Case report

Recurrent pulmonary mucormycosis after lobectomy in a non-smoking patient without predisposing risk factors

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Introduction

Mucormycosis (also termed as zygomycosis) is an opportunistic infection caused by fungi from the order of Mucorales, which are quite common in the environment. Clinical infections caused by such fungi usually occur in the presence of predisposing risk factors, such as diabetes mellitus, hematologic malignancies, hematopoietic stem cell transplantation, deferoxamine therapy, HIV infection, iron overload, trauma or burns, and use of corticosteroids or immunosuppressive drugs.1-2 Mucormycosis in patients without underlying conditions is rare, and when it occurs, it is likely to be a superficial infection.2 Pulmonary mucormycosis in such patients is exceedingly rare. To the best of the authors' knowledge, only ten cases have been previously reported3-12 in the literature, and most were elderly male smokers. Herein is reported a case of a non-smoking young male who was 12 years old at the onset of the disease. With the longest follow-up known in literature, this is also the first reported case of an immunocompetent patient who suffered from disease recurrence after lobectomy (two years) in an immunocompetent host. Treatment with an additional lobectomy and amphotericin B was successful in this patient.

Case presentation

In August, 2008, a 14-year-old boy was referred to this hospital with a two-month history of fever, cough, purulent sputum, and nasal discharge. Two years earlier, he had undergone a lobectomy of right inferior lobe at a local hospital due to fever and pulmonary mass in the right lung, with a post-operative
pathological diagnosis of ‘inflammatory pseudotumor’. After
the surgery, he was doing well until two months before this
admission. He was an otherwise healthy boy with no his-
tory of diabetes mellitus, hematologic malignancies, burns or
trauma, intravenous drug use, malnutrition or diarrhea, renal
failure, or use of corticosteroids or immunosuppressive drugs
or deferoxamine. He lived in a small village in the Shandong
province of China, with both parents working as corn farm-
ers. The boy sometimes helped with farming as well. He was
a non-smoker and had never consumed alcohol.

On examination, the patient was febrile with a tempera-
ture of 38 °C and normotensive. Purulent nasal discharges
associated with sinus pain were noted. Breath sounds were
low in both lower lungs with crackles heard on the left side.
Laboratory investigation showed the following results (normal
reference range in parenthesis): hemoglobin 12.1 (11.0-16.0)
g/dL; white blood cell count, 9.5 × 10⁹ (4.0-10.0 × 10⁹) cells/L;
raised erythrocyte sedimentation rate of 53 (<20) mm/h and
elevated C-reactive protein level of 91.4 (<3) mg/L; serum urea,
3.5 (2.5-6.5) mmol/L; creatinine, 64 (60-110) µmol/L; sodium,
136 (135-145) mmol/L; and potassium 4.0 (3.5-5.5) mmol/L.
Liver function tests were normal: total proteins, 71 (60-85)
g/L, alanine transaminase (ALT), 11 (10-40) IU/L; aspartate
transaminase (AST), 21 (8-40) IU/L; albumin, 40 (35-55) g/L; and
alkaline phosphatase (ALP) 60 (44-147) IU/L. Serum protein
electrophoresis showed elevated gammaglobulins. A 75 g oral
glucose tolerance test was normal. HIV serology was negative.

Results of serum iron studies were all within normal range:
serum iron concentration, 84 (60-150) microg/dL; plasma total
iron binding capacity, 288 (200-400) microg/dL; transferring
saturation, 29 (25-35)%; serum ferritin concentration, 46 (14-
336) ng/mL. Sputum cultures were negative for bacteria or
fungi. Sinus computed tomography (CT) scan revealed a dense
and non-homogeneous mass and sinusitis in the left max-
illa, and chest CT showed a mass with a diameter of 3 cm in
the left inferior lobe (Fig. 1A). Endoscopic evaluation of the
left maxillary sinus showed tissue necrosis and the pathology
of the specimen was ‘chronic inflammation’. A careful scruti-
nization of the chest CT confirmed that there was no lesion
in the left lung at the initial presentation of the disease, and
a review of the lung specimen taken from the right inferior
lobe two years before showed an unknown branched pathogen
with positive methenamine silver stain. Further, transtho-
racic lung biopsy exhibited inflammatory changes and some
broad, non-septate hyphae with positive methenamine silver
stain, suggestive of pulmonary mucormycosis. A left inferior
lobectomy was performed with thoracoscopic. Histopatho-
logical examination of the resected lung tissue showed broad,
irregularly branched and non-septate hyphae (Fig. 1B). Rhiz-
opus oryzae were identified in tissue specimen culture. A
diagnosis of mucormycosis involving the left lung and sinuses
was therefore confirmed. Surgical debridement of the sinuses
was undertaken, and amphotericin B therapy was initiated.
The patient was defervescent after the treatment, and the
erythocyte sedimentation rate and C-reactive protein level
returned to normal. The boy was doing well during the follow-
up and was healthy on his last follow-up visit in September,
2011.

Discussion

Mucormycosis is an opportunistic infection that is very
rare in patients without predisposing risk factors. Superfi-
cial infections (such as cutaneous/subcutaneous infections)
are the most representative clinical manifestation.2 Deep
organ involvement is not common in immunocompetent indi-
viduals, while pulmonary mucormycosis is so rare that, to
the authors’ knowledge, only ten other cases of pulmonary
mucormycosis (excluding mucormycosis involving only the
mediastinum without either lung) in patients without under-
lying disease have been reported in the English language
literature3-12 since 1950 (Table 1). The present case not only
adds a further illustration of this rare medical condition, but
is also of interest for several reasons.

First, although the previously reported cases all included
patients without obvious underlying diseases, several potent-
tial risk factors might have still existed in some of them;
such as mild diabetes, broad-spectrum antibiotic treatment
after a fracture, etc.4,5 Moreover, almost all patients were
chronic smokers (five out of six after excluding those with-
out a clear history of smoking, and a two month old infant);7
and smoking, which may enhance the virulence of fungi13
and compromise the protective barriers14 in airways, has been
demonstrated to be a risk factor in fungal infection other than
mucormycosis.15 Furthermore, patients from most of the pre-
vious reports were of older age (mean age, 53 years; excluding
the infant), which often leads to a greater chance of having

Fig. 1 - (A) Chest CT scan showed a mass in lower lobe of the left lung. (B) Broad, irregularly branched and non-septate
hyphae with positive methenamine silver stain observed in lung tissue (magnification, × 40).
underlying conditions. One of the patients, for example, was a 72-year-old male\textsuperscript{12} with a history of malaria and right clavicle and maxillary fracture. The present patient, at a much younger age and with no history of smoking, may provide more convincing evidence that a patient without any known risk factors can be a victim of mucormycosis. This might be due to the devastating nature of these filamentous fungi, capable of secreting several toxins or proteases,\textsuperscript{16} which may directly destroy endothelial cells in mucosal membranes and cause subsequent deep organ infection.

Second, although surgery alone has been proved successful in patients with pulmonary mucormycosis confined to one or two lobes,\textsuperscript{3,4,6,9,12} the present case showed that recurrent infection might be a problem in postoperative patients without continued treatment with anti-fungal drugs. To the best of the authors’ knowledge, this is the only reported case of an immunocompetent patient suffering from recurrent pulmonary mucormycosis after lobectomy surgery. This might be due to two possible reasons: first, the longer follow-up of the patient (five years after symptom onset and two years after recurrence of infection) compared to other cases (mean follow-up of 16 months). There is a possibility that the patients with surgical therapy alone might have increased risk of recurrent mucormycosis if the follow-up period were extended.

The other potential reason might have been the concomitant sinonasal involvement in this patient, as the sinus could serve as a fungi ‘reservoir’ after pulmonary lobectomy that leads to further recurrence. Therefore, the findings from the present case suggest that surgery and antifungal therapy might be of equal importance even for patients without underlying conditions, and the sinonasal involvement could serve as a potential risk factor for disease recurrence. Moreover, as the importance of combination therapy consisting of surgery and antifungal chemotherapy has been long recognized because it could improve patients’ survival,\textsuperscript{1} this case also indicates that combination therapy might prevent disease recurrence.

With a careful review of all the reported cases and the present case, it was found that almost all patients faced at some time in their life, with the only exceptions being the infant and those without reported occupational history. This finding possibly reflects the fact that fungi in the order of Mucorales often exist in decaying vegetation and in soils. Thus, farming could be a predisposing risk factor and taking a careful history might help.

Last but not the least, although cases of mucormycosis without obvious risk factors have been reported in many other countries,\textsuperscript{2} no such cases have been reported in China, the country with the largest population.\textsuperscript{2} Considering that the language barrier could be a contributing factor, no such cases were found in the Chinese language database CNKI (China National Knowledge Infrastructure, the largest academic database in China). This might be due to the under-recognition of this disease in the immunocompetent population in China, and in the present case, for example, the local hospital missed the diagnosis. The authors thus hope that this present case report can raise vigilance for the disease in China.

### Conclusion

Pulmonary mucormycosis in the absence of underlying disease is a very rare clinical condition. The reported case of a young male without history of smoking suggests that a patient without any known risk factors could have pulmonary mucormycosis. Surgical resection alone might be insufficient for eradication of pulmonary mucormycosis, even for localized lesions, and recurrence of disease could ensue after surgery. Antifungal therapy has proved to be beneficial for...
patient outcome. Farming might serve as a risk factor, and taking a careful history is warranted in suspicious cases.

Conflict of interest

All authors declare to have no conflict of interest.

Acknowledgements

The authors thank Dr. Yi Xiao, Dr. Hongbing Zhang, and Dr. Dingxin Qin for the support of the study and revision of the manuscript.

REFERENCES