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RESEARCH ARTICLE

A PULMONARY ASPERGILLUS NIGER INFECTION IN A DIABETIC KETOACIDOSIS PATIENT

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ABSTRACT

Pneumonia is the most common reason for diabetic ketoacidosis. Although the pathogen was uncommonly Aspergillus niger. Aspergillosis is opportunistically found in human individuals. The onset was insidious but the disease progressed quite rapidly. Herein we have reported a case of diabetic ketoacidosis that was associated with invasive pulmonary Aspergillus niger infection After receiving Fluconazole and amphotericin B, the patient recovered gradually three months later. Our experience suggested that timely bronchoscopy might play an important role in the early diagnosis and treatment of Aspergillus infection.

INTRODUCTION

The incidence of invasive aspergillosis infection has been commonly found in patients that present with immune injury such as in the settings of diabetes mellitus, long-term steroid treatment and immunosuppressive agent use. Invasive aspergillosis infection has five species have been reported to cause human infection, and these are: A. fumigatus, A. flavus, A. niger, A. terreus and A. nidulans .In our study, the cause was uncommonly "Aspergillus niger" in the diabetics, which is transmitted by inhalational exposure (Thomas, 2008). So we are difficult to recognize it. But it has been well documented that hyperglycemia and acidosis predispose the susceptible patient to fungal growth (Martin-Moro, 2008), such as diabetic acidosis patients. These two factors might increase the release of iron under conditions of acidosis and might enhance spore and hyphal growth (Khaled, 2010). Furthermore, some strains are found to produce ochra-toxi; however, there is scant additional information that is currently known about the biosynthetic mode of action of mycotoxin in this species. The way that A. Niger infiltrates the membrane covering the mucosa is described as invasive pulmonary aspergillosis (IPA) or Aspergillus tracheobronchitis (ATB). Normally, symptoms of this pulmonary infection are non-specific and usually mimic bronchopneumonia. The methods used to examine infection with aspergillosis or IPA include chocolate culture-medium, blood culture-medium and lactophenol cotton blue staining throughout the bronchoscopy. In addition, with the assistance of pathology and laboratory examinations throughout the bronchoalveolar lavage (BAL), the diagnosis is confirmed. The key feature in the diagnosis of Aspergillus infection is the presence of calcium oxalate crystals by pathological examination. Oxalic acid precipitates and forms crystals during fermentation. Although onset of Aspergillosis was insidious, but the symptoms developed quickly. Therefore, we are able to stress on the pathogen and acquire the correct treatment in time, the survival rate will be increasing. Herein we have reported a successful case of diabetic ketoacidosis that was associated with invasive pulmonary Aspergillus Niger infection.

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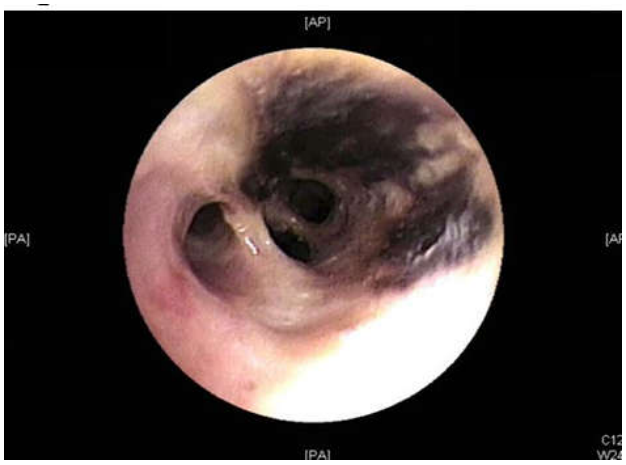
CLINICAL RECORD

MATERIALS AND METHODS

In January 2014, a 43-year-old Chinese female worker was transferred to an outpatient clinic for presentation of

progressive dyspnea and low-grade fever in a few days. She had a past history of poorly controlled type 1 diabetes mellitus (DM) for 10 years. But she ceased insulin use a few months before arriving at the medical center, and she appeared well until she had a tooth extracted one week ago before being admitted. She had no family history of DM. She was also a non-smoker. Review of this patient was unremarkable. The patient had a blood pressure of 105/75 mm Hg, and her temperature was 38.5□. On two liters of oxygen/min via a nasal canula, she was mildly tachypenic (i.e., 23 breaths/min) with an oxygen saturation of 96%. Her breath sounded clearly and there was no evidence of significant rales or wheezing. Heart rate was also tachycardic (i.e., 105 beats/min), and no irregular rhythm or murmur were found. On the fist day of admission, her blood glucose level was 818 mg/dL, and she was diagnosed with severe diabetic ketoacidosis according to abnormal blood gas measurements and biochemical analysis (i.e., pH 6.798, PaCO2 14.7 mmHg, PaO2 221 mmHg, bicarbonate 2.2mmol/L, lactate, 3.43mmol/L, and urine ketone levels >15 mmol/L). Routine blood tests showed that the differential white blood cell count (WBC) was 54.50 /mm3 including 82.0 % segment and her C-reactive protein (CRP) level was 200.84 mg/L. The blood culture did not growth any pathogen. Furthermore, the chest radiograph showed no positive findings. We aggressively administered as first-line management of severe diabetic ketoacidosi such as initial fluid resuscitation and insulin therapy. In addition, the antibiotic combination of ceftriaxone (1 g, twice daily) and levofloxacin (0.6 g four times per day) were administered due to unexplained infection. On the second day of admission, the blood sugar was controlled, but dyspnea developed that was accompanies by a higher fever (39.5 □).

Her vital signs were also unstable. Tracheal intubation was performed to overcome continuous hypoxia and volume expansion was used to treat shock. We found the black secretions which cover the vocal cords during the tracheal intubation. Repeated the chest radiography revealed pneumonia in the right lower and left middle lobe of the lungs. Eight hours later, a non-contrast-enhanced computed tomography (CT) scan showed extensive pneumonia in the right lung field. We found the dark secretions throughout bronchoscopy (Fig.1) and bronchoalveolar lavage (BAL) of the right middle lobe was performed.



(Fig.1) Bronchoscopy showed the dark tissue and secretions

These findings were sent for pathological and microscopic determination. The the secretions of sputum showed spores and mycelium by lactic acid phenol medan stain (Fig.2). The pathology of secretions showed spores and mycelium (Fig.3).

Fig.2. Lactic acid phenol medan stain the secretions of sputum. Total magnification, x 400

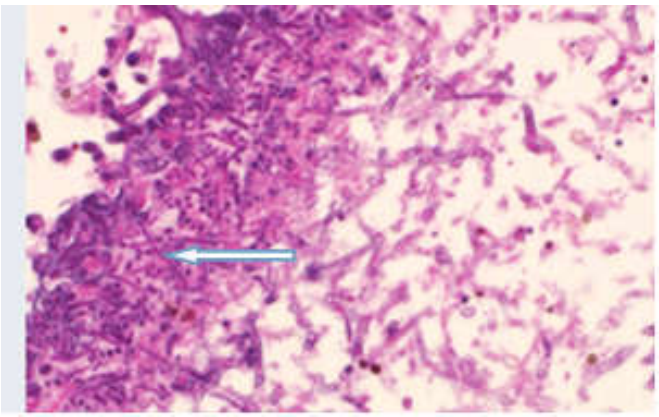


Fig. 3. Pathology of specimens from BAL showed spores and mycelium by the HE stain x 400.

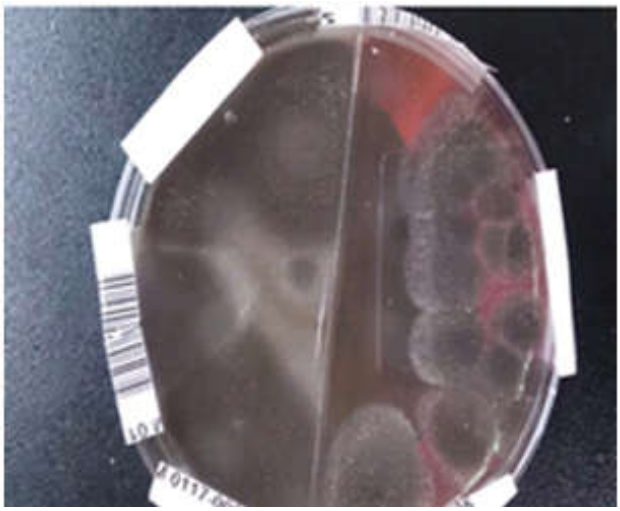


Fig.4.The sputum culture grew dark spores and hyphas after 3 days and demonstrated Aspergillus Niger Infection by the Chocolate plate culture medium

After 3 days the specimen culture grew dark spores and hyphas, finally, we demonstrated the "Aspergillus Niger Infection" by the Chocolate plate culture medium. (Fig.4).

RESULTS

According to the pathogen, the diagnosis of invasive pulmonary Aspergillus niger infection was established. Therefore, we quit the antibiotic use and changed into the antifungal agents such as Voriconazole (200 mg twice daily) was administered intravenously and Amphotericin B (10mg Q8H daily) was given by inhalation. Continuous supportive therapy and anti-fungal treatment was continued for 3 months. The patient recovered three months later which was approved by non-contrast Chest CT.

DISCUSSION

In nature, fungal species exist in soil, water, stale vegetables, any substrate that contains debris and human individuals themselves might give rise to opportunistic infection(3). Incidences of invasive aspergillosis infection have been commonly found in patients with immune injury such as that seen in diabetes mellitus, long-term steroidal therapy and following immunosuppressive therapy (Thomas, 2008). Five species of fungi that have beenassociated with lung infections have been previously reported: A. fumigatus, A. flavus, A. niger, A. terreus, and A. nidulans (Martin-Moro, 2008). In most cases, the cause of infection is following pulmonary exposure to A. fumigatus, which is transmitted by inhalation (Thomas, 2008). However, in our current report, the cause was uncommonly A.niger. Although fungal infections are found in diabetic patients with uncontrolled blood sugar levels due to immunosuppression, it is rare to find invasive aspergillosis in the same group of patients (Gallien, 2008). It has been well described that hyperglycemia and acidosis predisposes the patient to fungal growth (Martin-Moro, 2008). Both of these factors might increase the release of iron from transferring it under conditions of acidosis and enhancing spore and hyphal growth (Khaled, 2010). In aspergillus infections, the siderophore and spore pigmentation may be determined by the link in genes that might be involved in secondary metabolite synthesis (Mogensen, Jesper, 2009).

Aspergillus might also have the potential to produce mycotoxins such as that synthesized by A.niger, which produces black aspergillus toxins (Iwen, 1998). Furthermore, some strains produce ochra-toxin, but nothing else is known about the biosynthetic pathway leading to mycotoxin production in the species. In most cases, aspergillus might be introduced to the lower respiratory tract by inhalation of the infectious spores. The tracheobronchial tree was influenced primarily from evidence that pathogens infect the lower airways, and this strain is known Aspergillus tracheobronchitis. The ways by which these pathogens infiltrate the membrane covering the mucosa are described as invasive pulmonary aspergillosis (or IPA)(4). Besides, Aspergillus might infect locations near the lung, such as the sinuses, gastrointestinal tract or the skin via intravenous catheters, prolonged skin contact with adhesive tapes and burns (Samson, 2001). Normally, symptoms of this pulmonary infection are non-specific and usually mimic bronchopneumonia, for example, fever, unresponsiveness to antibiotics, cough, sputum production and dyspnea. Patients may also present with pleuritic chest pain due to thrombosis (Gallien, 2008). Chest X-ray is usually normal in the early stages but soon changes its state after a few days. In our case, after performing tracheal intubation, we inadvertently found dark secretions covering the glottis. Therefore, we arranged for bronchoscopy and took some samples by bronchoalveolar lavage (BAL). The methods of examination were chocolate culture-medium, blood medium and lactophenol cotton blue stain. Additionally, with the assistance of pathology and laboratory examinations of the BAL specimens, we adjusted the diagnosis and treatment accordingly. The timing of clinical management is crucial. The spores are regarded as minute clusters of cells that consist of a cell membrane, cytoplasm, pili, capsule, plasma membrane and ribosomes. The key feature in the diagnosis of Aspergillus infection is the presence of calcium oxalate crystals by pathological examination. Oxalic acid precipitates and forms crystals during fermentation. Hence, the association of calcium oxalate crystals and Aspergillus infection has been found, and even in the absence of visualized conidia, the presence of these crystals may indicate Aspergillus infection (Fang, 2012). Unfortunately, our case could not perform the exam. Mortality rates from mycoses often exceed 50%. In our case, the patient was successfully treated by voriconazole, which was one of the key anti-fungal agents, which includes polyenes (amphotericin b deoxycholate, and three lipid formulations of amphotericin b), triazoles (fluconazole, itraconazole, voriconazole, and posazole), and the echinocandins (caspofungin, micafungin, and anidulafungin), and flucytosine. One large randomized controlled trial demonstrated that voriconazole improved survival rates and decreased drug-related adverse events in a 12-week treatment regimen as compared with amphotericin B (Person, 2010).

Summary

As a group, we reported a patient diagnosed with invasive pulmonary Aspergillosis Niger with diabetic ketoacidosis. The onset was insidious but the disease progressed quite rapidly. We successfully used anti-fungal treatment that was based on pathological and microscopic examinations of tracheobronchal specimens. Our experience suggested that timely bronchoscopy might play an important role in the early diagnosis of Aspergillus infection, especially for those patients who are immunosuppressed as might be commonly found in the setting of diabetes mellitus.

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Conflict of Interest: The authors declare that they have no conflict of interests.

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