Invasive pulmonary aspergillosis: retrospective case record review

Mohamed Farouk Allam, Amparo Serrano Del Castillo, Carmen Díaz-Molina, Rafael Fernández-Crehuet Navajas

Department of Preventive Medicine and Public Health, Faculty of Medicine, University of Cordoba, Cordoba, Spain.

Summary

Invasive pulmonary aspergillosis is a severe infection, with a sharp increase during the last decades. Our study aimed at identification of the epidemiological characteristics of invasive pulmonary aspergillosis during a period of four years. All clinical records with pulmonary isolation of *Aspergillus* species were reviewed, as a part of surveillance program at Reina Sofia University Hospital, from January 1995 to December 1998. Diagnosis of invasive pulmonary aspergillosis was based on criteria of Centers for Disease Control and Prevention. Of the 50 patients identified 78% were males and 44% were current or ex-smokers. Chronic respiratory diseases were identified in 64% of them, and 60% were receiving immunosuppressives. Twenty percent of our patients had been subjected to lung transplantation and 28% to organ transplantation in general. Only 78% had received specific antifungal treatment and 56% had fatal prognosis. Our findings match with previous studies, apart from the high frequency of lung transplantation in our series. We recommend further studies on large prospective cohorts.

Key words

Invasive pulmonary aspergillosis, Surveillance program, Risk factors

Aspergilosis pulmonar invasora: revision retrospectiva de historias clínicas

Resumen

La aspergilosis pulmonar invasora es una infección severa que ha experimentado un brusco incremento en las últimas décadas. El objetivo del presente estudio ha sido establecer las características epidemiológicas de esta enfermedad en un periodo de cuatro años. Se revisaron todos los datos clínicos obtenidos de los casos con aislamiento de *Aspergillus*, parte de un programa de vigilancia del hospital universitario Reina Sofia, de enero de 1195 a diciembre de 1998. El diagnóstico de aspergilosis pulmonar invasora se basó en los criterios establecidos por los Centers for Disease Control and Prevention. De los 50 pacientes incluidos en el estudio, el 78% eran hombres y un 44% eran fumadores o ex-fumadores. Un 64% presentaba alguna enfermedad respiratoria crónica, y un 60% recibió tratamiento inmunosupresor. Un 28% de los pacientes fueron sometidos a trasplante de órgano, siendo un 20% del total trasplantados pulmonares. Solo el 78% de los pacientes recibieron tratamiento antifúngico, teniendo un 56% un pronóstico fatal. Nuestros hallazgos coinciden con lo descrito en estudios previos, al margen del alto porcentaje de trasplantados pulmonares de nuestro estudio. Son necesarios estudios prospectivos con grupos mayores de pacientes.

Palabras clave

Aspergilosis pulmonar invasora, Programa de vigilancia, Factores de riesgo

Address for correspondence:

Dr. Mohamed Farouk Allam
Department of Preventive Medicine and Public Health
Faculty of Medicine, University of Cordoba
Avda. Menéndez Pidal, s/n, Cordoba 14004, Spain
Phone: +34 957 218 278
Fax. +34 957 218 573
E-mail: fm2taehm@uco.es

Aceptado para publicación el 26 de noviembre de 2003

©2004 Revista Iberoamericana de Micología
Apdo. 699, E-48080 Bilbao (Spain)
1130-1406/01/10.00 Euros
Invasive pulmonary aspergillosis is a severe infection, which occurs mainly in immunosuppressed patients [1]. Diagnosis of the infection is often difficult and late made, and usually bears a dismal prognosis [6]. During the last decades there has been a sharp increase in the occurrence of invasive pulmonary aspergillosis with a high mortality, reaching 85% in immunosuppressed patients [10]. The use of powerful new chemotherapy protocols for malignancies and certain immunological disorders, and the increase use of organ transplantation may have contributed to this sharp increase [1,6,7]. In Spain, the commission of infection control of La Paz Hospital, Madrid has recommended aspergillosis surveillance system based on retrospective revision of medical records every 3 months [4]. Since January 1995, an active epidemiological surveillance program for isolation of Aspergillus was implemented in our university hospital. Constructions of new buildings and remodelling of the hospital prompted active registration of new cases with aspergillosis.

The main objective of this study is describing the epidemiological characteristics of invasive pulmonary aspergillosis patients who were identified during a period of four years.

Material and Methods

Medical records of all patients with positive isolation of Aspergillus species in Reina Sofia University Hospital from January 1995 to December 1998 were retrospectively studied. This hospital is a tertiary referral centre with 1500 beds, fully equipped to receive trauma patients. In addition, hospital activities extend to include organ and bone marrow transplantations. Owning to its location in the centre of Andalusia, it serves over one million persons.

In our study, all patients were diagnosed by the Microbiology Laboratory as positive by pulmonary isolation of Aspergillus. Since January 1995, an active epidemiological surveillance system based on retrospective revision of medical records every 3 months [4]. Since January 1995, an active epidemiological surveillance program for isolation of Aspergillus was implemented in our university hospital. Constructions of new buildings and remodelling of the hospital prompted active registration of new cases with aspergillosis.

In our study, all patients were diagnosed by the Microbiology Laboratory as positive by pulmonary isolation of Aspergillus species. Aspergillus species were identified on histopathological examination and tissue culture of lung biopsy.

Patients were considered to have definite diagnosis of invasive pulmonary aspergillosis if Aspergillus was identified on histopathological examination and tissue culture of lung biopsy.

Probable diagnoses of invasive pulmonary aspergillosis included patients whom Aspergillus was recovered either from a lower respiratory tract specimen obtained by bronchoalveolar lavage or from two or more sputum specimens. Confirmatory evidence for these patients consisted of characteristic findings suggestive of aspergillosis on chest radiograph and computerised tomography scan, and no evidence of a concurrent pathogen. Only 30% of these patients had a symptomatic pulmonary aspergillosis. The incidence rates of invasive pulmonary aspergillosis on chest radiograph and computerised tomography scan.

Of the 50 patients with invasive pulmonary aspergillosis, 78% were males, 44% were current or ex-smokers and 42% were living in a rural area. The mean age of the identified patients was 47.6 ± 21.14 years. Only 78% had received specific treatment for invasive pulmonary aspergillosis, and 56% had fatal prognosis. All patients who did not receive antifungal treatment were diagnosed post mortem, and of those who received specific antifungal treatment 43.6% had fatal prognosis. Antifungals used were amphotericin B, fluconazole, ketoconazole and itraconazole.

The table shows the principal epidemiological characteristics of diagnosed patients with invasive pulmonary aspergillosis. The incidence rates of invasive pulmonary aspergillosis according to the hospital admissions were 0.34, 0.26, 0.17, and 0.40 in years 1995, 1996, 1997, and 1998 respectively.

Discussion

Hospital surveillance programs, based on retrospective revision of medical records, are very important in invasive pulmonary aspergillosis, because this is a potentially preventable disease in many patients, and associated with high morbidity and mortality [4]. Revision of medical records has shown to be the most easy and rapid method to collect a sufficient sample for such rare events [9], and several researchers have employed such methods to study the occurrence of invasive aspergillosis [8,11,13-15].

Reviewing the medical literature, a variety of factors that increase the risk of invasive pulmonary aspergillosis have been described as; chronic respiratory diseases,
The CDC did not identify gender difference in invasive pulmonary aspergillosis, in contrast to our results where 78% of our patients were males. Forty four percent of our patients were current or ex-smokers, known risk factor for invasive pulmonary aspergillosis [1,3,6,7]. The higher prevalence of smoking among males in Spain could be the explanation for gender difference in our study.

Only 78% of our patients had received specific treatment for invasive pulmonary aspergillosis, which could be attributed to delay and difficulty in diagnosis. This problem has been previously reported [1,6,8,12,15], and could be responsible for part of the high fatal prognosis (56%) in our patients, although nearly similar figures (47.6%) was observed among patients who received specific antifungal treatment. This suggests a need for prospective cohort studies to evaluate the effectiveness of different antifungal treatment in invasive pulmonary aspergillosis.

The four years surveillance period was quite useful to our institution in establishing a baseline “endemic” rate of invasive pulmonary aspergillosis and determining groups of patients who were at risk. In addition, we have learned that the general health condition of the patient, roughly indicated by the number of hospital admissions in the past year, correlates with disease activity.

Our results suggest the need for prompt preventive measures and special attention for patients with these risk factors. These measures include, respectively, the use of granulocyte-colony-stimulating factors and intranasal application of amphotericin B or oral or systemic antifungal drug prophylaxis, this is together with reducing the exposure of patient under immunosuppressive therapy by using high-efficiency particulate air (HEPA) filters in the hospital environment [3,7,12]. Moreover, more attention by the physicians to Aspergillus as a causative agent of pulmonary infection among patients with previously reported risk factors, to be treated pre-emptively and aggressively.

Of course, these results pertain solely to our hospital and should not be considered to apply generally. However, the retrospective surveillance methodology can be applied in different hospitals. Inspection of our findings with their consistency and coherency strongly suggests the external validity of the study.

Our results call for further investigation of invasive pulmonary aspergillosis risk factors; future study preferably should be performed on large prospective cohorts, to increase their internal validity.

### Table. Descriptive analysis of 50 cases with invasive pulmonary aspergillosis.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Cases with invasive pulmonary aspergillosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years</td>
<td>47.6 ± 21.14</td>
</tr>
<tr>
<td>Gender (male)</td>
<td>39 (78)</td>
</tr>
<tr>
<td>Chronic respiratory disease</td>
<td>32 (64)</td>
</tr>
<tr>
<td>Chronic disease of relevance</td>
<td>29 (58)</td>
</tr>
<tr>
<td>Past history of immunosuppression</td>
<td>29 (58)</td>
</tr>
<tr>
<td>Immunosuppression in the last hospital admission</td>
<td>30 (60)</td>
</tr>
<tr>
<td>Granulocytopenia in the last 6 months</td>
<td>13 (26)</td>
</tr>
<tr>
<td>Granulocytopenia in de last hospital admission</td>
<td>12 (24)</td>
</tr>
<tr>
<td>Surgical intervention</td>
<td>24 (48)</td>
</tr>
<tr>
<td>Organ transplantation</td>
<td>14 (28)</td>
</tr>
<tr>
<td>Lung transplantation</td>
<td>10 (20)</td>
</tr>
<tr>
<td>Number of hospital admission in the last year</td>
<td>2.58 ± 1.81</td>
</tr>
</tbody>
</table>

* Quantitative data are expressed as mean ± SD; Number in parentheses adjacent to the actual number indicates percentage of cases.
References