Acta Scientific Cancer Biology

Volume 1 Issue 1 June 2017

Research Article

Retrospective Analysis of 49 Cases Pulmonary Mycosis in Immunocompetent Patients

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Received: June 06, 2017; **Published:** July 12, 2017

Abstract

Objective: This study aimed to investigate the etiology, clinical manifestations, radiographic features, diagnosis and managements of pulmonary mycosis. It also explores the incidence and clinical characters of coexist of pulmonary mycosis and lung cancer.

Methods: 49 patients identified by pathological examinations in Hunan Cancer Hospital from January 2010 to June 2015 were analyzed retrospectively. Clinical manifestations, radiographic characterization, diagnostic methods, management and prognosis were analyzed.

Results: Among 49 cases, 29 cases (59.2%) were pulmonary aspergillosis, 14 cases (28.6%) were pulmonary cryptococcosis. All the patients were identified by pathological examinations. 36 cases (73.5%) obtained lung or bronchi tissues by open-lung operation, 8 cases (16.3%) by trans-bronchial biopsy, and 5 cases (10.2%) by CT-guided percutaneous needle biopsy. Main symptoms include: cough 33 cases (67.3%), expectoration 23 cases (46.9%), haemoptysis 13 cases (26.5%), fever 8 cases (16.3%), and asymptomatic 9 cases (18.4%). The X-ray and chest CT showed masses or nodular lesions in 36 cases (73.5%), cavity formation in 10 cases (20.4%). Surgical resection was performed in 36 patients (73.5%). 15 cases (30.6%) received systemic antifungal therapy, 13 cases (26.5%) experienced complete responses or partial responses. There are pulmonary mycoses with lung cancer in 9 cases (18.4%). All the patients are smoker and with solitary pulmonary lesions. Pulmonary mycosis and lung cancer were found in the same site in 6 cases. All the patients further received surgical resection without recurrence.

Conclusions: The main pathogens of pulmonary mycosis were aspergillus, followed by cryptococcosis. Final diagnosis was mainly depended on pathological examinations. Coexist of pulmonary mycosis and lung cancer has been underestimated. Satisfactory results can be obtained by both anti-fungi treatments and surgical treatment.

Keywords: Pulmonary Mycosis; Etiology; Lung Cancer; Pulmonary Aspergillosis

Introduction

The etiology and incidence of pulmonary mycosis have changed during the past few decades. It has been estimated that fungi accounted for 12% of all the 177 human pathogens [1,2]. And both the absolute numbers of patients with pulmonary mycosis and the diversity of pathogens have changed dramatically [1,3]. However, due to lack of specific clinical manifestations and imaging features, the diagnosis of pulmonary mycosis is difficult.

Another important fact is that pulmonary infections and malignancies occasionally co-exist successively or simultaneously in the same patient [4,5]. As a cancer specialist hospital, the majority of patients received surgical resection, with a tendency to be malignant. It is great clinical challenging to make precise and complete diagnosis of comorbid diseases. And co-exist of lung cancer with pulmonary mycosis is life threating. Early diagnosis and prompt initiation of therapy could significantly improve the outcome. However, studies of comorbid diseases are rare.

In order to further investigate the pathogenesis, clinical manifestations, prognosis and the risk factors of pulmonary mycosis, also to explore the incidence and clinical characters of coexist of pulmonary mycosis and lung cancer, we performed a retrospective analysis of all patients with pathologically confirmed pulmonary mycosis from a single institution during January 2010 to June 2015.

Methods

Patient Selection

From January 2010 to June 2015, 49 patients were identified with pulmonary mycosis by pathological examination in Hunan Cancer Hospital in China. Inclusion in this analysis required patients with proven pulmonary mycosis based on the Revised Definitions of Invasive Fungal Disease from the European Organization for Research and Treatment of Cancer/Invasive Fungal Infections Cooperative Group and the National Institute of Allergy and Infectious Diseases Mycoses Study Group (EORTC/MSG) Consensus Group [6]. Proven pulmonary mycosis required histopathology or microbiologic documentation of infection from tissues obtained by biopsy or in culture samples from a normally sterile site. Approval from our hospital to use patients' records for this study was obtained and patients' confidentiality was maintained.

Clinical and radiographic manifestations analysis

Two chest radiologists with more than 10 years of experience independently reviewed imaging and clinical data from all patients, and decisions concerning the findings were reached by consensus. Clinical data were collected from electronic records. Medical records created at the time of admission were reviewed for complaints of chest pain, cough, sputum and fever. Chest CT images acquired for all patients at admission were examined to determine the presence of nodules, masses, areas of consolidation, atelectasis, ground-glass opacities, and the tree-in-bud pattern. For all nodules and masses (based on 3.0 cm size criteria), the location, size, margins, presence of cavitation, necrosis (determined by low attenuation), and number of lesions (solitary or multiple, based on two or more lesions criteria) were recorded.

Efficacy and Safety Evaluation

The overall efficacy and safety were defined according to specific criteria [7].

Statistical Analysis

Data among different groups were analyzed with χ^2 test. Groups were compared by SPSS16.0. A p value < 0.05 was considered statistically significant.

Results

Etiology

Among the 49 patients, 29 cases (59.2%) were identified as pulmonary aspergillosis, 14 cases (28.6%) as pulmonary cryptococcosis, while 2 cases (4.1%) as pulmonary candidiasis and 4 cases (8.2%) as other undifferentiated types.

Demographics

Among the 49 patients, males represented 38 cases (77.6%), female 11 cases (22.4%), with a male to female ratio of 3.5:1. Patients' median age was 46.3 (ranged from 33 to 68) years. There were 38 patients were with underlying diseases (77.6%), including 9 cases of lung cancer (18.4%), 6 cases of COPD (12.2%), 5 cases of bronchiectasis and tuberculosis respectively (10.2%), 4 cases of diabetes, coronary disease and hypertension respectively (8.2%), 1 case of pulmonary cysts, gout and SLE respectively. No patient used corticosteroids and immunosuppressive agents for more than 6 months. None of the cases are with HIV infection. The incidence of underlying diseases in pulmonary aspergillosis was 82.8% and the incidence in pulmonary cryptococcosis was 64.3%. Details of patients' demographic are given in Table 1.

	Pulmonary Aspergillosis	Pulmonary Cryptococcosis	Pulmonary Candidiasis	Other undifferentiated types	Total
	N = 29	N = 14	N = 2	N = 4	
Male/female	4.8:1	2.5:1	1:1	3:1	3.5:1
Mean age	44.1	38.5	41	41.5	41.3
Underlying diseases	24	9	2	3	38

Table 1: Demographic data for 49 patients with pulmonary mycosis.

Diagnostic methods

Among the 49 patients, 36 cases was diagnosed by open-lung biopsy (73.5%); 8 cases were confirmed by trans-bronchial biopsy (16.3%); 5 cases were diagnosed by CT guided percutaneous needle biopsy (10.2%). Among the 8 cases of non-surgical pulmonary aspergillosis, 7 patients (87.5%) were confirmed by trans-bronchial biopsy. All the 4 cases of non-surgical pulmonary cryptococcosis cases were confirmed by CT guided percutaneous needle biopsy. Details of diagnostic methods, and final diagnoses are given in Table 2.

	Pulmonary Aspergillosis	Pulmonary Cryptococcosis	Pulmonary Candidiasis	Other undifferentiated types	Total
	N = 29	N = 14	N = 2	N = 4	
Open-lung biopsy	21	10	2	3	36
Trans-bronchial biopsy	7	0	0	1	8
CT guided percutaneous needle biopsy	1	4	0	0	5

Table 2: Diagnostic methods used in the 49 patients with pulmonary mycosis.

Clinical manifestations

The most common clinical findings were: cough in 33 cases (67.3%), expectoration in 23 cases (46.9%), hemoptysis in 13 cases (26.5%), fever in 8 cases (16.3%); chest pain

in 2 cases; 9 patients (18.4%) were asymptomatic. Hemoptysis was much more common in pulmonary aspergillosis cases, with 11 of 29 patients (37.9%) having hemoptysis; while only 2 cases (14.3%) of pulmonary cryptococcosis cases had hemoptysis. The incidence of hemoptysis in pulmonary aspergillosis was higher. The difference was significant ($P < 0.05$). While asymptomatic was much more common in pulmonary cryptococcosis cases, with 6 out of 14 patients (42.9%) without any symptoms; only 2 cases (6.9%) of pulmonary aspergillosis without any symptoms. The incidence of asymptomatic in pulmonary cryptococcosis was higher. The difference was significant ($P < 0.05$). Details of clinical characteristics are given in Table 3.

	Pulmonary Aspergillosis	Pulmonary Cryptococcosis	Pulmonary Candidiasis	Other undifferentiated types	Total
	N = 29	N = 14	N = 2	N = 4	
Cough	19	9	2	3	33
Expectoration	14	4	2	3	23
Hemoptysis	11	2	0	0	13
Fever	4	4	0	0	8
Asymptomatic	2	6	0	1	9

Table 3: Main clinical manifestations of 49 patients with pulmonary mycosis.

Radiographic characteristics

The median lesion size was 38.5 (ranged from 8 to 82) mm. CT findings included masses or nodule lesions in 36 cases (73.5%), patchy lesions in 3 cases (6.1%), cavity formation in 10 cases (20.4%). In 29 pulmonary aspergillosis cases, 8 patients (27.6%) showed the formation of cavities; while just 2 cases (10.0%) showed cavities in other pulmonary mycosis. Pulmonary aspergillosis was with a higher incidence of cavity formation than other pulmonary mycosis. The difference was significant ($P < 0.05$). The lesions of pulmonary cryptococcal were located in the peripheral lung fields and were closed to the pleura. Other signs include: lung hilum or mediastinal lymphadenectasis in 21 cases (42.9%), pleural thickening and adhesion in 5 cases. Details of clinical characteristics are given in Table 4.

	Pulmonary Aspergillosis	Pulmonary Cryptococcosis	Pulmonary Candidiasis	Other undifferentiated types	Total
	N = 29	N = 14	N = 2	N = 4	
Masses or nodule lesions	19	13	2	2	36
Patchy lesions	2	0	0	1	3
Cavity formation	8	1	0	1	10

Table 4: Chest imagine features of 49 patients with pulmonary mycosis.

Treatment and prognosis

In 49 patients, 36 cases (73.5%) underwent surgical resection of pulmonary lesions. 15 cases (30.6%) received systemic antifungal therapy, 13 cases (26.5%) experienced complete responses or partial responses, and 2 cases showed no response or progressing.

Characters of pulmonary mycosis with lung cancer

In our study, there are pulmonary mycoses with lung cancer in 9 cases (18.4%) in total, including squamous cell carcinoma in 5 cases, adenocarcinoma in 4 cases. Among 9 cases, 7 cases are pulmonary aspergillosis, 2 cases are pulmonary cryptococcosis. All the patients are smoker and all the patients had solitary pulmonary lesions. Pulmonary mycosis and lung cancer were found in the same site in 6 cases. Pulmonary mycosis lesions were found in lymph nodes in 3 cases. All the patients underwent bronchoscopy and biopsy, and three of them were found neoplasm in the airway and had been confirmed as pulmonary aspergillosis. All the patients further received surgical resection without recurrence and pathologically proved pulmonary mycosis with lung cancer post-operation. All the patients are immunocompetent. None of the 9 cases are with diabetes, autoimmune diseases, HIV infection, solid tumor or hematologic malignancy.

Discussion

Pulmonary mycoses are diseases caused by microscopic fungi, according to the patient's immunity status, which due to deficiencies at either local or general level and can involve the respiratory system [8]. However, in present study, none of the patient used corticosteroids and immunosuppressive agents for more than 6 months. The most common underlying diseases are lung cancer, COPD, bronchiectasis and tuberculosis. It indicates that, besides immunity status, pulmonary mycoses are also closely associated with organic abnormity of respiratory system.

Hao., *et al*. reported that, according to autopsy, aspergillus is the first pathogen for deep fungal diseases, followed by cryptococcosis [9]. Chen reported that the most prevalent three species of pulmonary mycosis were pulmonary aspergillosis (57%), pulmonary cryptococcosis (21%) [10]. Our report also confirmed these results with the most prevalent organisms isolated from pulmonary mycosis being pulmonary aspergillosis (59.2%), pulmonary cryptococcosis (28.6%). The incidence of pulmonary candidiasis is also very high [11]. However, as we known, pulmonary candidiasis and mold fungi are easily complicated by hematogenous spread, while pulmonary aspergillosis and cryptococcosis are easily to form a focal mass. Only for masses or nodule lesions, we can get the pathological results by surgical operations, trans-bronchial biopsy or CT guided percutaneous needle biopsy [11,12].

In our study, pulmonary fungal disease was mainly found in male and smoker, the average age was 45 years old, and lung cancer was also predominant in male and smoker, among patients age from 40 - 60 years [13,14]. Since both diseases have quite similar high incidence population and ago, the probability of coexistence of two diseases is on the rise. The co-incidence rate of pulmonary fungal disease and lung cancer is about

2.7~9.3% [15,16]. According to our data, the association of untreated lung cancer with co-existing pulmonary mycosis in immunocompetent patients is not rare. Retrospective investigation of comorbid diseases should be valued since the incidence rate is about 18.4%. Potential explanation for such a high incidence rate is the majority of patients in such a cancer specialist hospital, with a tendency to be malignant. Another potential explanation is that pulmonary lesions such as calcification, cavity, and the chronic inflammatory stimulation of bronchial mucosa and alveolar epithelial cells may be related to the occurrence of lung cancer. And tumor oppression of the bronchus and lung tissue, disrupted the local drainage, blood and lymphatic circulation, can also lead to increased risk of pulmonary fungal disease. We summarize the clinical data, and give an overview of the current knowledge on the etiology, diagnosis and treatment of this condition. Patients with lung cancer may be more prone to pulmonary aspergillus infection on the basis of abnormal airways, cavity formation and long-term smoking. However, as reported before, cryptococcosis remained a rare mycosis in patients with cancer [17].

Pulmonary mycosis occasionally present with clinical and radiological features that are indistinguishable from thoracic malignancy [18]. This situation presents a diagnostic challenge and may delay treatment significantly. Imaging findings of pulmonary mycosis are not easy to identify with peripheral lung cancer [19]. Peripheral lung cancer showed lung solitary, lobulated mass or associated with satellite nodules, mass around accompanied by burr, the eccentric hollow, multiple lymph node enlargement, which are the main features of lung cancer, but these imaging findings are also visible in pulmonary mycosis. The nodular lesions in pulmonary mycosis, particularly in the peripheral lung, can sometimes be confused with lung cancers [20,21]. Comorbid diseases make a complete and precise diagnosis difficult, partly due to nonspecific symptoms and radiological findings. Diagnosis of pulmonary mycosis within pulmonary carcinoma can be especially difficult in immunocompetent hosts.

The treatment of pulmonary mycosis includes surgical resection and antifungal drugs. In our report, 36 patients (73.5%) received surgical resection, and no patients had no recurrence. 15 cases received drug treatment, 13 cases experienced complete responses or partial responses. Both anti-fungi and surgical treatment can obtain satisfactory results. When lung cancer is coexisting with pulmonary mycosis, clinicians should properly manage these two diseases simultaneously [22]. As for the lung cancer, in early stage, with pulmonary mycosis and cancer lesions in the same site, surgical resection is feasible and effective. In our group, six patients removed both lung cancer and mycosis at the same site by pneumonectomy. It also has been reported a case of adenocarcinoma where pneumonectomy concomitantly enabled radical cure of the underlying disease and invasive pulmonary aspergillosis against which different antifungal drugs had been ineffective [23]. Extended surgery such as pneumonectomy under an adequate pulmonary reserve might be warranted as a therapeutic option for comorbid diseases. However, there is still some confusion about systemic treatment. Both antifungal therapy and chemotherapy will affect the liver and kidney function and bone marrow hematopoietic function. Therefore, clinical treatment is very difficult. Followed the fungal mass surgical resection, continue to use antifungal treatment will cure pulmonary mycosis, but the minimal postoperative antifungal drug dosage and period of treatment is inconclusive.

Some limitations of the present study should be emphasized. First, the retrospective selection of patients, enrolled in cancer hospital under strong tendency of malignancy, clearly introduced selection bias into our series. Second, our analytical methodology prevented the identification of predictive clinical or radiological factors that could aid in the diagnosis of fungal infection, especially in the presence of clinical and radiological characteristics suggestive of malignancy.

Conclusion

In conclusion, the main pathogens of pulmonary mycosis were aspergillus, followed by cryptococcosis. Final diagnosis was mainly depended on pathological examinations. Because the management and outcomes of fungal infection and malignancy are entirely distinct, the establishment of a specific diagnosis is critical to provide appropriate therapy. We show interest in comorbid diseases that are sometimes underestimated. Satisfactory results can be obtained by both anti-fungi treatments and surgical treatment.

Acknowledgement

The study was supported by a grant from the National Natural Science Foundation of China (NO. 81401631).

Conflict of Interest Statement

None of the authors has any conflict of interest to declare in relation to the subject matter of this manuscript.

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Volume 1 Issue 1 June 2017