Original Article

Clinical features of patients showing Candida hypersensitivity: an observational study

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Abstract. *Background:* The significance of Candida albicans as an allergen is still unclear. This study aimed at investigating the clinical features of patients monosensitized to Candida.
Methods: Thirty-four adult patients monosensitized to the yeast Candida albicans selected from a population of >7000 subjects and referred for suspect respiratory allergy were studied. Ninety subjects monosensitized to different airborne allergens served as controls. Both patients and controls underwent a clinical examination at the ENT department to detect possible nasal polyps.
Results: Male and female patients were equally distributed (17/17). The mean age of the patients was 58.4 years (range 23-75 years; median 59 years) vs 29.9 years (range 9-62 years) in controls ($p < 0.001$). At baseline examination, 15 (44%) patients vs 5/90 (6%) controls were diagnosed as having nasal polyposis ($p < 0.001$). Polyposis was bilateral in 13/15 (87%) patients; 3 had "massive" polyps, and 4 had a clinical history of prior surgical intervention to remove nasal polyps. Eight patients (24%) had asthma, previously diagnosed as intrinsic in six cases. No patient had a history of aspirin-induced asthma (i.e. ASA triad). After one year 1/11 (9%) patients without polyps at the baseline examination had developed bilateral nasal polyposis.
Conclusion: Candida-hypersensitivity is uncommon, occurs in older ages, and is strongly associated with nasal polyposis.

Key words: Candida, Allergy, Chronic rhinitis, Nasal polyposis, Asthma.

Introduction

While the role of several molds (e.g. Alternaria, Aspergillus, and Cladosporium) as aeroallergens has long been established, the significance of the yeast Candida albicans in allergic diseases is still unclear [1]. Studies of Candida as a potential allergen are rather few. Candida albicans hypersensitivity has been observed in patients with allergic bronchopulmonary aspergillosis [2], and earlier studies found that sensitization to this yeast is associated with chronic asthma and rhinitis both in children [3,4] and adults [5,6]. Moreover, we recently observed that skin reactivity to Candida is frequently associated with nasal polyposis [7,8]. However, in the clinical practice most patients sensitized to Candida albicans are sensitized to other seasonal and/or perennial airborne allergens as well, a fact that certainly hampers a clear definition of the allergological significance of this yeast. Studies of monosensitized patients would be helpful to better define the clinical relevance of Candida in allergic disorders. This study aimed at investigating the clinical expression of Candida sensitization in a cohort of patients monosensitized to this yeast.

Patients and methods

Patients

All 34 adult patients (M/F 17/17) monosensitized to the yeast Candida albicans out of >7000 subjects referred to the allergy centers of Bollate hospital and Paderno Dugnano by their general practitioners during the last 8 years for a possible respiratory allergy were studied.

Monosensitization was defined as a positive skin test to Candida in the absence of any reactivity to all other airborne allergens (see below). Ninety patients monosensitized to one of several airborne allergens (28 grass, 11 ragweed, 5 mugwort, 7 pellitory, 13 birch, 21 house dust mite, 3 cypress, 1 Alternaria, and 1 cat dander) served as controls. Both patients and controls underwent a thorough interview with the purpose to ascertain the clinical features of their respiratory symptoms (including duration, seasonal changes, presence of cough or dyspnea, aspirin intolerance), and a clinical examination at the ENT department in order to detect possible nasal polyps. In doubtful cases diagnosis of polyposis was confirmed both by plain radiographic means and coronal CT scans. In suspect cases, diagnosis of asthma was confirmed by spirometric means. Local (nasal, bronchial) corticosteroid therapy was given where needed. Both patients and controls without nasal polyps on the baseline ENT evaluation were offered a free follow-up control visit after one year.

Skin tests

All subjects underwent skin prick tests (SPT) with a standard panel of commercial extracts (Allergopharma, Reinbeck, Germany) of the main seasonal and perennial allergens present in this geographical area, including pollen (grass, pellitory, ragweed, birch, cypress, olive, mugwort, and plantain), molds (Alternaria tenuis, Aspergillus fumigatus, Hormodendrum cladosporides, Candida albicans, and Tricophyton mentagrophytes), house dust mites, and cat and dog dander. All skin tests were carried out on the volar side of the forearm using sterile 1mm-tip lancets (Dome-Hollister/Stier, Spokane, WA, USA) and were performed in duplicate. Readings were taken after 15 min. Reactions were expressed as mean wheal diameter (adding the longest diameter to the orthogonal diameter and dividing it by 2). A diameter of 3 mm or more was considered positive [9]. Histamine 10 mg/ml and saline were used as positive and negative control, respectively.

Statistical methods

Means were compared by Student's t test. Proportions were compared by chi-square test with Yates' correction. Probability (p) values less than 5% were considered statistically significant.

Results

Patients were significantly older (mean 58.4 years, range 23-75 years; median 59 years) than controls (mean 29.9 years, range 9-62 years)($p< 0.001$). All 34 (100%) patients reported long-lasting perennial rhinitis, which was mainly characterized by airflow obstruction; none of these subjects gave a history of acute symptoms such as sneezing, itching and watery rhinorrea. In all patients physical examination revealed the classical pale blue tone of allergic nasal mucosa [10]. At baseline examination, 15 (44%) patients vs 5/90 (6%) controls were diagnosed as having nasal polyposis ($p< 0.001$). In 13/15 (87%) patients polyposis was bilateral, and 3 patients had "massive" polyps (grade IV after Rasp & Bujia [11]). Four of these patients had a clinical history of prior surgical intervention to remove nasal polyps. Eight patients (24%) had asthma, previously diagnosed as intrinsic in six cases. No patient had a history of aspirin-induced asthma (i.e. ASA triad).

One out of 11 (9%) patients without nasal polyposis at the baseline examination who accepted to undergo the ENT follow-up visit one year later had developed bilateral polyposis (0/21 in controls). Notably, in this patient polyps appeared despite long-term nasal corticosteroids given to control her perennial rhinitis. In the remaining 10 patients the nasal mucosa still showed the typical aspect of allergic rhinitis.

Discussion

Our Candida-allergic patients showed several interesting features. First, their mean age (58 years) was fairly greater than that of atopic controls. Sensitization to airborne allergens generally occurs in children and young adults [12]; this might suggest that long-term exposure to the yeast present in the upper airways is needed for sensitization to occur. The second striking feature was the high prevalence of nasal polyposis. Including the follow-up visits, 48% of patients were finally diagnosed as having nasal polyps, which were bilateral in most cases. Such prevalence largely exceeds the one observed both in our atopic controls and in unselected subjects with respiratory allergies [13], but it keeps with our previous observations in unselected patients showing skin reactivity to Candida [7,8]. This finding further confirms the association between Candida sensitization and nasal polyposis. Finally, 24% of patients had asthma that had been diagnosed as "intrinsic" in 6/8 cases, which suggests that, in subjects whose upper airways are colonized by Candida (both sensitive or not sensitive to the yeast), Candida-derived allergenic proteins may reach the lower airways. The relatively small number of patients included in the present study reflects the low prevalence of "pure" Candida sensitivity, but the association between Candida hypersensitivity and nasal polyposis also applies to the much larger number of patients who are co-sensitized to other airborne allergens. This study suggests that Candida should be included in the standard series of allergenic extracts used to carry out skin tests, particularly in patients with a clinical history of perennial rhinitis and/or asthma, in order to detect subjects prone to developing nasal polyps. Candida is a common human

saprophyte and is normally found in the microbial flora of the nasopharynx [14]. Most probably, neither excessive growth of this yeast in sinuses and nose, nor candidal infection (as a result of either local or systemic immunocompromise) is needed for subjects genetically predisposed to develop Candida sensitivity to become sensitized. As a consequence, no preventive effect from local anti-fungal treatment should be expected in Candida-hypersensitive patients. Long-term follow-up studies will be needed to assess whether specific immunotherapy with Candida extracts is able to prevent the onset of nasal polyposis in patients sensitized to this yeast.

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