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Clinical features and diagnosis of chronic pulmonary aspergillosis in Chinese patients

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Abstract

Chronic pulmonary aspergillosis (CPA) has recently been recognized as a significant global health burden. In China, the diagnosis of CPA is still unfamiliar to most doctors. The aim of this study was to demonstrate the clinical manifestations and diagnoses of CPA in China.

A multidisciplinary team of doctors retrospectively screened 690 records of patients diagnosed with pulmonary aspergillosis from January 2000 to December 2016 at Peking Union Medical College Hospital, Beijing, China. Of these, 69 patients were diagnosed with CPA. The patients' clinical characteristics were then retrieved and analyzed. Demographic, laboratory, and radiological data for these patients were compared by CPA type.

Of the 69 patients diagnosed with CPA, 10 patients were diagnosed with chronic cavitary pulmonary aspergillosis (CCPA), 15 patients with semi-invasive aspergillosis (SAIA), 41 patients with simple aspergilloma, and 3 patients with Aspergillus nodule. Further, 53.3% of the SAIA patients were obviously immunocompromised, and 60% of the CCPA patients, 26.7% of the SAIA patients, 7.3% of the simple aspergilloma cases were mildly immunocompromised. Previous underlying lung abnormalities were observed in 20% of CCPA patients, 53.3% of SAIA patients, and 80.5% of simple aspergilloma patients. The most common symptoms in the CPA patients were cough (92.8%), hemoptysis (63.8%), chronic sputum (23.2%), and fever (17.4%). The most common computerized tomography abnormalities were cavities (94.2%), nodule (84.1%), consolidation (4.3%), pleural thickening (2.9%), and infiltration (2.9%). CCPA, SAIA and simple aspergilloma patients were significantly different with respect to their course before diagnosis, constitutional symptoms, fever, hemoptysis, breathlessness, white blood cell count, erythrocyte sedimentation rate, high-sensitivity C-reactive protein count, presence of nodule, and presence of a solitary lesion (all $P < .05$). Furthermore, SAIA patients had a significantly shorter course before diagnosis and a significantly higher white blood cell count compared with CCPA patients (both $P < .01$).

In China, underlying systemic immunocompromising conditions and lung diseases with mechanical impediments contribute to CPA. Simple aspergillosis was the most common diagnosis in CPA patients. The imaging characteristics of simple aspergillosis and Aspergillus nodules were quite discriminable, while CCPA, and SAIA were similar in their clinical and radiological features. Distinguishing between CCPA and SAIA depends mainly on the physician's clinical judgment.

Abbreviations: CCPA = chronic cavitary pulmonary aspergillosis, CPA = chronic pulmonary aspergillosis, CT = computerized tomography, EOS = eosinophil, ESR = erythrocyte sedimentation rate, hsCRP = high-sensitivity C-reactive protein, SAIA = semi-invasive aspergillosis, WBC = white blood cells.

Keywords: Chinese, chronic pulmonary aspergillosis, clinical features, predisposing factors

1. Introduction

Chronic pulmonary aspergillosis (CPA) refers to a group of infectious consuming diseases that typically cause prolonged and relapsing cough, dyspnea, and hemoptysis. CPA most often affects patients with underlying pulmonary conditions and common immunosuppressive conditions. CPA is further divided into several subtypes, including chronic cavitary pulmonary aspergillosis (CCPA), chronic fibrosing pulmonary aspergillosis (CFPA), aspergillus nodule, single aspergilloma, and subacute invasive pulmonary aspergillosis (usually occurs in moderately immunocompromised patients with more progressive features within 3 months).

CPA has recently been recognized as a significant global health burden.[1] It is associated with significant morbidity and mortality, but the optimal diagnosis and treatment strategy has yet to be determined. The prevalence of CPA varies widely, with a higher prevalence in developing countries compared with developed countries. A previous study by Denning et al[1] reported that 21% (US) to 35% (Taiwan, China) of post tuberculosis patients developed pulmonary cavities and about 22% of these patients developed CPA.

The diagnosis of CPA is still unfamiliar to most doctors in China. Indeed, the China National Knowledge Infrastructure

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does not contain any clinical studies performed to investigate either the clinical manifestations of CPA or appropriate standards of diagnosis for CPA. Therefore, we sought to gain a better understanding of the diagnosis and clinical features of CPA in China.

2. Methods

We retrospectively reviewed the medical records of the 690 hospitalized patients who were diagnosed with "pulmonary aspergillosis" from January 2000 to December 2016 at Peking Union Medical College Hospital, a major referral center in China. Because of the retrospective nature of the study, informed consent was waived. The study was approved by the Ethical Committee of Peking Union Medical College Hospital (protocol number: S-K247). Of these 690 patients, 96.0% were Han Chinese, 1.0% were Hui, 0.5% were Mongolian, and the remaining patients were either Tujia or Korean. The patients' clinical characteristics were retrieved, and the data were reviewed and identified by a multidisciplinary team, including one senior pulmonologist, one infectious disease physician, one radiologist, and one pathologist. Of the 690 patients reviewed, 69 patients were determined to meet all of the 5 diagnostic requirements for CPA (the case do not meet any one out of the 5 diagnosis requirements would be removed). These requirements were as follows:

1. At least a 3-month duration of pulmonary or systemic symptoms, with at least a 1-month duration of subacute invasive aspergillosis. A duration of less than 3 months was acceptable for simple aspergilloma patients who received their diagnosis prior to surgery at the beginning of their clinical course.
2. Radiological evidence of chronic pulmonary lesion with surrounding inflammation, with or without an intracavitary mass.
3. Direct evidence of *Aspergillus* from sputum or lung tissue biopsy.
4. Exclusion of other pulmonary pathogens that might explain the present clinical course, such as tuberculosis mycobacteria.
5. Exclusion of major discernible immunodeficiency, such as AIDS, leukemia, or organ transplant. Modest immunocompromising factors, such as diabetes mellitus, chronic liver disease, history of malignancy, or prolonged corticosteroid administration[2] were considered acceptable.

After extensive review of the clinical and radiological data, all diagnosed 69 cases were classified into 5 categories:

1. Chronic cavitary pulmonary aspergillosis (CCPA), 10 patients: Patient is immunocompetent or mildly immunocompromised, with formation and expansion of one or more pulmonary cavities over at least 3 months of observation.
2. Chronic fibrosing pulmonary aspergillosis (CFPA), 0 patients: Patient shows severe fibrotic destruction of at least 2 lobes of the lung leading to major loss of lung function
3. Semi-invasive aspergillosis (SAIA), 15 patients: Patient is immunocompromised to some degree and presents with progressive features over 1–3 months as well as variable radiological features, including cavitation, nodules, or progressive consolidation with abscess formation.
4. Simple aspergilloma, 41 patients: Patient is immunocompetent and shows single pulmonary cavity containing a fungal ball with microbiological evidence implicating *Aspergillus spp*. and with no radiological progression over at least 3 months of observation: Duration before diagnosis may be less than 3 months if the patient warrants diagnosis with simple aspergilloma before surgery at the very beginning of the clinical course.
5. *Aspergillus* nodule, 3 patients: Patient is immunocompetent and presents with one or more nodules which may or may not cavitate.

Clinical characteristics were retrieved from the patients' medical records. The following data were collected for further analysis: age, sex, underlying diseases, symptoms, chest computerized tomography (CT) images, white blood cell (WBC) and eosinophils (EOS) counts from a blood routine examination, high-sensitivity C-reactive protein (hsCRP), erythrocyte sedimentation rate (ESR), and serum 1,3 b-D glucan testing.

2.1. Statistical analysis

The main statistical objective of this investigation was to compare CCPA, SAIA, and simple aspergilloma patients with respect to their demographic, laboratory, and radiological characteristics. We also compared CCPA and SAIA to determine any group difference. The sample size is of study is small especially as it is further divided into subgroups. So we choosed Fisher exact test and Kurskal–Wallis test for this study. The Kruskal–Wallis test was applied to investigate the differences in age, course before diagnosis, and laboratory test results, including levels of WBC, EOS, ESR, hsCRP, and serum 1,3 b-D glucan. Fisher exact test was applied to investigate differences in sex, symptoms, and imaging features. A 2-sided $P < 0.05$ was considered to indicate statistical significance. Continuous variables are presented as a mean ± standard deviation, and categorical variables are presented as numbers and percentages. All analyses were performed using R Studio Version 3.3.2.

3. Results

A total of 69 patients were finally diagnosed with CPA from the 690 pulmonary aspergillosis patients. These included 10 patients with CCPA, 15 with SAIA, 41 with simple aspergilloma, and 3 with Aspergillus nodule. No patients were diagnosed with chronic fibrosing pulmonary aspergillosis.

3.1. General characteristics

Of the 69 CPA patients, 28 (41%) were male. The ages ranged from 19 to 74 years, with a median age of 53 (40, 59 y) years. The course of the disease was variable, and the longest duration before diagnosis was 8 years.

3.2. Predisposing conditions

Of the 69 patients determined to have CPA, 8 (11.5%) patients were obviously immunocompromised, including 1 patient with allergic bronchopulmonary aspergillosis, 1 patient with systemic vasculitis, 1 patient with nephrotic syndrome, 3 patients with different types of interstitial lung disease, 1 patient with systemic lupus erythematosus who was being treated with immunosuppressive therapy, and 1 patient with esophageal cancer who was receiving chemotherapy. We considered patients who had no major discernible immunodeficiency but showed a certain degree of immunocompromise because of immunosuppressive therapy to be obviously immunocompromised. All of these 8 patients were considered to have SAIA. Thirteen patients (18.8%) showed

Table 1

Predisposing factors in all chronic pulmonary Aspergillosis patients.

	Total (n = 69)	CCPA (n = 10)	SAIA (n = 15)	AN (n = 3)	SA (n = 41)
Immunocompetent	48 (69.6%)	4 (40%)	3 (20%)	3 (100%)	38 (92.7%)
Mildly immunocompromised	13 (18.8%)	6 (60%)	4 (26.7%)	0 (0%)	3 (7.3%)
Obviously immunocompromised	8 (11.5%)	0 (0%)	8 (53.3%)	0 (0%)	0 (0%)
Previous lung abnormality	43 (62.3%)	2 (20%)	8 (53.3%)	0 (0%)	33 (80.5%)

Data are presented as number (%).

AN = Aspergillosis nodule, CCPA = chronic cavitary pulmonary aspergillosis, SA = simple aspergilloma, SAIA = semi-invasive aspergillosis.

mild immunodeficiency. These cases stemmed from ankylosing spondylitis, idiopathic thrombocytopenic purpura, nephrotic syndrome with a history of immunosuppressive therapy, diabetes, chronic hepatitis B, and history of esophageal cancer or breast cancer. We considered patients who had relevant systematic diseases or a history of obvious immunocompromise that may affect immune status to be mildly immunocompromised. Of these 13 patients, 6 were determined to have CCPA, 4 to have SAIA, and 3 were determined to have simple aspergilloma. Finally, 48 patients (69.6%) were found to have normal immunity, and these included 4 patients with CCPA, 3 with SAIA, 3 with aspergillosis nodule, and 38 with simple aspergilloma. In addition, 43 patients (62.3%) presented with a history of lung abnormality, including bronchiectasis from a known or unknown cause, COPD, asthma, allergic bronchopulmonary aspergillosis, and congenital lung and heart disease (Table 1).

3.3. Symptoms

The most common symptoms in the CPA patients were cough (92.8%), hemoptysis (63.8%), sputum production (23.2%), fever (17.4%), breathlessness (7.2%), chest pain (5.8%), and constitutional symptoms (5.8%). Four patients (5.8%) were asymptomatic. The symptoms varied by CPA type (Table 2).

3.4. Laboratory examinations

All of the 69 CPA cases had direct evidence of *Aspergillus* infection. The pathogen was identified from sputum (33.3%), lung resection surgery (62.3%), percutaneous lung biopsy (1.4%), or bronchoscopy biopsy (2.9%). Blood routine examination results revealed that the mean WBC in our patient group was $8.1 \pm 4.4 \times 10^9$/L (normal range, 3.5–9.5×10^9/L), the mean EOS level was $0.2 \pm 0.2 \times 10^9$/L (normal range, 0.02–0.5×10^9/L), the mean hsCRP level was 38.5 ± 57.9 mg/L (normal range, 0–3.0 mg/L), the mean ESR was 30.9 ± 29.9 mm/h (normal range, 0–15 mm/h), and the mean 1,3 b-D glucan testing result was 281.2 ± 598.2 pg/mL (normal range, 0–50 pg/mL). These examination results varied by CPA type (Table 3).

3.5. Radiological examinations

All patients underwent chest CT imaging. The most common CT abnormalities were cavity (94.2%), nodules (84.1%), consolidation

Table 2

Symptoms by type of chronic pulmonary Aspergillosis.

Symptoms	Total (n = 69)	CCPA (n = 10)	SAIA (n = 15)	AN (n = 3)	SA (n = 41)
Constitutional symptoms	4 (5.8%)	1 (10%)	3 (20%)	0 (0%)	0 (0%)
Cough	64 (92.8%)	10 (100%)	14 (93.3%)	0 (0%)	40 (97.6%)
Sputum production	16 (23.2%)	3 (30%)	6 (40%)	0 (0%)	7 (17.1%)
Chest pain	4 (5.8%)	0 (0%)	3 (20%)	0 (0%)	1 (2.4%)
Fever	12 (17.4%)	3 (30%)	7 (46.7%)	0 (0%)	2 (4.9%)
Hemoptysis	44 (63.8%)	7 (70%)	5 (33.3%)	0 (0%)	32 (78.0%)
Breathlessness	5 (7.2%)	1 (10%)	4 (26.7%)	0 (0%)	0 (0%)
Asymptomatic	4 (5.8%)	0 (0%)	0 (0%)	3 (100%)	1 (2.4%)

Data are presented as number (%).

AN = Aspergillosis nodule, CCPA = chronic cavitary pulmonary aspergillosis, SA = simple aspergilloma, SAIA = semi-invasive aspergillosis.

Table 3

Laboratory features by chronic pulmonary Aspergillosis type.

	Total (n = 69)	CCPA (n = 10)	SAIA (n = 15)	AN* (n = 3)	SA (n = 41)
WBC ($\times 10^9$/L)	8.1 (4.4)	6.8 (3.9)	12.9 (5.8)	8.01, 7.67, 5.33	6.5 (2.0)
EOS ($\times 10^9$/L)	0.2 (0.2)	0.1 (0.1)	0.2 (0.2)	0.19, 0.13, 0.02	0.2 (0.2)
G-testing (pg/mL)	281.2 (598.2)	194.8 (318.8)	411.4 (796.1)	NA	67.0 (62.5)[a]
ESR (mm/h)	30.9 (29.9)	38.4 (28.4)	56.5 (29.0)	NA	9.1 (6.6)[b]
hsCRP (mg/L)	38.5 (57.9)	15.1 (16.0)	65.4 (71.9)	NA	5.1 (8.8)[c]

Data are presented as mean (SD).

* Data presented as actual values.

[a] = Data available from 8 patients.

[b] = Data available from 20 patients.

[c] = Data available from 6 patients.

AN = Aspergillosis nodule, CCPA = chronic cavitary pulmonary aspergillosis, EOS = eosinophil count, ESR = erythrocyte sedimentation rate, G-testing = Serum 1,3 b-D glucan testing, hsCRP = high-sensitivity C-reactive protein, NA = Not available, SA = simple aspergilloma, SAIA = semi-invasive aspergillosis, WBC = white blood cell count.

Table 4

Radiological characteristics by chronic pulmonary Aspergillosis type.

	Total (n = 69)	CCPA (n = 10)	SAIA (n = 15)	AN (n = 3)	SA (n = 41)
Nodule	58 (84.1%)	7 (70%)	7 (46.7%)	3 (100%)	41 (100%)
Cavity	65 (94.2%)	10 (100%)	14 (93.3%)	0 (0%)	41 (100%)
Consolidation	3 (4.3%)	0 (0%)	3 (20%)	0 (0%)	0 (0%)
Infiltration	2 (2.9%)	2 (20%)	0 (0%)	0 (0%)	0 (0%)
Pleural thickening	2 (2.9%)	0 (0%)	2 (%13.3)	0 (0%)	0 (0%)
Solitary	56 (81.2%)	5 (50%)	7 (46.7%)	3 (100%)	41 (100%)

All data are presented as number (%).

AN = Aspergillosis nodule, CCPA = chronic cavitary pulmonary aspergillosis, SA = simple aspergilloma, SAIA = semi-invasive aspergillosis.

(4.3%), pleural thickening (2.9%), and infiltration (2.9%). Most of these (81.2%) were solitary lesions. Table 4 presents the radiological characteristics listed by CPA type.

3.6. Comparison of clinical features by CPA types

The comparisons of clinical and radiological data in CCPA, SAIA, and simple aspergilloma are summarized in Table 5. CCPA, SAIA, and simple aspergilloma patients significantly differed with respect to many clinical characteristics, including course before diagnosis ($P = .0022$), constitutional symptoms ($P = .011$), fever ($P = .0005$), hemoptysis ($P = .0077$), breathlessness ($P = .0046$), WBC count ($P = .0001$), ESR ($P = .0002$), and hsCRP count ($P = .0138$). Only 1 patient, in the simple aspergilloma group, was asymptomatic. With regards to the radiological results, presence of a nodule and presence of a solitary lesion were found to differ significantly among these three groups (both $P < .0001$). No significant differences were found for any other characteristics.

The comparisons of clinical and radiological data between CCPA and SAIA are summarized in Table 6. SAIA patients had a significantly shorter course before diagnosis compared with CCPA patients (7.4 ± 12.0 months vs 20.8 ± 19.8 months; $P = .0034$) and a significantly higher WBC count ($12.9 \pm 5.8 \times 10^9$/L versus $6.8 \pm 3.9 \times 10^9$/L; $P = .0025$). No significant differences were found in any other clinical or radiological characteristics, and there was no significant difference in age ($P = .5977$) or sex ($P = .2262$) between the 2 patient groups.

4. Discussion

Chronic pulmonary aspergillosis (CPA) is an uncommon and problematic pulmonary disease. In 2016, Denning and others published clinical guidelines for global diagnosis and management of CPA.[2] However, the definition of CPA still contains some degree of uncertainty, especially with regard to the division of phenotypes. A chronic and characteristic feature of thoracic imaging, direct or indirect evidence of *Aspergillus* infection and exclusion of alternative diagnoses is essential for the diagnosis of CPA. By convention, a diagnosis of CPA usually also requires that the disease has been present for at least 3 months, and patients are usually not severely immunocompromised by

Table 5

Comparison of clinical features in types of chronic cavitary pulmonary aspergillosis, semi-invasive aspergillosis, and simple aspergilloma.

	CCPA (n = 10)	SAIA (n = 15)	SA (n = 41)	*P*
Female, n (%)	3 (30.0%)	9 (60.0%)	28 (68.3%)	.925[a]
Age, y, mean (SD)	52.7 (10.4)	53.7 (13.0)	47.7 (13.6)	.2216[b]
Course before diagnosis, mo, mean (SD)	20.8 (19.8)	7.4 (12.0)	28.6 (31.4)	.0022[b]
Constitutional symptoms present, n (%)	1 (10.0%)	3 (20.0%)	0 (0.0%)	.0110[a]
Fever present, n (%)	3 (30.0%)	7 (46.7%)	2 (4.9%)	.0005[a]
Hemoptysis present, n (%)	7 (70.0%)	5 (33.3%)	32 (78.0%)	.0077[a]
Cough present, n (%)	10 (100.0%)	14 (93.3%)	40 (97.6%)	.6177[a]
Expectoration present, n (%)	3 (30.0%)	6 (40.0%)	7 (17.1%)	.1872[a]
Breathlessness present, n (%)	1 (10.0%)	4 (26.7%)	0 (0.0%)	.0046[a]
Chest pain present, n (%)	0 (0.0%)	3 (20.0%)	1 (2.4%)	.0503[a]
Symptomatic, n (%)	10 (100.0%)	15 (100.0%)	40 (97.6%)	1.0000[a]
WBC, $\times 10^9$/L, mean (SD)	6.8 (3.9)	12.9 (5.8)	6.5 (2.0)	.0001[b]
EOS, $\times 10^9$/L, mean (SD)	0.1 (0.1)	0.2 (0.2)	0.2 (0.2)	.4987[b]
ESR, mm/h, Mean (SD)	38.4 (28.4)	56.5 (29.0)	9.1 (6.6)	.0002[b]
hsCRP, mg/L, Mean (SD)	15.1 (16.0)	65.4 (71.9)	5.1 (8.8)	.0138[b]
G-testing, pg/mL, Mean (SD)	194.8 (318.8)	411.4 (796.1)	67.0 (62.5)	.3883[b]
Cavity present, n (%)	10 (100.0%)	14 (93.3%)	41 (100.0%)	.3788[a]
Nodule present, n (%)	7 (70.0%)	7 (46.7%)	41 (100.0%)	<.0001[a]
Consolidation present, n (%)	0 (0.0%)	3 (20.0%)	0 (0.0%)	.0126[a]
Pleural thickening present, n (%)	0 (0.0%)	2 (13.3%)	0 (0.0%)	.0699[a]
Solitary lesion present, n (%)	5 (50.0%)	7 (46.7%)	41 (100.0%)	<.0001[a]

[a] Fisher exact test.

[b] Kruskal-Wallis test.

CCPA = chronic cavitary pulmonary aspergillosis, EOS = eosinophil count, ESR = erythrocyte sedimentation rate, G-testing = Serum1,3 b-D glucan testing, hsCRP = high-sensitivity C-reactive protein count, SA = simple aspergilloma, SAIA = semi-invasive aspergillosis, WBC = white blood cell count.

Table 6

Comparison of clinical and radiological features between patients with chronic cavitary pulmonary aspergillosis and those with semi-invasive aspergillosis.

Clinical features	CCPA (n = 10)	SAIA (n = 15)	*P*
Female, n (%)	3 (30.0%)	9 (60.0%)	.2262[a]
, y, mean (SD)	52.7 (10.4)	53.7 (13.0)	.5977[b]
Course before diagnosis, mo, mean (SD)	20.8 (19.8)	7.4 (12.0)	.0034[b]
Constitutional symptoms present, n (%)	1 (10.0%)	3 (20.0%)	.6265[a]
Fever present, n (%)	3 (30.0%)	7 (46.7%)	.6785[a]
Hemoptysis present, n (%)	7 (70.0%)	5 (33.3%)	.1107[a]
Cough present, n (%)	10 (100.0%)	14 (93.3%)	1.0000[a]
Expectoration present, n (%)	3 (30.0%)	6 (40.0%)	.6913[a]
Breathlessness present, n (%)	1 (10.0%)	4 (26.7%)	.6146[a]
Chest pain present, n (%)	0 (0.0%)	3 (20.0%)	.2500[a]
Symptomatic, n (%)	10 (100.0%)	15 (100.0%)	
WBC, $\times 10^9$/L, mean (SD)	6.8 (3.9)	12.9 (5.8)	.0025[b]
EOS, $\times 10^9$/L, mean (SD)	0.1 (0.1)	0.2 (0.2)	.4534[b]
ESR, mm/h, mean (SD)	38.4 (28.4)	56.5 (29.0)	.1489[b]
hsCRP, mg/L, mean (SD)	15.1 (16.0)	65.4 (71.9)	.0522[b]
G-testing, pg/mL, Mean (SD)	194.8 (318.8)	411.4 (796.1)	.2328[b]
Cavity present, n (%)	10 (100.0%)	14 (93.3%)	1.0000[a]
Nodule present, n (%)	7 (70.0%)	7 (46.7%)	.4139[a]
Consolidation present, n (%)	0 (0.0%)	3 (20.0%)	.2500[a]
Pleural thickening present, n (%)	0 (0.0%)	2 (13.3%)	.5000[a]
Single lesion present, n (%)	5 (50.0%)	7 (46.7%)	1.0000[a]

[a] Fisher exact test.

[b] Kruskal-Wallis test.

CCPA = chronic cavitary pulmonary aspergillosis, EOS = eosinophil count, ESR = erythrocyte sedimentation rate, G-testing = Serum 1,3 b-D glucan testing, hsCRP = high-sensitivity C-reactive protein count, SAIA = semi-invasive aspergillosis, WBC = white blood cell count.

HIV-infection, cancer chemotherapy, or immunosuppressive therapy. In contrast, SAIA can be diagnosed after just a 1-month period, and this diagnosis can occur with or without an underlying immunocompromising disease. We report that the most common form of CPA in China is simple aspergilloma.

The clinical presentation of *Aspergillus* lung disease is determined by the interaction between fungus and host. Invasive aspergillosis develops in severely immunocompromised patients. Except in cases of SAIA, CPA occurs in patients who are not obviously immunocompromised.[3] Although CPA patients may have been treated with some level of immunosuppressant therapy,[2] CPA is more likely to develop after progression of previous anatomical alterations, such as in cases of inactive tuberculosis with residual cavities.[1] By far, the most common local predisposing factor for CPA is previously treated tuberculosis, sarcoidosis, asthma, or COPD.[1,4–6] In our study, the predispositions for CPA varied. Fifty-three percent of SAIA patients were observed to be obviously immunocompromised. Further, 60% of CCPA patients, 26.7% of SAIA patients, and 7.3% of simple aspergilloma patients were observed to be mildly immunocompromised by underlying conditions, including ankylosing spondylitis, idiopathic thrombocytopenic purpura, nephrotic syndrome with a history of immunosuppressive therapy, diabetes, chronic hepatitis B, and a history of esophageal cancer or breast cancer. Previous underlying lung abnormalities were observed in 20% of CCPA patients, 53.3% of SAIA patients, and 80.5% of simple aspergilloma patients. These abnormalities included bronchiectasis, COPD, asthma, allergic bronchopulmonary aspergillosis, and especially congenital lung and heart diseases. These congenital diseases included pulmonary sequestration and Tetralogy of Fallot, both of which have seldom been mentioned in previous studies. The nature of the underlying lung diseases that we observed suggests that both systemic immunodeficiency and mechanical impediments of the lung contribute to increasing the susceptibility to CPA.[7]

Patients with CPA usually suffer from chronic productive cough, hemoptysis, breathlessness, and chest pain. In addition, these patients occasionally experience constitutional symptoms such as weight loss, malaise, sweats, or anorexia. Hemoptysis occurs in all types of CPA and can occasionally develop into life-threatening massive hemoptysis.[8,9] However, the specific symptoms of the different subtypes of CPA remain unclear. Our results suggest that the most common symptoms of CPA are cough (92.8%), hemoptysis (63.8%), chronic sputum (23.2%), and fever (17.4%). Hemoptysis appears most often in simple aspergilloma patients, even though these patients experience a relatively quiet clinical course. Hence, hemoptysis does not necessarily indicate CPA exacerbation. In the present study, fever and constitutional symptoms were observed to be more common in SAIA and CCPA patients. This suggests that there was a larger systemic inflammatory response in these CPA patients.

The clinical manifestations of *Aspergillus* infections largely depend on the immune status of the host.[3] The CPA patients in the current study were in the middle or lower intervals of the immune status spectrum. Hence, the peripheral eosinophil count of our CPA patients remained normal. The WBC levels obtained from the blood routine examinations were significantly higher in SAIA patients compared with CCPA and simple aspergilloma patients. WBCs are essential in the initiation and execution of the acute inflammatory response and the subsequent resolution of fungal infection by mechanisms such as respiratory bursts.[10] Therefore, although WBC levels have little diagnostic value in CPA, they may help to distinguish between SAIA and other noninvasive CPA subtypes. Antibody testing is important to the diagnosis of CPA, and *Aspergillus*-specific IgG is always raised in this disease. Antibody levels are also used to monitor treatment response in CPA.[11] The diagnostic value of galactomannan in bronchoalveolar lavage fluid has been demonstrated to be high for invasive pulmonary aspergillosis in nonhematological patients, especially in patients with immunosuppressive conditions.[12] Unfortunately, testing for *Aspergillus*-specific Ig G is not yet practiced in our hospital. Serum 1,3 b-D glucan testing is unreliable, and it was reported that 1,3, b-D glucan positivity was only observed in 15.4% in CPA patients.[13] Comparison of 1,3 b-D glucan test results showed no significant differences between the CPA subgroups. With an increasing number of diagnosed CPA cases, galactomannan, and *Aspergillus*-specific IgG testing should become a more common practice in the clinic.

Radiographic features of CT scan secondary to *Aspergillus* infection range from a typical appearance of a fungus ball within the lung cavity to complex pleuroparenchymal features related to progressive destructive cavitary disease. CCPA generally presents first as indistinct regions that progress to form more distinct cavities.[14,15] Single and multiple nodules can also be present in CPA. Such nodules have been noted to be moderately or strongly positive on positron emission tomography scanning and can mimic carcinoma of the lung.[16] SAIA and CCPA are difficult to radiographically distinguish from each other because they both show features of chronic pulmonary infiltrates, progressive cavitation, and subsequent aspergilloma formation. It has been suggested that pre-existing cavities showing pericavitary infiltrates with or without aspergilloma indicate CCPA.[17] In the current study, the imaging characteristics of simple aspergillosis and *Aspergillus* nodules were quite discriminable, whereas CCPA and SAIA were quite similar in manifestation of nodules and cavity and consolidation features.

The different forms of *Aspergillus* infection are associated with significantly different morbidity and mortality rates.[18] If the lung function permits, surgical removal of the lesion is the best choice for patients with simple aspergilloma.[19] However, benefit from the operation in CCPA patients is much less.[20] Clinical distinctions between SAIA and CCPA are necessary because the treatment and prognosis goals for these 2 conditions are different.[2,15] Many authors have sought to distinguish the 2 entities by cavity features, host immune status, and the degree of suspected tissue invasion.[21] SAIA usually occurs in immunocompromised or very debilitated patients and is more rapid in progression than CCPA despite showing similar clinical and radiological features.[22] In addition, SAIA patients are more likely to have detectable *Aspergillus* antigen in the blood and to show hyphae invading the lung parenchyma.[23] The comparison of subgroups in our study revealed that course before diagnosis and WBC count significantly differed between SAIA and CCPA, and these results may aid in distinguishing these 2 conditions.

5. Conclusions

In China, the nature of the underlying systemic immunocompromise and mechanical impediments from lung disease contribute to increased susceptibility to different types of CPA. Hemoptysis is a predominant symptom in CPA patients, but direct evidence of *Aspergillus* is important in the diagnosis of CPA. Simple aspergillosis was the dominant diagnosis for all CPA patients. The imaging characteristics of simple aspergillosis and *Aspergillus* nodules were quite discriminable, whereas CCPA and SAIA were quite similar. CCPA and SAIA were also quite similar in their clinical features. Distinguishing between these 2 types of CPA requires the clinical judgment of an experienced physician. Because of the uncertainty of the definitions, the possible unfamiliarity of clinicians with the diagnosis, and the low incidence of CPA, the sample size is relatively small especially in the need to compare between groups in the current study. However, in the field of such a fresh definition, our findings might be clinically beneficial and may inspire future studies in China.

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