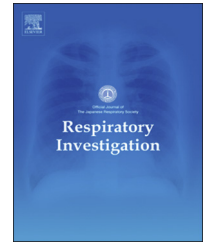


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## Original article

# Clinical characteristics of patients with *Aspergillus* species isolation from respiratory samples: Comparison of chronic pulmonary aspergillosis and colonization



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## ABSTRACT

**Background:** With advancements in anti-fungal drugs, it has become more important to correctly diagnose chronic pulmonary aspergillosis (CPA); however, it is not easy to distinguish CPA from colonization when *Aspergillus* species are isolated from respiratory samples. The aim of the study was to clarify the particular clinical characteristics of patients with CPA vs. those with colonization. **Methods:** We retrospectively reviewed the medical records of 110 patients with *Aspergillus* species isolation from respiratory samples, to analyze and compare the differences between CPA and colonization of the *Aspergillus* species.

**Results:** The median age of all analyzed was 71 years (range: 31–92 years); 64 were female (58%). The most frequently cultured *Aspergillus* species was *Aspergillus fumigatus* (48.3%), followed by *A. niger* (29.2%). Thirty patients (27.4%) were diagnosed with CPA, vs. 75 (68.2%) with colonization and 5 (4.5%) with allergic bronchopulmonary aspergillosis. Compared with the colonization group, the CPA group included more males (CPA vs. colonization: 49.3% vs. 13.3%) and subjects with a low body mass index (18.45 kg/m<sup>2</sup> vs. 21.09 kg/m<sup>2</sup>). As for the underlying pulmonary diseases, the patients with CPA showed a significantly higher prevalence of sequelae of pulmonary tuberculosis (40% vs. 8%) and a history of thoracic surgery (43% vs. 13%) than those with colonization. Asthma was less frequent in the CPA group than in the colonization group (0% vs. 20%). We found no significantly important underlying extrapulmonary diseases.

**Conclusions:** Patients with CPA display clinical characteristics distinct from those seen in subjects with colonization.

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Abbreviations: CPA, chronic pulmonary aspergillosis; ABPA, allergic bronchopulmonary aspergillosis; IPA, invasive pulmonary aspergillosis; SD, standard deviation; Asp, *Aspergillus*; COPD, chronic obstructive pulmonary disease; BMI, body mass index.

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## 1. Introduction

*Aspergillus* species, which are commonly found in humid solid, water, and other materials, can cause a variety of illnesses in humans. We inhale several hundred spores per day and, although these spores are generally cleared from the body without resulting in disease in most people, some are affected by several *Aspergillus* species that can cause pulmonary diseases, such as allergic bronchopulmonary aspergillosis (ABPA), chronic pulmonary aspergillosis (CPA) and simple aspergilloma [1], even if they are not immunocompromised.

When isolating *Aspergillus* species from respiratory samples, it is important to confirm whether the isolates simply indicate colonization, meaning that the species are a component of the normal flora and are not pathogenic. In this study, we reviewed the characteristics of patients seen in our hospital, in whom *Aspergillus* species were isolated from respiratory samples, to clarify the differences in clinical characteristics between CPA and colonization.

## 2. Patients and methods

### 2.1. Study design

We retrospectively reviewed the laboratory data of a series of consecutive samples from which *Aspergillus* species were isolated between January 2002 and December 2011 at the NTT Medical Center Tokyo, Tokyo, Japan. Only patients with *Aspergillus* species isolates from respiratory samples, without hematological malignancy, were included in this study. The subjects' electronic medical records were reviewed to obtain clinical and demographic data, including gender; age; category of pulmonary aspergillosis; laboratory data (white blood cell count, serum albumin, and *Aspergillus* antigen levels, and [1–3] *beta*-D glucan titer); underlying pulmonary diseases; comorbidities; treatment; and survival rates. The study protocol was reviewed and approved by the Ethics Committee of NTT Medical Center Tokyo on May 17, 2012 (approval number 12-116).

The patients were categorized into the following 5 groups based on their diagnosis: (1) CPA; (2) simple aspergilloma; (3) invasive pulmonary aspergillosis (IPA); (4) ABPA; and (5) colonization [2]. Since there is no definitive definition of CPA [3], in this study, a diagnosis of CPA was given when all of the following criteria were met: (1) isolation of *Aspergillus* species from respiratory samples; (2) the presence of clinical symptoms, such as weight loss, malaise, coughing, hemoptysis, increased sputum, dyspnea, and fever; and (3) radiological findings, such as the new appearance or the enlargement of paracavitary infiltration, adjacent pleural thickening, fungus ball, or nodule formation [4]. Immunocompromised patients expressing neutropenia with respiratory symptoms and radiological findings, such as the halo sign, the air-crescent sign, and consolidation with cavitary lesions within the previous month were categorized as having IPA [5]. Radiological findings were determined by 2 physicians (S.O. and K.U.) who specialize in respiratory medicine. If these 2 physicians had different findings, they

discussed it in order to come to an agreement. The diagnosis of ABPA was made by the physician in charge, although patients diagnosed with ABPA were confirmed to have a history of asthma, an elevated serum total immunoglobulin E level, and central bronchiectasis on chest computed tomography [6]. Colonization was defined as the lack of radiological or clinical findings suggestive of the above 3 categories in patients.

The (1-3) *beta*-D glucan assays were conducted using a product manufactured by MP Biomedicals, Inc (Santa Ana, Calif). The *Aspergillus* antigen tests were performed using the Platelia *Aspergillus* AG EIA device (Siemens Healthcare, Erlangen, Germany); the cut-off value for *Aspergillus* antigens was set at  $\geq 0.5$ .

### 2.2. Statistical analysis

The data are expressed as either the mean (standard deviation [SD]) or the median (range). Non-categorical variables were compared using the *t* test. Categorical variables were expressed as percentages and compared using the Chi-square test. A *P* value of  $<0.05$  was considered statistically significant, and survival rates were analyzed according to the Kaplan–Meier method using the log-rank test. The data were analyzed using the StatView version 5.0J software package (Statistical Analysis Systems, Cary, NC).

## 3. Results

Fig. 1 shows a diagram of the study cohort. Of the 368 samples with *Aspergillus* species isolates, 188 were respiratory samples obtained from 125 patients. Fifteen patients were excluded due to hematological malignancy, for a total of 110 patients included in the study.

Table 1 shows the patient characteristics. The median age (range) was 71 years (range: 31–92 years); 64 (58%) were male. The samples were mostly of sputum (85 samples [77%]), followed by bronchoalveolar lavage fluid (23 samples [21%]) and lung biopsy specimens (2 samples [2%]). The most commonly isolated *Aspergillus* species were *Aspergillus fumigatus* (48.3%), followed by *Aspergillus niger* (29.2%), *Aspergillus*

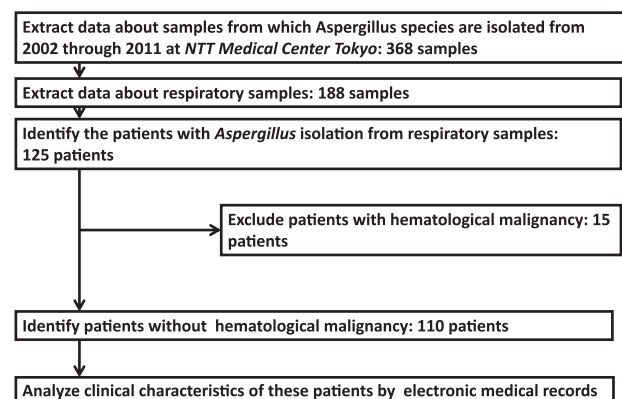


Fig. 1 – Flow chart of the study.

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