Case Report

Pulmonary Mucormycosis in a Patient with Systemic Lupus Erythematosus: A Diagnostic and Treatment Challenge

Hung-Chang Hung,1 Gang-Yu Shen,2 Shiuan-Chih Chen,3,4,5 Kai-Jieh Yeo,4,6 Shih-Ming Tsao,4,5,7 Meng-Chih Lee,3,4,5,8 and Yuan-Ti Lee4,5,7

1Division of Gastroenterology, Department of Internal Medicine, Nantou Hospital, Ministry of Health and Welfare, No. 478, Fuxing Road, Nantou City, Nantou County 540, Taiwan
2Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Chiu General Hospital, No. 137, Chenggong First Road, Lingya District, Kaohsiung 802, Taiwan
3Department of Family and Community Medicine, Chung Shan Medical University Hospital, No. 110, Section 1, Jianguo North Road, Taichung 402, Taiwan
4School of Medicine, Chung Shan Medical University, No. 110, Section 1, Jianguo North Road, Taichung 402, Taiwan
5Institute of Medicine and School of Medicine, Chung Shan Medical University, No. 110, Section 1, Jianguo North Road, Taichung 402, Taiwan
6Division of Allergy, Immunology, Rheumatology, Department of Internal Medicine, Chung Shan Medical University Hospital, No. 110, Section 1, Jianguo North Road, Taichung 402, Taiwan
7Division of Infectious Diseases, Department of Internal Medicine, Chung Shan Medical University Hospital, No. 110, Section 1, Jianguo North Road, Taichung 402, Taiwan
8Department of Family Medicine, Taichung Hospital, Ministry of Health and Welfare, No. 199, Section 1, Sanmin Road, Taichung 403, Taiwan

Correspondence should be addressed to Yuan-Ti Lee; leey521@yahoo.com.tw

Received 24 February 2015; Revised 1 June 2015; Accepted 3 June 2015

Academic Editor: Larry M. Bush

Copyright © 2015 Hung-Chang Hung et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Pulmonary mucormycosis is commonly encountered in patients with diabetic ketoacidosis, hematologic malignancies, neutropenia, organ or hematopoietic stem cell transplantation, and malignancy, but it rarely occurs in high-risk patients with systemic lupus erythematosus (SLE). We present the case of a 40-year-old SLE female with fulminant pneumonia after remission of nephritis treated with rituximab, who developed severe pulmonary mucormycosis that led to her rapid death from acute respiratory failure and acute respiratory distress syndrome. Pulmonary mucormycosis has a high mortality rate. However, with early diagnosis and antifungal therapy with lipid formulation-liposomal amphotericin B and surgical removal of the infected area, the outcome can be improved.

1. Introduction

The most common invasive fatal opportunistic diseases (Rhizopus 47% and Mucor 18%) are of the order Mucorales. These include Rhizopus, Mucor, Cunninghamella, Apophysomyces, Absidia, Saksenaea, Rhizomucor, Cokeromyces, and Syncephalastrum species. Infections caused by both mucormycosis and entomophthoramycosis were previously called zygomycosis. The class Zygomycetes has disappeared from current taxonomy. The infections caused by the order Mucorales are now termed mucormycosis [1–3].

There are several potential contributing factors to mucormycosis including poorly controlled diabetes mellitus (both types 1 and 2), diabetic ketoacidosis, metabolic acidosis, persistent neutropenia, high-dose glucocorticoid therapy, trauma or burns, and iron overload due to chelation therapy with deferoxamine in patients on dialysis or chronically transfusion dependent [1, 4]. Invasive fungal infection is
rarely encountered among SLE patients. Of these, the most common pathogens are cryptococcosis, candidiasis, and aspergillosis [5]. The mortality rate of mucormycosis ranges from 5 to 95% and that of pulmonary mucormycosis is 50–95% [1, 3, 6–8]. There are very few reports of mucormycosis among SLE patients and the mortality could be over 50% [9–11]. The clinical features of mucormycosis include rhinocerebral (39–66%), pulmonary (16–24%), central nervous system (9%), and gastrointestinal (7%) and local cutaneous involvement (10–19%) forms [3, 7].

This paper describes a patient receiving rituximab for SLE nephritis after remission that presented with severe pneumonia which was complicated by acute respiratory distress syndrome because of invasive mucormycosis.

2. Case Report

A 40-year-old female patient arrived at the Emergency Department of the Chung Shang Medical University Hospital, Taichung, Taiwan, because she had a fever, chills, and shortness of breath for a period of one week. Her past medical history was SLE nephritis for which she was put on a monthly dose of rituximab target therapy for the previous three months at a medical center hospital in Taipei, Taiwan. She did not have any pulmonary problems prior to this episode. On physical examination, the patient had a body temperature of 38.8°C (101.8°F), a heart rate of 140/min, and respirations at 24/min. Blood pressure was 142/89 mm Hg and oxygen saturation on room air was 90%. A complete blood count revealed hemoglobin levels of 11.4 g/dL, white cell counts of 2,010 cells/µL (myeloblasts 4%, metamyelocytes 8%, bands 7%, neutrophils 78%, and leukocytes 3%), absolute lymphocyte count 353 cells/µL (9%), absolute CD19 B lymphocyte 64 cells/µL (18.1%), absolute CD4 T-cell count 177 cells/µL, and absolute CD8 T-cell count 127 cells/µL. A chest X-ray after admission revealed the presence of bilateral infiltration and poorly defined nodular, cavitary opacities in both lower lungs (Figures 1(a) and 1(b)) and a clinical diagnosis of pneumonia was made. After admission, she was treated with piperacillin/tazobactam and azithromycin, but the patient experienced rapid progression to acute respiratory distress. Fluconazole and methylprednisolone were put on hospital day two. On the third day of hospitalization, she developed septic shock and acute respiratory failure and required urgent ventilation and extracorporeal membrane oxygenation (ECMO). Piperacillin/tazobactam, azithromycin, fluconazole, and methylprednisolone were discontinued and meropenem, sulfamethoxazole/trimethoprim for pneumocystis pneumonia, and micafungin (3.5 mg/kg/day) for invasive fungal infection were started at that time. Three days after admission, bronchoalveolar lavage (BAL) showed blood tinged mucous fluid and numerous macrophages and a bit of Gram-negative bacilli and yeast on a Gram stain. A chest computed tomography (CT) image reveals a minimal amount of pleural effusion and poorly defined nodular, cavitary opacities and ground-glass opacities in both lower lungs (Figures 1(c) and 1(d)). Microbiological and serological studies for Legionella pneurnophila, Human Immunodeficiency Virus-1, Epstein-Barr virus, Cytomegalovirus, Cryptococcus neoforms, Streptococcus pneumoniae, Chlamydia pneumoniae, Mycoplasma pneumonia, and tuberculosis were all negative. Three sets of blood cultures drawn at admission and bacteria cultures of sputum were sterile after seven days of incubation. The patient’s condition deteriorated in the intensive care unit. On hospital day 11, the patient was declared dead. Cultures from BAL yielded Rhizopus species on hospital day 13 (Figures 2(a) and 2(b)). By now there was a clinical diagnosis of pulmonary infection with mucormycosis.

3. Discussion

There has been a marked increase in the incidence of opportunistic fungal infections worldwide and an even more pronounced increase with mucormycosis [3, 8]. The clinical manifestations of mucormycosis are broad and depend on the patient’s immune status and underlying conditions [3]. There has been an increase in the number of reports of mucormycosis in patients with SLE [11]. All patients with SLE that are immunocompromised involve intrinsic defects in immune function and hypogammaglobulinemia and as such are typically receiving immunosuppressive medicine anti-CD20 monoclonal antibody (mAb) rituximab and glucocorticoid therapy for control of SLE nephritis. Thus, such patients, including the patient described in this case report, are at high risk of invasive fungal infection.

Long-term corticosteroid therapy enhances a patient’s susceptibility to mucormycosis by causing defects in macrophages and neutrophils [1, 12]. The adverse events of mAb include infusion-related acute anaphylaxis, serum sickness, infections, dermatitis, cancer, autoimmune disease, and cardiotoxicity [13]. Types of infectious complications related to rituximab include bacterial infections, viral reactivation, mycobacterial infections, fungal infections, and protozoal infections [13]. Invasive aspergillosis and candidiasis have been reported in high-risk patients; however, pulmonary mucormycosis related to rituximab treatment has not been reported before [13, 14]. In this case, the use of rituximab might have affected CD4 T-cell dysfunction and was suspected as contributing to pulmonary mucormycosis [14].

At first, she suffered from dyspnea and fever intermittently for 7 days. A chest X-ray revealed both cavitary lower lungs and opacity infiltration. Hence, the tentative diagnosis was SLE relapse and a pulmonary infection. The high level of CRP was probably indicative of a bacterial or fungal infection. She was initially treated with a broad-spectrum antimicrobial agent and preemptive antifungal agent such as fluconazole and micafungin. The clinical course of pneumonia was so fulminant that despite using ECMO in the ICU the patient still died. The sputum culture showed Rhizopus species after her death.
Figure 1: (a) Admission anteroposterior chest radiography shows multilobar solitary nodules and consolidation. (b) Anteroposterior chest radiography on hospital day 10 shows diffuse consolidation of bilateral lungs and pneumothorax with subcutaneous emphysema in soft tissues. (c) Chest CT scan (contrast) shows diffuse irregular rim of consolidation and multiple solitary nodules of bilateral lungs. (d) Chest CT scan (lung window) shows diffuse consolidation with multiple air lucencies and solitary nodules of bilateral lungs.

Pulmonary mucormycosis develops after inhalation of fungal sporangiospores, by spreading from hematogenous or lymphatic system to the lungs or angioinvasion causing necrosis and infarction of the affected tissues [8]. Pulmonary mucormycosis can present as mild to severe such as fever unresponsive to antibiotics, dyspnea, cough, pleuritic chest pain, and hemoptysis [7]. It may invade organs adjacent to the lungs, such as the mediastinum, pericardium, and chest wall, or it may disseminate systemically. Invasion of the large mediastinal vessels can lead to massive hemoptysis, which has occasionally been fatal [1]. The signs of pulmonary mucormycosis on chest images are nonspecific and indistinguishable from those of pulmonary aspergillosis [8]. Findings include consolidation, nodules, masses, cavities, pleural effusion, atelectasis, posterior tracheal band thickening, and hilar or mediastinal lymphadenopathy. Chest radiograph can even be normal [7]. When reading chest CT images, the air crescent sign (a thin rim of air between the necrotic lung and the surrounding parenchyma) and the halo sign (consolidation with a rim of surrounding) suggest the presence of an invasive fungal infection [7, 8]. The reverse halo sign may be an early indicator of pulmonary mucormycosis. These images are also able to detect lesions [8]. But these cannot distinguish mucormycosis from aspergillosis.

Direct examination of sputum, paranasal sinus secretions, or BAL fluid is frequently nondiagnostic, but isolation of Mucorales organisms in such specimens from a susceptible host with pneumonia or rhinocerebral infection should be considered a strong indicator of mucormycosis [8]. Direct histological examination of a tissue biopsy remains the gold standard for diagnosis [8, 12]. In the patient, the clinical diagnosis of pulmonary mucormycosis was based on the
Figure 2: Microscopic features of the *Rhizopus* species isolated from bronchoalveolar lavage culture of the patient. (a) Sporangiophores are long and nondichotomous, usually terminating in large globose sporangia (100×). (b) Sporangiophore with sporangium contains numerous sporangiospores (400×).

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

Authors’ Contribution

Gang-Yu Shen made an equal contribution as first author.

Acknowledgments

The authors would like to thank the Institute of Medicine and School of Medicine, Chung Shan Medical University, Taichung, Taiwan, for the chemicals and instrumental facilities use.

References


