

Coexisting Pulmonary Tuberculosis and Rhino-Orbital Mucormycosis in Diabetes Mellitus — A Case Report

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Abstract

Mucormycosis occurs predominantly in patients with diabetes and other immunosuppressed patients. It is acute, fulminant, and often fatal. Tuberculosis, in contrast, is insidious, chronic debilitating, and may be fatal within several years if untreated. We report a 66-year-old male with fever, epistaxis, shortness of breath and pulmonary infiltration. Diabetes mellitus with ketoacidosis was found after admission. Pulmonary tuberculosis and rhino-orbital mucormycosis were diagnosed by tissue biopsy. The patient received anti-tuberculosis chemotherapy, sinusoscopic debridement and amphotericin B. Despite our vigorous treatment, the patient died 35 days after admission. The coexistence of tuberculosis and mucormycosis in a patient is rare. On searching Medline database, we can not find a similar case record dated back from 1966 till now. (J Intern Med Taiwan 2004; 15: 86-90)

Key Words : Tuberculosis, Mucormycosis, Diabetes mellitus

Introduction

There are several unusual infections occur predominantly or even exclusively in patients with diabetes mellitus (DM), among them, rhinocerebral mucormycosis continues to be of great concern. The clinical course of mucormycosis is usually acute, fulminant, and often fatal.

Tuberculosis (TB), despite effective screening measures and chemotherapy regimen, remains a major threat to diabetes as well as general population here in Taiwan. The clinical course of TB is usually insidious and chronic debilitating.

We report a rare DM case in which coexisting pulmonary TB and rhino-orbital mucormycosis were found. The patient received standard anti-TB chemotherapy, surgical debridement and amphotericin B. However, despite our vigorous treatment, the patient died 35 days after admission. On searching Medline database, we can not find a similar case record dated back from 1966 till now.

Case Report

A 66-year-old male sugar cane farmer, with a 30 pack-year cigarette exposure, presented with acute onset of fever, epistaxis, and shortness of breath for one day before admission. The patient had a history of chronic obstructive pulmonary diseases, with several acute exacerbation episodes which required admission treatment. A DM history was denied.

On physical examination, the patient appeared acute ill-looking and moderate dyspneic. The temperature was 39 degrees Celsius. The eyes were grossly normal with adequate extraocular movements and age-matched visual acuity. Some blood clots were found in the nostrils. There were bilateral coarse rhonchi on chest auscultation. The other examinations were unremarkable.

The laboratory data were significant for a leukocytosis of 13,370/cumm with left-shift. The sugar level was 513 mg/dL with ketoacidosis. Arterial blood gas analysis revealed a PaCO₂ of 17.6 mmHg and a pH of 7.334. The sputum specimen grew *Escherichia coli*, *Klebsiella pneumoniae*, and *Serratia marcescens*. The blood cultures were negative, as was the sputum mycobacterial culture. A test for anti-human immunodeficiency virus antibody (IgG) was negative.

The chest radiograph and computed tomography (CT) showed bilateral pulmonary infiltration (Fig. 1,2). He was first treated as bacterial pneumonia with empiric antibiotics.

Because of persistent fever and respiratory symptoms, a CT-guided lung biopsy was performed. Pulmonary tuberculosis was diagnosed by typical histologic findings (Fig. 3A & 3B). Standard anti-TB chemotherapy with isoniazid, rifampicin, ethambutol and pyrazinamide was started.

Despite the aforementioned treatment, the patient still appeared very uneasy and had persistent fever. Two weeks after admission, right eye chemosis, blurred vision and periorbital swelling developed. Epistaxis was also reported. A magnetic resonance imaging (MR) study of orbits (Fig. 4) demonstrated paranasal sinusitis, abnormal enhancement of right optic nerve, retrobulbar fat and adjacent soft tissue. The cerebrum was intact. Sinoscopic biopsy and debridement was performed, with multiple black eschar, destructive tissue and pus removed. The histologic finding was consistent with mucormycosis (Fig. 5). *E. coli* and mold-like organisms were isolated from the pus sample. On fungal stain, *Absidia* species was identified (Fig. 5).

Incremental doses of amphotericin B was initiated, in addition to the previous anti-TB therapy. However, despite our vigorous treatment, the patient died of acute renal failure and sepsis 35 days after admission.

Discussion

Although a common belief, increased susceptibility to infection in DM is not

supported by strong evidence 1-2. Nevertheless, there are several uncommon infections occur predominantly or even exclusively in diabetic patient, such as malignant external otitis, rhinocerebral mucormycosis, emphysematous pyelonephritis, and emphysematous cholecystitis¹. Mucormycosis, caused by a group of saprophytic fungi of the order Mucorales, is typically seen in debilitated patients, patients with diabetic ketoacidosis, and patients who are severely immunosuppressed. It occasionally occurs in healthy individuals³. The clinical course is acute, fulminant, and often fatal.

Clinical subtypes of mucormycosis include rhino-orbito-cerebral or rhinocerebral, pulmonary, gastrointestinal, disseminated, and cutaneous forms. Among them, the rhino-orbito-cerebral form is the most common and carries the highest mortality rate⁴. Approximately 50% of rhinocerebral mucormycosis occur in diabetic patients, ketoacidosis is the most important risk factor².

Rhino-orbital mucormycosis, a variant of rhino-orbito-cerebral mucormycosis, is characterized by sinusitis, and a painless, necrotic black palatal or nasal septal ulcer or eschar³. Without early treatment, the fungus may rapidly disseminated by the vascular route, causing death within days. Histopathological studies show hyphal invasion of blood vessels, including the carotid arteries and cavernous sinuses; vasculitis with thrombosis; hemorrhage; and tissue infarction³.

Early surgical intervention plus systemic amphotericin B is the hallmark of treatment. The major side effect of amphotericin B is nephrotoxicity which can be reduced by the use of the later developed liposomal forms. With the combination of surgical and antifungal treatment, the prognosis remains poor, a cure rate of 30-80% has been reported, the lowest rate is associated with intracranial involvement⁵.

TB, once a proven threat to diabetics and the general population, is now a less serious health problem owing to effective screening programs and chemotherapy regimen⁶. However, TB persists as a major public health issue as each year, between 3.5 and 4 million new cases were reported worldwide where 90% were from developing countries⁷. In Taiwan, we have a total of 16,089 new TB cases reported in 2002, among them 14,250 (87%) were pulmonary TB⁸.

A coexistence of such acute, fulminant infection as rhino-orbital mucormycosis and chronic, debilitating pulmonary TB in diabetic mellitus is extremely rare. One of the reasons may be the consistently poor prognosis of mucormycosis and its fulminant nature. On searching Medline database, we can not find a similar case record of coexisting tuberculosis and mucormycosis dated back from 1966 till now.

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Fig.1. Chest anteroposterior view with portable machine, showing bilateral pulmonary infiltration

Fig.2. High resolution CT of chest at the level of carina, showing bilateral airspace disease and interstitial infiltraiton

Fig.3A. Chronic granulomatous inflammation, focal areas of caseating necrosis with surrounding inflammatory cells and nuclear debris in the lung tissue (Hematoxylin & Eosin, 400X).

Fig.3B. Numerous acid-fast bacilli are found. (Acid-fast stain, 1000X)

Fig.4. T1-weighted axial MR image of the orbits with fat suppression and contrast enhancement shows paranasal sinusitis (arrows), marginal enhancement of the right optic nerve (arrow head), abnormal enhancement of the retrobulbar fat and adjacent soft tissue (asterisks). There is no cerebrum involvement.

Fig.5. Inflammatory exudate with fungal elements is found in the necrotic nasal tissue. The hyphae are ribbon-shaped, nonseptate, broad with right-angle branching (arrow) which are characteristics of mucormycosis. (Periodic acid-Schiff stain, 400X). Sporangia characteristic of *Absidia* species are found on lactophenol cotton blue stain (Inset, 200X)

於糖尿病人身上同時發生的肺結核與鼻-眼眶白黴菌病：一病例報告

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摘 要

白黴菌病常見於糖尿病或免疫受抑制的病人，其病程常是急性，猛爆性且常常致死。相反的，肺結核剛開始時症狀較不明顯，多造成慢性虛弱，如不治療會在數年內死亡。我們報告一個 66 歲男性因發燒，流鼻血，氣喘及肺浸潤住院。住院後發現有糖尿病合併酮酸中毒。肺結核及鼻-眼眶白黴菌病依切片得到証實。其後病人接受抗結核藥物，外科清創及 amphotericin B 治療。雖經積極治療，病人仍於住院後 35 天死亡。白黴菌病與結核病同時發生很罕見，經查 Medline 資料庫，從 1966 至今並無相似個案報告。