Environmental variables associated with an increased risk of invasive aspergillosis

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Abstract

Information on the environmental variables that may affect the incidence of invasive aspergillosis (IA) is scarce. We sought to determine the relationship between airborne spore counts, climatic conditions and IA. We also examined whether circulating respiratory viruses predispose patients to IA in a multicentre cohort study of hospitalized adults with IA. Data on environmental mould spores, climatic conditions and circulating respiratory viruses were obtained from the Environmental Department of the Autonomous University of Barcelona, the Meteorological Service of Catalonia and the Acute Respiratory Infection Surveillance Project in Catalonia, respectively. Between 2008 and 2011, 165 patients with IA were identified. Diagnosis was based on one or more of the following: culture (125 cases), galactomannan antigen (98) and histology (34). One hundred and twenty-seven cases (77%) had criteria for probable IA and the remainder for proven IA. Environmental mould spore counts from the period 28–42 days preceding infection presented significant associations with admissions due to IA. None of the climatic conditions were associated with an increased risk of IA, but the presence of circulating respiratory viruses was associated with a higher risk of infection: the most strongly associated viruses were respiratory syncytial virus, influenza A(H1N1)pdm09 and adenovirus. In conclusion, the presence of high numbers of spores in the air increases the risk of admission due to IA. Circulating respiratory viruses appear to be associated with a higher risk of developing IA. Physicians should be aware of this association in order to optimize prevention and diagnosis strategies for IA during viral epidemic periods.

Keywords: Airborne mould counts, climatic conditions, environmental variables, invasive aspergillosis, respiratory viruses
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Introduction

Invasive aspergillosis (IA) is a life-threatening infection that affects mainly severely immunocompromised patients. Despite advances in diagnosis and treatment, mortality rates associated with IA range from 40 to 90% [1,2]. More detailed knowledge of factors contributing to the pathogenesis of invasive aspergillosis is needed in order to optimize the management of this infection and to improve prophylactic measures.

The development of IA is a multistage process that begins with the inhalation of conidia dispersed in the air and continues with the host response against infection [3,4]. Individual host factors that increase the risk of infection have been well defined [5–7]. However, our understanding of the natural history of infection, the inocula required and the incubation period of the disease are still poorly understood. In particular, information regarding the possible effect of certain environmental factors on the risk of IA is scarce. A previous study

showed that climatic conditions may influence the airborne spore count in some geographical areas [8]. However, the relationship between climatic conditions, airborne spore counts and rates of admission due to IA is less clear. It is tempting to speculate that circulating respiratory viruses may hinder the host response to infection. It could be related to an increased risk of IA.

We sought to identify the relationship between airborne mould spore count in the community and hospital admissions due to IA. We also aimed to assess the effect of climatic variables on airborne spore counts and/or the risk of IA in our area, and whether circulating respiratory viruses predispose patients to IA.

Methods

Setting, patients and study design

We performed a retrospective multicentre study of all episodes of invasive aspergillosis occurring in hospitalized adult patients between January 2008 and December 2011 at three tertiary teaching institutions in Barcelona, Spain. Only outpatients hospitalized for newly developed signs or symptoms of IA have been included. All haematological severely immunocompromised patients stayed in rooms with strict HEPA filtration. Patients who developed IA were identified by assessment of clinical, microbiology and pathology records, and by review of the diagnostic codes on hospital discharge. Only patients with proven and probable IA in accordance with the definitions of the European Organization for Research and Treatment of Cancer/National Institute of Allergy and Infectious Diseases Mycosis Study Group (EORTC/MSG) [9] were included. The following information was carefully collected from medical records: demographic characteristics, clinical features and day of IA diagnosis (the day on which the first diagnostic test was performed). For patients whose diagnosis was obtained from post-mortem examination, the day of death was considered to be the day of diagnosis.

This observational study was approved by the Institutional Review Board.

Environmental data

Daily median airborne mould concentrations were calculated from environmental data collected from the Institute of Environmental Science and Technology at the Autonomous University of Barcelona. The estimations were based on continuous measurements taken in the centre of the city. Data on climatic conditions were obtained from the Catalan Meteorological Service and were based on continuous measurements taken at the weather station in our urban area. Daily median records for rainfall, measured in litres/m^2, humidity, wind and wind speed were used for the analysis. Data on circulating respiratory viruses were obtained from the acute respiratory infection surveillance project in Catalonia (PIRIDAC). The numbers of cases of influenza A, influenza B, adenovirus and respiratory syncytial virus (RSV) were used for the study.

Statistical analysis

Categorical variables were described using counts and percentages. Continuous variables were expressed as the mean and standard deviation or median and interquartile range depending on the Kolmogorov-Smirnov test.

Patients admitted for IA were recorded according to cases occurring during 2-week periods. The effect of environmental variables in each 2-week period was analysed. The Spearman ρ correlation was used to detect significant temporal associations between groups. For the analysis of quantitative associations between environmental mould spores and admissions due to IA in a 2-week period, a Poisson regression model was used. To assess potential confounding by environmental variables, we performed a multivariate analysis. A partial Spearman ρ correlation analysis and a Poisson relation with addition covariants were performed. The results were analysed using SPSS version 15.0 (SPSS Inc., Chicago, IL, USA). Statistical significance was established at $\alpha = 0.05$. All reported p-values are two-tailed.

Results

General features of the study population

During the 4 years of the study period, 165 patients with IA were hospitalized. The most frequent co-morbid conditions were haematological malignancies (67 cases; 40.6%, including 13 stem cell transplantations), solid organ transplantation (33 cases; 20%), solid cancer (14 cases; 8.4%) and AIDS (nine cases; 5.4%). Other factors predisposing to IA were neutropenia (49 cases; 29.7%), corticosteroid use (87 cases, 52.7%) and use of other immunosuppressive drugs (97 cases; 58.8%). The diagnosis of IA was established by using one or more of the following methods: culture (125 cases), galactomannan (98 cases) and histology (34 cases). One hundred and twenty-seven cases (77%) had criteria for probable IA. Most cases were caused by *Aspergillus fumigatus* (78.4%), followed by *A. flavus* (7.3%), *A. terreus* (4.2%) and *A. niger* (3.6%). Table 1 summarizes the major epidemiological and clinical characteristics of the patients.