
◎原 著

Difference in specific IgG and IgG₄ antibodies against *Candida albicans* between healthy and asthmatic subjects in the elderly

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Abstract : Specific IgG and IgG₄ antibodies against *Candida albicans* were examined in 48 healthy and 69 asthmatic subjects to analyze the mechanism causing an increased production of these immunoglobulins.

1. The level of *C.albicans*-specific IgG and IgG₄ antibodies was higher, not significantly in IgG₄, in asthmatics under 30 years of age, compared with healthy subjects of the same age group.
2. Specific IgG and IgG₄ antibody levels in both healthy and asthmatic subjects showed a tendency to increase with aging, and significant difference was present between cases under 30 years and cases over 70 years of age.
3. Any difference in the production of specific IgG and IgG₄ was not observed in elderly cases older than 60 years between healthy and asthmatic subjects.

Key words : *Candida albicans*, Specific IgG, IgG₄, Bronchial asthma, Aging

Introduction

Candida albicans plays a role in the pathogenesis of bronchial asthma as an antigen¹⁻⁵⁾. IgE, IgA and IgG antibodies are produced in *C.albicans*-specific immune response, and the production of IgG antibodies is more predominant than that of the other immunoglobulins in some of atopic subjects^{1, 6)}.

It is well known that IgE antibodies participate in the onset mechanism of bronchial

asthma. It is, however, still difficult to assess a role of specific IgG antibodies in *C.albicans*-induced immune response, because the production of IgG antibodies and positive delayed cutaneous hypersensitivity to *C.albicans* are common in healthy population⁷⁾.

In the present study, serum levels of specific IgG and IgG₄ antibodies against *C.albicans* were examined to estimate a clinical significance of these immunoglobulins in asthmatics, and the results were compared

with healthy subjects.

Subjects and Methods

The Subjects were 28 healthy and 44 asthmatic subjects whose age was over 60 years. Twenty healthy and 25 asthmatic subjects whose age was under 30 years were selected as control subjects.

Candida albicans-specific IgG antibodies were measured by the method modified from that described by Engvall et al.⁸⁾ ELISA plates were coated with 100 μ l of *C.albicans* extract at a 1 : 20000 dilution in phosphate buffered saline (0.1M sodium phosphate, 0.15M sodium chloride, pH 7.2) (PBS) at 4 °C overnight and then washed three times with PBS-Tween 20. After washing, 200 μ l of 1% BSA-PBS-T-20 were added to the wells with incubation for 1 hr at 37°C and then discarded. Reference serum or serum sample at a 1 : 4000 dilution in PBS-T20 was added and incubated at 37°C for 2 hr. After washing, 100 μ l of alkaline phosphatase conjugated anti-human IgG (Miles Co. U.S.A.) was added to the wells at a 1 : 2000 dilution in PBS-T20 and then incubated at 4°C overnight. After another washing, conventional substrate, p-nitrophenyl phosphate (NPP) was added to the wells with incubation for 1 hr at 37°C. The reaction was stopped by addition of 0.1ml 1N NaOH. Absorbance was measured in a spectrophotometer at 405 nm.

Candida albicans-specific IgG_a antibodies were measured by an indirect enzyme-linked immunosorbent assay⁹⁾. The procedure in this assay was the same as in the measurement of specific IgG antibodies except for the followings : (1) murine monoclonal anti-human IgG_a (Yamasa Shoyu Co.Japan) was used instead of anti-human IgG ; (2) The wells were further incubated with peroxidase-conjugated anti-

mouse IgG ; (3) the wells were developed with o-phenylenediamine ; (4) Optimal density of the wells were determined at 500 nm. These assays were carried out in duplicate. The results of specific IgG_a were expressed as arbitrary units per milliliter against an positive serum pool.

Results

The level of specific IgG antibodies against *Candida albicans* in asthmatics aged between 61 and 70 was similar to the level in healthy subjects of same age group. The IgG antibody level in cases over age 71 was more increased compared to healthy subjects of same age group. The difference between healthy and asthmatic subjects was, however, not significant. The specific IgG antibody level in cases between 0 and 30 was not significantly different between healthy and asthmatic subjects, although the mean level in asthmatics was higher than the level in healthy subjects (Fig.1).

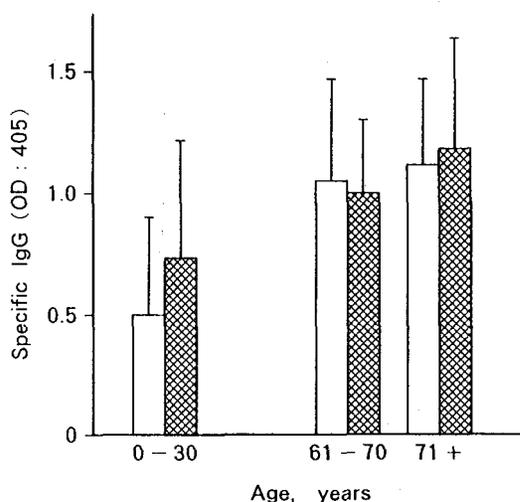


Fig. 1. *Candida albicans*-specific IgG antibodies in healthy (□) and asthmatic subjects (▨).

The difference in the level of *C. albicans*-specific IgG₄ antibodies was significant between healthy and asthmatic subjects whose age was under 30 years ($p < 0.05$). In cases between 61 and 70 and cases over 71, any significant difference was not present in specific IgG₄ antibody level between healthy and asthmatic subjects. The specific IgG₄ level showed a tendency to increase with aging in both healthy and asthmatic subjects. In healthy subjects, the IgG₄ antibody level was significantly higher in cases between 61 and 70 ($p < 0.05$) and in cases over 71 ($p < 0.01$) compared with cases between 0 and 30. While in asthmatics, the level of specific IgG₄ antibody was significantly more increased only in cases over 71 than in cases between 0 and 30 ($p < 0.05$) (Fig.2).

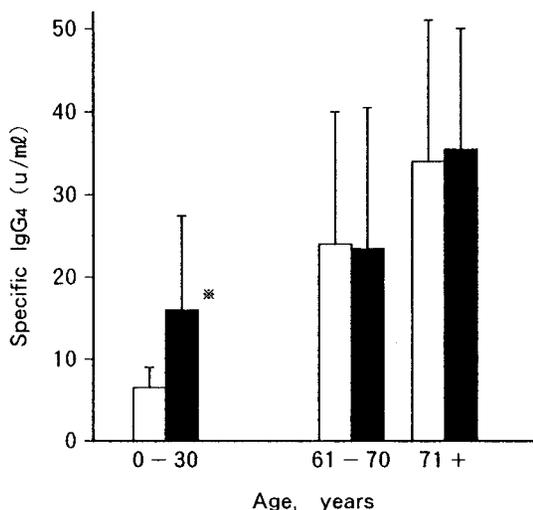


Fig 2. *Candida albicans*-specific IgG₄ antibodies in healthy (□) and asthmatic subjects (■). *significant difference from healthy subjects at $p < 0.05$

Discussion

It has been speculated that specific IgG and IgG₄ antibodies against *C. albicans* play a role in the pathogenesis of bronchial asthma related to IgE-mediated allergic reaction. Analysis for the mechanism causing an increased production of IgG and IgG₄ is necessary to assess clinical significance of the rise in these immunoglobulins. The increase of *C. albicans*-specific IgG antibodies has been shown in atopic subjects^{4, 6}. The level of *C. albicans*-specific IgG₄ antibodies has been also reported to increase in atopics and during immunotherapy¹⁰⁻¹², although the function of IgG₄ antibodies, anaphylactic or protective, is still controversial¹⁰⁻¹⁵.

Several mechanisms causing an increased production of *C. albicans*-specific IgG and IgG₄ have been proposed. Firstly, the increase of IgG and IgG₄ production in atopic subjects has been speculated to be due to suppressed cell-mediated immune response. The cell-mediated immune response plays the major role in defence against *C. albicans*¹⁶. The suppression of the response in atopics causes the saprophytic *C. albicans* growth and induces an increased production of IgG and IgG₄ antibodies⁶. The results of this study showed the increased production of IgG and IgG₄ antibodies in asthmatics between 0 and 30, the majority of whom was atopic. The results are in agreement with those reported in the literatures^{10, 11, 15}.

Secondly, it has been reported IgE is predominantly produced in the lymphoid tissue of the respiratory tract¹⁷, and IgG₄ mainly in the intestinal lymphoid tissue¹⁸. The production of IgG₄ antibodies is therefore induced predominantly when subjects are sensitized through the intestinal tract.

Thirdly, the rise of C.albicanns-specific IgG and IgG₄ can be found in gerontic subjects. In this study, the level of specific IgG and IgG₄ antibodies was significantly higher in cases over age 71 compared with the level in cases between 0 and 30. The reason why the increase of IgG and IgG₄ antibodies can be often observed in elderly subjects is not known. The reason may be due to suppressed cell-mediated immunity or due to an increase in sensitization through the intestinal tract. Extensive and long-term sensitization with C.aibicans may lead to an increased production of specific IgG and IgG₄ antibodies. Further studies are necessary to analyze these phenomena.

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高齢者健常人および気管支喘息患者におけるカンジダ特異的 IgG および IgG₄ 抗体について

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高齢者(61才以上)の健常人48名および気管支喘息患者69例を対象に, カンジダ特異的IgGおよびIgG₄抗体を測定し, その増加の機序について若干の検討を加えた。なお, 対照としては, 30才以下の健常人および気管支喘息患者を選んだ。

1. カンジダ特異的IgGおよびIgG₄抗体価は, 30才以下では, 健常人に比べ気管支喘息症例で高い傾向が見られ, 特異的IgG抗体では両者間に有意の差が見られた($P < 0.05$)。
2. カンジダ特異的IgGおよびIgG₄抗体は, 健常人および気管支喘息症例いずれも加齢とともに増加する傾向が見られ, 71才では, 30才以下の症例に比べ有意に高い抗体価を示した。
3. 61才以上の高齢者では, 特異的IgG, IgG₄抗体いずれにおいても, 健常人と気管支喘息患者との間に有意の差は見られなかった。

キーワード: カンジダ特異的IgG, IgG₄, 気管支喘息, 加齢