87% of the 15 AIP patients assayed in this study. Allergic mechanisms may be related to the occurrence of AIP.

The authors state that they have no Conflict of Interest (COI).

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