Case Report

Acta Hæmatologica

Acta Haematol 1998;100:85–87

Received: July 4, 1997
Accepted: January 15, 1998

V. Lévy[a]
P.R. Burgel[b]
A. Rabbat[b]
M. Cornet[c]
T. Molina[d]
R. Zittoun[a]

Services
[a] d'Hématologie, de
[b] Réanimation, de
[c] Microbiologie et
[d] d'Anatomo-Patholgie, Hôtel-Dieu de Paris, France

Respiratory Distress due to Tracheal Aspergillosis in a Severely Immunocompromised Patient

Key Words
Acute respiratory failure
Aspergillosis, fungal
Pseudomembranes
Tracheal ulceration

Abstract
A 23-year-old man, intensively treated for acute lymphoblastic leukaemia in relapse and with documented pulmonary aspergillosis, was admitted to the intensive care unit for acute respiratory failure. The diagnosis of invasive tracheal aspergillosis was made by bronchoscopy and biopsy. The lesions consisted of extensive necrotizing bronchitis with transmural and peribronchial extension associated with tracheal and bronchial obstruction due to the presence of pseudomembranes almost entirely composed of fungal hyphae. Despite treatment with amphotericin B and itraconazole, mechanical ventilation and bronchoscopy, the patient died 3 weeks later of massive bleeding.

Introduction

Pulmonary aspergillosis presents a wide spectrum of pathology in humans, ranging from saprophytic manifestations to invasive forms including aspergilloma, allergic bronchopulmonary aspergillosis, bronchocentric granulomatosis and invasive aspergillosis. Invasive pulmonary aspergillosis is a common lethal complication for patients treated for haematological malignancies with or without bone marrow transplantation [1, 2]. We report the case of an acute respiratory failure due to an invasive tracheal aspergillosis complicating the course of a documented pulmonary aspergillosis in a severely immunocompromised patient.

Case Report

J.F., a 23-year-old man, was treated in 1993 for a Philadelphia chromosome-negative acute lymphoblastic leukaemia. Treatment consisted in induction chemotherapy (vincristine, corticosteroids, cyclophosphamide, daunorubicin, asparaginase) and intrathecal methotrexate. Complete remission was achieved and was consolidated with cytarabine and cyclophosphamide. Postconsolidation treatment involving brain irradiation was also given. In June 1996, 3 weeks before the end of maintenance treatment, the patient relapsed with thrombocytopenia and fever. Bone marrow aspiration disclosed an infiltration with 90% blasts. Treatment with daunorubicin, dexamethasone, vindesine and cyclophosphamide was ineffective and high dose cytarabine (3 g/m^2/12 h, day 1 to day 5) was added on day 10. The patient remained febrile despite broad-spectrum antibiotics without any bacterial identification. Weekly chest roentgenograms were normal. By the end of aplasia (day 19), the patient complained of a moderate cough without chest pain or haemoptysis. The chest roentgenogram showed a 4-cm round ill-defined infiltrate of the right upper lobe surrounded with ground glass opacity on CT scan. The suspected diagnosis of invasive aspergillosis was documented

KARGER
Fax + 41 61 306 12 34
E-Mail karger@karger.ch
www.karger.com

0001–5792/98/1002–0085$15.00/0

Accessible online at:
http://BioMedNet.com/karger

V. Lévy
Service d'Hématologie, Hôtel-Dieu de Paris
1 place du Parvis Notre-Dame
F–75181 Paris (France)
Tel. +33 1 42 34 82 34, Fax +33 1 42 34 84 62

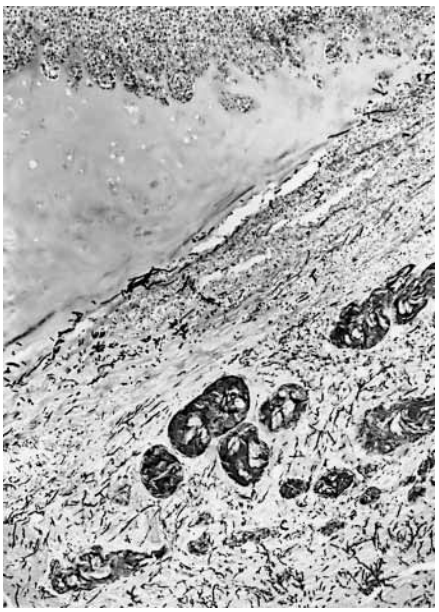

Fig. 1. Ulceration of the cartilage ring associated with numerous fungal hyphae of *Aspergillus* in the tracheal mucosae. HE and Grocott. × 73.

2 days later on day 21 by a positive culture of *Aspergillus fumigatus* in one of the two sputum specimens analyzed. *Aspergillus* antigens were positive in the serum (Latex agglutination test). Amphotericin B started on day 6 (1 mg/kg/day) was increased up to 1.5 mg/kg/day. On day 24 the patient experienced severe dyspnoea, wheezing and inspiratory stridor, nonresponsive to inhaled β_2-agonists and steroids. The chest roentgenogram remained unchanged. The patient was admitted to the intensive care unit. Intubation and mechanical ventilation were required because of the development of exhaustion with severe hypoventilation, cyanosis and major hypercapnia despite the initial use of noninvasive facial mask ventilation (BiPAP). Bronchoscopy, performed after transient removal of the tracheal tube, showed a partial tracheal obstruction (>50%) secondary to the presence of pseudomembranes from the distal part of the trachea to the main right bronchus. The bronchoalveolar lavage performed was positive for *A. fumigatus* (few colonies). Biopsy disclosed an invasive aspergillosis with ulceration and necrosis of the tracheal mucosa. These lesions reached the cartilage rings where numerous fungal hyphae were present (fig. 1). A second thoracic CT scan done on day 30 showed an excavation of the parenchymatous nodule and evidence of tracheal involvement. Despite the addition of itraconazole (600 mg/day) on day 24, repeated fibroscopy showed no improvement. The patient's condition worsened with increasing difficulties of the mechanical ventilation because of high airway pressure due to tracheal stenosis. He died of massive bleeding on day 42. Repeated attempts of deobstruction under bronchoscopy were unsuccessful and the five bronchial aspirations analyzed were positive for *A. fumigatus* with many colonies. He had received a total amount of 2.5 g amphotericin B and had therapeutic serum itraconazole levels. Postmortem examination was not performed because of the family's refusal.

Discussion

Bronchitis due to aspergillus is known to occur in 5–8% of the patients with disseminated aspergillosis [3] and is commonly symptomless and diagnosed at autopsy. By contrast, pseudomembranous necrotizing bronchial aspergillosis appears as a new distinct entity with severe clinical features [4]. It was first described in 1985 in a 15-year-old haemophiliac with AIDS and severe neutropenia, who developed a rapidly progressive respiratory failure with intermittent wheezing, nonresponsive to bronchodilators and steroid therapy.

In 1993, Kemper et al. [5] reported 4 cases of AIDS patients, who developed severe airway obstruction due to *Aspergillus* species with ulcerative and plaque-like tracheobronchitis. Only 16 out of the 58 cases registered by Kemper et al. in the literature were diagnosed before death. More than half of the patients had neutropenia as an underlying factor and/or histological evidence of parenchymal lung involvement. Only 5 patients were treated for acute leukaemia. The authors show that this invasive form is generally rapidly progressive with almost 40% of deaths. In our patient, tracheal involvement occurred as a terminal evolution of an invasive pulmonary disease. He had several recognized risk factors for aspergillosis including acute leukaemia in relapse, treatment with high dose steroids and cytarabine [6], and prolonged neutropenia [7]. The lesions consisted of an extensive necrotizing bronchitis with transmural and peribronchial invasion. There was a significant tracheal obstruction secondary to the presence of pseudomembranes almost entirely composed of fungal hyphae. Massive bleeding could have resulted from the rupture of pulmonary vessels as previously described in invasive aspergillosis [8]. This case was thus similar to the initial case previously recognized in 1985.

In conclusion, respiratory symptoms such as wheezing in a heavily immunocompromised patient, even when the chest roentgenogram is normal, can be the first symptoms of a tracheobronchial aspergillosis and can lead to severe respiratory failure due to tracheal obstruction. Sputum culture, when positive, may be helpful to make the diagnosis. Despite the use of amphotericin B and then intraconazole the condition is frequently fatal due to massive haemorrhage.

References

1 Dennings WD, Stevens DA: Antifungal and surgical treatment of invasive aspergillosis: Review of the 2,121 published cases. Rev Infect Dis 1990;12:1147–1201.

2 Wingard JR, Beals SU, Santos GW, Merz GW, Saral R: Aspergillus infection in bone marrow transplant recipient. Bone Marrow Transplant 1987;2:175–181.

3 Youg RC, Bennett JE, Vogel CL, Carbone PP, DeVita VT: Aspergillosis: The spectrum of disease in 98 patients. Medicine 1970;49:147–173.

4 Pervez NK, Kleinerman J, Kattan M, Freed JA, Harris MB, Rosen MJ, Schwartz IS: Pseudomembranous necrotizing bronchial aspergillosis. Am Rev Respir Dis 1985;131:961–963.

5 Kemper CA, Hostetler JS, Follansbee SE, Ruane P, Covington DC, Leong SS, Deresinski SC, Stevens DA: Ulcerative and plaque-like tracheobronchitis due to infection with aspergillus in patients with AIDS. Clin Infect Dis 1993;17:344–352.

6 O'Donnell M, Schmidt GM, Tegmeier BR, Fauceett C, Fahey JL, Ito J, Nademanee A, Niland J, Parker P, Smith EP: Prediction of systemic fungal infection in allogeneic bone marrow recipient: Impact of amphotericin prophylaxis in high-risk patients. J Clin Oncol 1994;12:230–238.

7 Gerson SL, Talbot GH, Hurwitz S, Strom BL, Lusk EJ, Cassileth PA: Prolonged granulocytopenia: The major risk factor for invasive pulmonary aspergillosis in patients with acute leukemia. Ann Intern Med 1984;100:345–351.

8 Albeda SM, Talbot GM, Gerson SL, Miller WT, Cassileth PA: Pulmonary cavitation and massive hemoptysis in invasive pulmonary aspergillosis. Influence of bone marrow recovery in patients with acute leukemia. Am Rev Respir Dis 1985;131:115–122.