Respiratory Medicine (2005) **99**, 887–893

ELSEVIER

respiratoryMEDICINE

Prevalence of allergic bronchopulmonary aspergillosis in cystic fibrosis in an area with a high frequency of atopy

Marianne Skov[a,b,*], Karen McKay[a,c], Christian Koch[b], Peter J. Cooper[a]

[a]*Department of Respiratory Medicine, The CF Clinic, The Children's Hospital at Westmead*
[b]*The CF Centre, Department of Pediatrics, National University Hospital, Rigshopitalet, Copenhagen, Denmark*
[c]*School of Paediatrics and Child Health, The University of Sydney, Sydney, Australia*

Received 10 July 2004

KEYWORDS
ABPA;
Atopy;
CF;
Diagnosis;
Humidity;
Prevalence

Summary *Background*: Lower airway colonisation with *Aspergillus fumigatus* and the complicating hypersensitivity reaction allergic bronchopulmonary aspergillosis (ABPA) is well recognised in patients with cystic fibrosis (CF). There is a wide range in reported prevalence of ABPA in CF. Differences in predisposing factors such as atopy and climatic humidity, but also differences in reporting may in part explain this observation. In the Australian population there is a high frequency of atopy and the climate is relatively humid.

Patients and methods: Children and adolescents with CF ($n = 277$) from the CF Clinic, Children's Hospital at Westmead, Sydney, Australia were included in a retrospectively conducted study of *Aspergillus* colonisation and ABPA (1998–2003).

Results: The prevalence of *Aspergillus* colonised patients increased significantly from 7.4% in 1998 to 18.8% in 2002. No seasonal variation in initial positive *Aspergillus* culture or in humidity was observed. A total of 13 patients (4.7%) were diagnosed with ABPA over the study period, with a significant increase in prevalence from 0.3% in 1998 to 4.0% in 2002. In addition, the criteria used for reporting ABPA in the study population were in agreement with the recently published diagnostic criteria for ABPA in CF.

Conclusions: In spite of a high frequency of atopy and a relatively humid climate in the Sydney area, *Aspergillus* colonisation and ABPA in CF patients was not disproportionate. Moreover, criteria for reporting of ABPA in this setting was not different from that in the Northern Hemisphere.

*Corresponding author. The CF Centre, Department of Pediatrics, National University Hospital, Rigshopitalet, Copenhagen, Denmark. Tel.: +45 4580 0836.
E-mail address: mskov@dadlnet.dk (M. Skov).

0954-6111/$ - see front matter © 2004 Elsevier Ltd. All rights reserved.
doi:10.1016/j.rmed.2004.11.018

Introduction

Colonisation with *Aspergillus fumigatus* (*A. fumigatus*) in the lower airways is prevalent in $<5\%$ and up to 57% of patients with cystic fibrosis (CF).[1,2] The prevalence of patients who develop the complicating hypersensitivity reaction allergic bronchopulmonary aspergillosis (ABPA) ranges from 1% to 14% in various studies.[3–6] Factors predisposing to ABPA have been considered to be climate humidity, resulting in higher *Aspergillus* spore counts,[6] and atopy.[1,7] Differences in these factors between populations may partly explain the wide range in prevalence. Since diagnostic criteria for ABPA have primarily been based upon studies performed in patients with asthma and since symptoms in ABPA overlap with other common features in CF, the diagnosis of ABPA is difficult to establish. Thus, the diagnosis and reporting of ABPA may often rely upon a variety of diagnostic criteria. A set of diagnostic criteria for ABPA in patients with CF, as well as a screening program, has recently been proposed by a CF Foundation sponsored Consensus Conference panel.[8]

In an attempt to investigate some of the possible factors responsible for differences in the reported prevalence of ABPA, we performed a 5-year retrospective study of patients with CF at The Children's Hospital at Westmead, Sydney, Australia to assess (a) *Aspergillus* colonisation and presence of ABPA in an area with a high frequency of atopy, (b) the influence of humidity on *Aspergillus* colonisation and (c) the agreement between clinically used ABPA criteria in a southern hemisphere centre and the recently proposed CF Foundation Consensus criteria for ABPA in CF.[8] Data obtained in this setting were compared to data previously reported for the USA and Europe.[9]

Patients and methods

Residents of the state New South Wales (NSW) represents 33.6% of the patients in the Australasian CF Data Registry (Australia and New Zealand). Approximately 58% of children and adolescents with CF in NSW attend The Children's Hospital at Westmead in Western Sydney. Thirty-seven of the children attend a twice-yearly CF clinic conducted by the hospital in Canberra, 300 km from Sydney, but they were excluded from this study due to differences in climatic conditions (drier year round as well as hotter in summer and colder in winter). The remaining 277 patients attending the hospital for their CF care in 2002 were the subjects of this study.

According to the data submitted to the Australasian CF Registry by the hospital in 2000, patients with CF have 3–5 visits per year in the centre, and the number of sputum samples per patient sent for microbiological culture per year is 1.14 in the age group 0–4 years and 1.9 cultures in the age group $\geqslant 5$ years.[10] Serological screening for ABPA is performed once-a-year, primarily with measurement of total IgE and eosinophil count. Patients who are suspected of having ABPA on clinical grounds have cutaneous skin prick to *Aspergillus*, precipitating antibodies to *Aspergillus* and occasionally specific IgE antibodies to *Aspergillus* measured. Within the study period from January 1998 to April 2003 (5.25 years) a total of 109 patients (56 females/53 males, mean age 12.2 years) had positive *Aspergillus* cultures. Data pertained to these patients were retrospectively reviewed and, where relevant, compared with that from patients with no *Aspergillus* found on culture sputum samples ($n = 168$).

The data for this study were obtained from a number of sources including the electronic patient medical and pathology record (Powerchart, Cerner Corp; version 2002.03), the patient pulmonary function record (Vmax Spectra, SensorMedics Corp; version 10-1A) as well as the patient's record in the Australasian CF Registry. The following data were recorded:

(a) Total IgE as determined using the UniCap system with results expressed as kIU/L with a normal range less than 200 kIU/L.
(b) Specific IgE antibodies (RAST) to *Aspergillus* as measured by the CAP system according to the manufacturers instructions (Pharmacia, Uppsala, Sweden). Results were expressed as negative or positive, and positive results were further subdivided into high and very high levels.
(c) Eosinophil count as measured by automated electronic detection system. Results were expressed as 10^9/L. Eosinophilia was defined as eosinophil counts $>0.3 \times 10^9$/L.
(d) Precipitating antibodies to *Aspergillus* as measured by radial immunodiffusion. Results were expressed as positive or negative relative to two somatic extracts, 1#: 20 mg/mL and 2#: 2 mg/mL and two filtrate antigens, 3#: 20 mg/mL and 4#: 2 mg/mL.
(e) Chest X-ray and chest CT-scan results.
(f) Lung function measured using spirometry and expressed as a percentage of that predicted for gender and height.[11] Data from 1999 to 2003 were included.