Received: 2012.05.13
Accepted: 2012.07.06
Published: 2012.08.01

A near fatal case of invasive aspergillosis

Gustavo Cumbo-Nacheli[1], Jorgelina de Sanctis[2]

[1] Respiratory Institute, Cleveland Clinic Foundation, Cleveland, OH, U.S.A.
[2] Infectious Diseases, Cleveland Clinic Foundation, Cleveland, OH, U.S.A.

Summary

Background: Invasive aspergillosis (IA) rarely presents with endobronchial nodules or pseudomembranes on bronchoscopy. We describe a case of invasive aspergillosis in a patient with systemic lupus erythematosus (SLE), in which a fungal etiology was suspected after visualization of scattered, white endobronchial nodules.

Case Report: A 36-year-old-female with history of SLE developed cardiorespiratory shock. Bronchoscopy indicated the presence of endobronchial lesions, and serologic studies were consistent with IA. Given high index of suspicion for fungal disease in an immunocompromised host, empiric antifungals were discontinued and voriconazole initiation resulted in a successful therapy.

Conclusions: This case highlights the importance of a high index of suspicion for fungal diseases, especially among critically ill hosts with endobronchial lesions, who develop rapid cardio-respiratory impairment. Failure to recognize endobronchial patterns of fungal infection may lead to treatment delay and adverse clinical outcomes.

key words: **invasive aspergillosis • endobronchial lesions • systemic lupus erythematosus**

Full-text PDF: http://www.amjcaserep.com/fulltxt.php?ICID=883320

Word count: 1094
Tables: –
Figures: 4
References: 14

Author's address: Gustavo Cumbo-Nacheli, Respiratory Institute, Cleveland Clinic Foundation, Cleveland, OH, U.S.A., e-mail: gustavocn@hotmail.com

Background

Clinical presentations from *Aspergillus fumigatus* infections range from mild (single organ involvement) to life-threatening invasive disease. Classically, these infections occur in immunosuppressed patients (neutropenic patients, bone marrow and solid organ transplant recipients, HIV/AIDS patients) or patients on immunosuppressive regimens such as corticosteroids and or, chemotherapy. There has been also increasing reports of IA in patients with non-classic risk factors (surgery, cirrhosis, chronic obstructive pulmonary disease, malignancy, and cystic fibrosis) as well as described in patients with systemic lupus erythematosus (SLE).

Occasionally, A. fumigatus infection displays unusual clinical features, posing a challenging diagnosis for the clinician. Failure to recognize and delays in treatment of these fungal infections increases the risk of an adverse clinical outcome. We present a case of invasive aspergillosis with unusual endobronchial features.

Case Report

A 36-year-old-female with history of SLE was admitted to the ICU with hypoxemic respiratory failure. Her initial complaints included fever, shortness of breath, cough with sputum production, and ulcers in oral region for two weeks. The patient denied hemoptysis. Her SLE had affected the cutaneous and musculoskeletal systems. Although she was previously on metothrexate treatment, she had not been taking immunosuppresants for 6 months. She had a history of 20 pack/year tobacco use.

In the emergency department vital signs were significant for hypotension, tachycardia and tachypnea along with fever of 101.6°F (38.7°C) and spO2 93% on 4L/min via nasal cannula. Her physical exam was remarkable for respiratory distress, bibasilar lung dullness, and distal phalanx erythematous nodules (Figure 1). Her complete blood cell count showed a WBC 2.5×10^3 cells/uL (neutrophilis 83%, lymphocytes 14%), hemoglobin 8.5 mg/dl, and platelet count 116 cells/uL. Her arterial blood gases were remarkable for hypoxemia. Chest radiograph displayed bilateral pulmonary infiltrates and pleural effusions (Figure 2).

Upon deterioration of her respiratory status and severe hypoxemia, she was admitted to the intensive care unit (ICU) and mechanical ventilation was initiated. On ICU day 1 a chest computed tomogram (CT) showed bibasilar infiltrates and bilateral pleural effusions (Figure 3). A flexible bronchoscopy (FB) with bronchoalveolar lavage (BAL) was performed. Right mainstem bronchus and right lower lobe endobronchial lesions were present (Figure 4). These white papular areas were amenable to sampling using a protected endobronchial brush. As her condition progressively deteriorated, antifungal coverage and stress dose steroids were initiated.

On ICU day 2, the BAL revealed growth of septated hyphae, consistent with *A. fumigatus*. Serum and BAL galactomannan assays were positive. Antifungal agent was changed to voriconazole. Her hospital stay was complicated with cardiogenic shock requiring Intra aortic balloon pump (IABP) and inotropics. Although an endomyocardial biopsy was not obtained secondary to her labile status, it was suspected that there was fungal involvement of her cardiovascular system. Prompt initiation of voriconazole resulted in progressive overall clinical improvement, and she was able to be weaned from the IABP, vasopressors, and mechanical

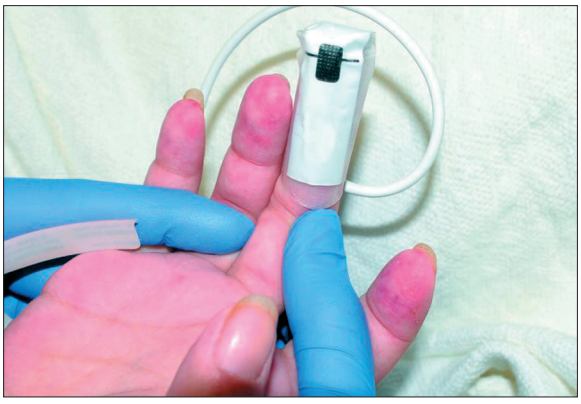

Figure 1. Cutaneous manifestations of invasive aspergillosis.

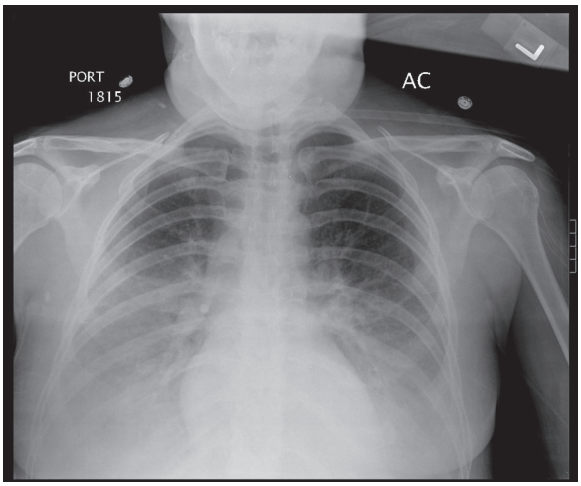

Figure 2. Chest Xray. Bibasilar opacities.

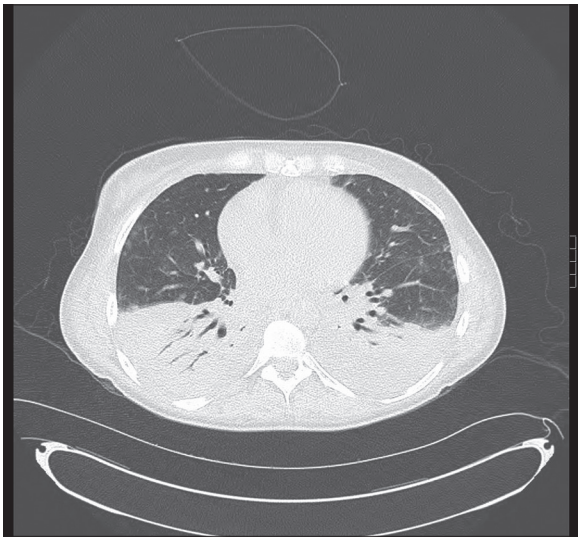

Figure 3. CT Chest. Bibasilar alveolar infiltrates.

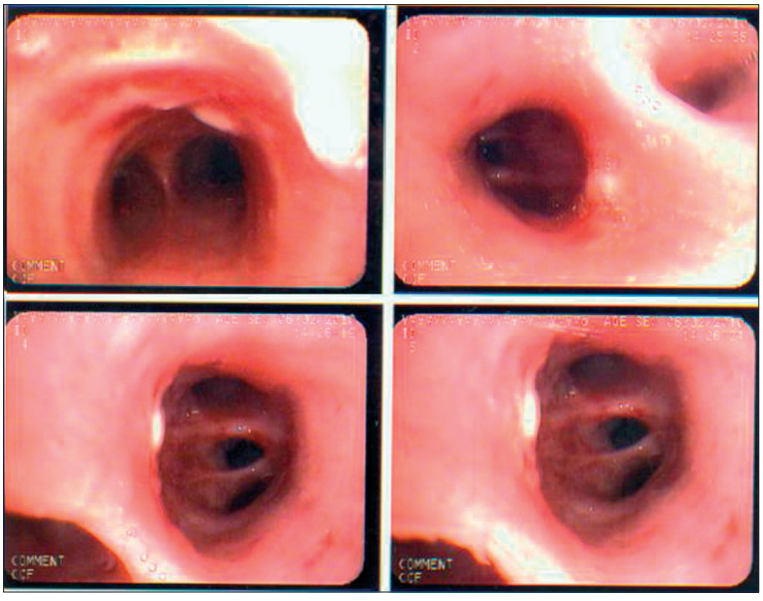

Figure 4. Bronchoscopic examination demonstrating endobronchial lesions.

ventilation. She remained hospitalized for a total of 30 days, to be discharged to skilled nursing facility. At one month outpatient follow-up the patient had returned to her baseline.

Discussion

We describe an unusual presentation of aspergillus fumigatus infection, in which extensive endobronchial and possibly endomyocardial fungal involvement resulted in cardiorespiratory collapse. A variety of clinical manifestations have been described in *Aspergillus fumigatus* infection: 1) allergic bronchopulmonary aspergillosis (ABPA), 2) pulmonary aspergilloma, 3) chronic necrotizing pneumonia, and 4) invasive aspergillosis. In a series among intensive care unit patients, 3% of the autopsies displayed evidence of disseminated *A. fumigatus* infection. [1,2] Patterns of endobronchial aspergillosis include: 1) mucous plugs in bronchiectatic areas; 2) endoluminal mass-like obstructive lesions; 3) bronchiolithiasis; 4) airway narrowing and abundant granulation tissue, especially in surgical anastomosis; 5) polypoid lesions; 6) eroded bronchial walls [2–6]. In cases of suspected aspergillus fumigatus pulmonary infection, a bronchoscopy with bronchioalveolar lavage is warranted, as this diagnostic modality is >90% specific for detection of this organism [7]. Our patient displayed signs of endobronchial involvement, although there was no visible obstruction, airway narrowing or mucosal erosion at the time of bronchoscopic examination.

Invasive aspergillosis complicating systemic lupus erythematosus is a rare entity, which carries a high mortality (>95%) and may result in various sequelae [8,9]. It has been described that SLE induced vasculitis may result in mucocutaneous breakdown, and impaired humoral and cellular immunity predispose these immunocompromised hosts to more severe forms of aspergillus fumigatus infection [10,11].

Cutaneous manifestations of IA are a rare entity, and may be encountered in up to 2% of the patients with disseminated disease. Skin examination may display plaques or papules, often violaceous to erythematous. Later in the course of the disease, these lesions evolve into black eschars. The skin lesions present in our patient resolved within days of initiation of antifungal regimen [12,13].

Although unconfirmed, it is possible that IA may have affected our patient's cardiovascular system. Aspergillus endomyocarditis carries a >50% associated mortality, and should be included in the differential diagnosis in immunocompromised patients presenting with cardiocirculatory shock. In confirmed aspergillus endocarditis case, prompt surgical consultation should be sought, as an early aggressive surgical approach may be warranted [14].

Pulmonary involvement in IA is usually multifocal and macronodular. Secondary invasion by A. fumigatus should be suspected in patients with evidence of new focal or nodular disease, especially on those with a history of previous fungal disease. Radiologically, nodules and cavitation may be encountered. The "halo" (mass with peripheral ground glass opacification) and "air crescent" (radiolucid crescents surrounding nodules) signs suggest pulmonary aspergillosis, although these finding may be absent among non-neutropenic patients [2].

Especially in the fungal replication and growth phase, laboratory studies assist in the diagnosis of A. fumigatus infection. Galactomannan assay detects A. fumigatus wall components in body fluids. Brochioalveolar galactomannan positivity indicates respiratory involvement, whereas positive serum galactomannan assays raise the possibility of invasive fungal disease.

Treatment in invasive aspergillosis consists of intravenous antifungals (azoles, polyenes, echinocandins) and aggressive supportive measures. Early involvement of an infectious diseases specialist is suggested.

Conclusions

This case highlights the importance of a high index of suspicion for fungal diseases, especially in critically ill hosts with

endobronchial lesions. Our objective is to raise awareness of uncommon features of invasive aspergillosis, as adverse clinical outcomes may occur if these patterns are unrecognized by the clinician. The increasing incidence of IA in patients with active rheumatologic conditions, and its associated mortality among critically ill subjects warrants further research in this field.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing interests

The authors declare that they have no competing interests.

REFERENCES:

1. Dimopoulos G et al: Disseminated aspergillosis in intensive care unit patients: an autopsy study. J Chemother, 2003; 15(1): 71–75
2. Franquet T et al: Spectrum of pulmonary aspergillosis: histologic, clinical, and radiologic findings. Radiographics, 2001; 21(4): 825–37
3. Tsubochi H et al: Endobronchial aspergillosis and actinomycosis associated with broncholithiasis. Eur J Cardiothorac Surg, 2007; 31(6): 1144–46
4. Quoix E et al: [Endobronchial aspergillosis associated with a carcinoid tumor]. Rev Mal Respir, 1990; 7(6): 609–12
5. Sammut PH et al: Unusual form of endobronchial Aspergillosis in a patient with cystic fibrosis. Pediatr Pulmonol, 1993; 16(1): 69–73
6. Verea-Hernando H et al: Bronchoscopy findings in invasive pulmonary aspergillosis. Thorax, 1989; 44(10): 822–23
7. Angelotti T et al: Nodular invasive tracheobronchitis due to Aspergillus in a patient with systemic lupus erythematosus. Lupus, 2002; 11(5): 325–28
8. Gonzalez-Crespo MR, Gomez-Reino JJ: Invasive aspergillosis in systemic lupus erythematosus. Semin Arthritis Rheum, 1995; 24(5): 304–14
9. Katz A et al: Aspergillosis in systemic lupus erythematosus. Semin Arthritis Rheum, 1996; 26(3): 635–40
10. Rivero SJ, Diaz-Jouanen E, Alarcon-Segovia D: Lymphopenia in systemic lupus erythematosus. Clinical, diagnostic, and prognostic significance. Arthritis Rheum, 1978; 21(3): 295–305
11. Cerqueira Macêdo DP, de Souza-Motta CM, Milan EP, Pereira Neves R: Invasive aspergillosis associated with systemic lupus erythematosus and cardiac postoperative complication. Braz J Microbiol, 2009; 40(1): 180–83
12. Schimmelpfennig C et al: Skin involvement as the first manifestation of systemic aspergillosis in patients after allogeneic hematopoietic cell transplantation. Bone Marrow Transplant, 2001; 27(7): 753–55
13. La Nasa G et al: Voriconazole for the treatment of disseminated nodular cutaneous aspergillosis in a patient affected by acute myeloid leukemia. Hematol J, 2004; 5(2): 178–80
14. Attia RQ, Nowell JL, Roxburgh JC: Aspergillus endocarditis: a case of near complete left ventricular outflow obstruction. Interact Cardiovasc Thorac Surg, 2012; 14(6): 894–96