



Case report

Pulmonary coccidioidomycosis in China: Case reports and literature review

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ABSTRACT

Coccidioidomycosis is a fungal infection commonly found in the tropical regions of southwestern United States, such as Arizona, the Central Valley of California, parts of New Mexico, and western Texas. The endemic regions also extend into northern Mexico and include focal endemic areas in sections of Central America and Argentina. Coccidioides species have also been reported in central and southern Utah, Nevada, and the central part of Washington State., the pathogenic bacteria commonly colonize the lungs. China, which is outside the traditionally established endemic area, is witnessing a rise in reported cases of pulmonary coccidioidomycosis. Meanwhile, the comorbidities of the disease began to become complicated. We reported two Chinese patients with pulmonary coccidioidomycosis complicated by organizing pneumonia and reviewed 42 cases of Chinese patients in the literature from 1958 to 2024. Out of the 44 patients from 13 different provinces (Including Hong Kong Special Administrative Region and Taiwan), the average age was (43.08 ± 3.03) years. Among them, 34 (76.7 %) were male, while 10 (23.3 %) were female, cough/sputum (81.8 %) are the most common symptoms, the cases are concentrated in coastal areas. 27(61.4 %) were Imported and 17(38.6 %) were domestic primary cases, showing a higher proportion of imported cases compared to domestic primary cases. Misdiagnosis and mistreatment have a significant impact on patients, the combination of new technologies and traditional pathology diagnosis have substantially promoted precise diagnosis for clinician in non-endemic areas. Interestingly, the histopathological findings of the two patients we report showed evident organizing pneumonia and an increased eosinophil count, the application of corticosteroid drugs notably improved the patients' conditions. Overall, at least 84.1 % of patients had a favorable prognosis. Considering the changing epidemiology of pulmonary coccidioidomycosis, Chinese healthcare providers should be cautious about their patients' travel history, particularly among male individuals.

Introduction

Coccidioidomycosis (Valley fever) can be a severe systemic mycosis caused by the dimorphic fungus species *Coccidioides immitis* (CI) and *Coccidioides posadasii* (CP). Coccidioidomycosis occurs mainly in the southwestern United States, including the Central Valley of California, and the states of Arizona, California, New Mexico, and Texas [1]. While the number of coccidioidomycosis cases in these endemic regions has been increasing annually, there have been few reported cases in China. The research indicates that while 60 % of individuals infected with *Coccidioides* may be asymptomatic, the condition of symptomatic

patients can exhibit a wide range of severity and complexity, from flu-like symptoms to devastating acute meningitis [2]. Recently, the number of confirmed pulmonary coccidioidomycosis cases in China has increased [3]. To better understand the changing situation of pulmonary coccidioidomycosis in China, we also reviewed coccidioidomycosis-related online literature, aiming to emphasize the importance of combining travel history with clinical presentations and appropriate diagnostic tests. This approach intends to enhance medical workers' awareness of this disease in non-endemic areas. Based on our research findings, we present a novel perspective that seeks to offer assistance and guidance in the treatment of pulmonary

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¹ Huanhuan Bi and Feng Hou contributed equally to the work.

Table 1
Literature Review of Pulmonary Coccidioidomycosis Cases in China.

ID	Author	Clinical presentation	Dissemination	Misdiagnosis/ mistreatment	Provinces	Sex	Age	Past history	Exposure history	Imaging examination	Pathological results	Treatment	Prognosis
1	XC Wu et.al[4]	Cough and sputum	No	Yes	Jiangxi Province	male	31	None	None	Chest X-ray shows two lungs with heavy texture, bronchitis	The sputum fungus cultured coccidioides lophores	Clotrimazole	Improved
2	XC Wu et.al	Cough and sputum	No	No	Jiangxi Province	female	32	None	None	Chest radiographs showed enhanced lung texture	Sputum fungus culture	Unknown	Unknown
3	XX Fu et.al[5]	Fever, cough, chest pain	Yes	Yes	Shanghai	female	26	None	None	Chest radiograph showed both lung consolidation; X-rays of the thoracic vertebrae showed vertebral destruction and paravertebral abscess	The left cervical lymph node biopsy showed coccidioides	Ketoconazole	Improved
4	A. P. Koehler. al[6]	Fever, cough,	Yes	No	Hong Kong	male	32	None	California	Chest CT showed lymph node enlargement and paratracheal soft tissue mass	Cervical lymph biopsy showed coccidioides cysts	Ketoconazole,Itraconazole, Amphotericin B	Improved
5	P Liu et. al[7]	Unknow	Yes	No	Jiangsu Province	male	37	Drug abuse	None	None	Coccidioides were found in brain exudate and right lung abscess	None	Death
6	XJ Zeng et.al[8]	Cough and bloody sputum	No	Yes	Hu Bei Province	female	44	None	None	Chest CT showed a mass in the upper right lung	Microscope showed a large number of coccidioides	Surgery	Unknown
7	YQ Xu et.al[9]	Cough	No	Yes	Zhejiang Province	male	75	None	Arizona	Chest CT revealed a 30 cm × 38 cm subpleural mass in the right lung's middle lobe with irregular edges and peripheral obstructive inflammation. Enlarged lymph nodes were noted in the right hilar and	Postoperative histopathology revealed coccidioides	Surgery	Unknown

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Table 1 (continued)

ID	Author	Clinical presentation	Dissemination	Misdiagnosis/mistreatment	Provinces	Sex	Age	Past history	Exposure history	Imaging examination	Pathological results	Treatment	Prognosis
8	HENRY K.H. KWOK [10]	Fever, weakness,	Yes	No	Hong Kong	male	50	None	Nevada+Arizona	mediastinum, suggesting a high possibility of lung cancer with mediastinal lymph node metastasis. Left medial lobe atelectasis with air bronchogram, bilateral lower lobe pulmonary nodules and multiple mediastinal enlarged lymph nodes	Lymph node biopsy showed cyst	Fluconazole	Improved
9	HENRY K.H. KWOK [10]	Cough, fever, swelling of the chest wall	Yes	No	Hong Kong	male	42	Radiotherapy for nasopharyngeal carcinoma, HBV	California	Chest radiographs showed spots, pleural effusion and multiple masses in ribs, muscles and vertebrae	Biopsy of chest wall mass indicated coccidioides	Amphotericin B, Fluconazole	Death
10-17	NF Lian et.al [11]	Cough, chest pain, hemoptysis, fever	No	No	Fu Jian Province	5male,3female	42.87 ± 4.93	None	None	The chest CT showed nodular density and cavity in 4 cases	Lung biopsy showed granuloma formation and coccidioides cyst	Fluconazole, Itraconazole, Fluorocytosine orally/amphotericin B inhaled	7, Improved, 1 lost to follow-up.
18	BY Yu et.al [12]	Cough and sputum	No	Yes	Zhejiang Province	male	81	Chronic bronchitis	None	Chest CT scan showed a nodule in the upper left lung	Lung biopsy showed multiple necrotic foci and cyst, accompanied by granuloma formation	Surgery+Fluconazole	Improved
19	F Zong et.al [13]	Cough and sputum	No	Yes	Jiangsu Province	male	74	Sicca syndrome	None	Chest CT showed multiple nodules in both lungs	Caseous necrogranuloma and numerous cysts	Surgery+Fluconazole+Voriconazole	Improved
20	ZY Wang et.al [14]	Fever, cough, fatigue	No	Yes	Zhejiang Province	male	71	None	Arizona	Chest CT showed an irregular marginal opaque shadow in the right middle lobe subpleural area with a diameter of 3.0 cm × 3.8 cm. Enlargement of	Pathological findings of the mass showed granulomatous inflammation and cyst	Surgery	Improved

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Table 1 (continued)

ID	Author	Clinical presentation	Dissemination	Misdiagnosis/mistreatment	Provinces	Sex	Age	Past history	Exposure history	Imaging examination	Pathological results	Treatment	Prognosis
21	CB Wang et.al [15]	None	No	Yes	Shan Xi Province	female	49	Nephrotic syndrome, thrombocytopenic purpura	None	the right hilar and mediastinal lymph nodes Chest CT showed nodules in the left inferior lobe of the lung	Pathology showed granulomatous nodules with cyst inside	Surgery	Improved
22	HT Zong et.al [16]	Fever, cough, bloating, lymph node enlargement	Yes	Yes	Beijing	female	53	None	Nevada+California	CT showed lung consolidation, miliary nodules, pleural effusion, and lymph node enlargement	Pathological examination of the lymph nodes reveals granulomatous inflammation with necrosis, with encapsulation observed internally.	Itraconazole, Fluconazole+Amphotericin B	Improved
23	Y Ma et.al [17]	Cough and sputum	No	No	Jiangsu Province	female	22	None	California	CT showed two lung infections, bilateral pleural effusion, multiple enlarged lymph nodes in mediastinum and right hilum, and pericardial effusion.	The pathology after CT-guided percutaneous lung biopsy showed a large spherical spore structure	Fluconazole	Improved
24	ML Gao et.al [18]	None	No	Yes	Zhejiang Province	male	53	None	None	Tubercle of upper lobe of right lung	Postoperative lung tissue suggests a spherical spore structure	Fluconazole	Improved
25	MR Wang et.al [19]	Fever, cough, phlegm	No	No	Shanghai	male	61	None	Arizona	Patchy shadow in the middle lower lobe of the right lung	MALDI-TOF MS	Fluconazole 800 mg	Improved
26	H Liang et.al [20]	Multiple lumps, fever	Yes	No	Shanghai	male	24	None	California	CT showed a mass of the upper lobe of the right lung, multiple mediastinal lymph node enlargement, bilateral chest wall collapse, and subcutaneous gas accumulation	Pathological fungal granuloma was followed by suppurative inflammation with coagulation necrosis, abscess formation, and sporangium	Amphotericin B liposome(2180 mg)+Fluconazole200 mg/d	Improved

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Table 1 (continued)

ID	Author	Clinical presentation	Dissemination	Misdiagnosis/ mistreatment	Provinces	Sex	Age	Past history	Exposure history	Imaging examination	Pathological results	Treatment	Prognosis
27	W Zhou et.al [21]	Fever, cough, chest tightness	No	Yes	Guangdong Province	male	55	None	California	CT showed patchy solid shadow in the upper and lower lungs with uneven density and blurred edges. Diffuse multiple nodules were observed in both lungs with blurred boundaries and multiple lymph node enlargement in the right hilum and mediastinum.	Tissue biopsy indicated coccidioides	Amphotericin B , Fluconazole400mg/d	Improved
28	Y Li et. al[22]	Sternal pain	No	No	Guangdong Province	female	24	None	Washington	Multiple lytic bone destruction in the middle part of the sternum, and local soft tissue mass was formed. Multiple dense nodules in the right superior apical segment of the lung	The puncture biopsy showed several round thick-walled spores filled with endospores, consistent with coccidioidal granuloma	Itraconazole	Improved
29	YC Gu et.al [23]	Fever	No	No	Zhejiang Province	male	61	Hypertension	Arizona	Left inferior lobe lesions with peripheral inflammatory exudation	Ultrasound-guided percutaneous punctured lung histology showed spore and spore contents	Fluconazole400mg/d	Improved
30	GZ Liang et. al[24]	Coughing with blood in the sputum.	No	Yes	Beijing	male	29	None	Arizona	A cavity of the lower right lung with a few exudative changes around the lesion	Sputum culture of coccidioides	Unknown	Improved
31	CL Mei et.al [25]	Chest wall mass, rash	Yes	No	Hu Bei Province	male	22	None	Arizona	Ligule and patchy high-density shadows were seen in the lingual lobe of the left lung	NGS, Coccidioides posa, 15256 sequences		Improved
32	CY Wang	Headache, epilepsy, and	Yes	No	Taiwan	male	71	None	California	Chest CT showed bilateral	Coccidioides were detected in	Fluconazole , Amphotericin B	Death

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Table 1 (continued)

ID	Author	Clinical presentation	Dissemination	Misdiagnosis/ mistreatment	Provinces	Sex	Age	Past history	Exposure history	Imaging examination	Pathological results	Treatment	Prognosis
	et.al [26]	loss of consciousness								diffuse nodular pulmonary lesions and meningeal lesions	cerebrospinal fluid		
33	S Zhang et.al [27]	Pain in the right hip, pain in the right hip	Yes	No	Jiangsu Province	male	28	None	Arizona	Chest CT showed multiple lymph node enlargement in the whole body, multiple spots in the two lungs, and multiple bone destruction in the bones	The cervical lymph node biopsy showed coccidioides	Itraconazole 200 mg	Improved
34	Q Shen et.al [28]	Cough and sputum	No	No	Zhejiang Province	male	55	None	Arizona	Chest CT showed infection of the left inferior lobe and multiple mediastinal lymph node enlargement	Mass spectrometry, NGS Coccidioides oescasadas, human herpesvirus type 6 A	Voriconazole tablet 200 mg	Improved
35	CH Chen et.al [29]	Cough and sputum	Yes	No	Taiwan	male	25	Unknown	Arizona	None	Both the pathology of submandibular lymph nodes and scratching smears of skin lesions contain coccidioides	Ketoconazole	Improved
36	XY Yang et.al [30]	Dry cough and fatigue	No	No	Hebei Province	male	63	Asthma	Mexico	Pulmonary nodule	Laser capture microdissection and PCR sequencing showed multiple granulomas with caseous necrosis. Scattered thick-walled spherules containing endospores were observed after PAS and GMS staining	Fluconazole	Improved
37	XX Guo et.al [31]	Fever, cough, weight loss	Yes	No	Shanghai	male	42	Unknown	Mexico	Chest CT showed tubercle of right superior lobe. Enlargement of hilar and mediastinal	Tissue biopsy indicated coccidioides	Itraconazole, Fluconazole	Improved

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Table 1 (continued)

ID	Author	Clinical presentation	Dissemination	Misdiagnosis/ mistreatment	Provinces	Sex	Age	Past history	Exposure history	Imaging examination	Pathological results	Treatment	Prognosis
38	XX Guo et.al [31]	Fever,cough	Yes	No	Shanghai	male	27	Unknown	Arizona	lymph nodes; Pleural effusion Chest CT showed bilateral miliary tubercles. Left inferior lobe subpleural fibrosis	Lymph node biopsy, bone marrow culture	Itraconazole 200 mg/d	Improved
39	XX Guo et.al [32]	Fever,cough, weight loss	Yes	No	Shanghai	male	28	Unknown	California	Chest CT showed bilateral miliary tubercles. Lower right lobe consolidation; Right pleural effusion	Lymph node biopsy, skin pus mNGS	Fluconazole , Itraconazole	Improved
40	XX Guo et.al [33]	Fever,cough	No	No	Shanghai	male	21	Unknown	Arizona+California	Chest CT showed bilateral nodules and plaques	Tissue biopsy	Itraconazole	Improved
41	XX Guo et.al [34]	Fever,cough	Yes	No	Shanghai	male	27	Unknown	California	Chest CT showed bilateral patchy opacity. There is a small cavity in the lower left lobe; Mediastinal lymph node enlargement; Pleural effusion	Cerebrospinal fluid culture and Mngs	Itraconazole	Improved
41	XX Guo et.al [35]	Fever,cough	Yes	No	Shanghai	male	37	Unknown	Arizona+California	Chest CT showed bilateral miliary tubercles. Single foci patchy consolidation in lower right lobe; Enlarged mediastinal lymph nodes	Bronchoscopic biopsy, bone marrow culture, BALF, and mNGS in lung tissue	Itraconazole , Fluconazole	Improved
43	Case 1	Fever,cough and sputum	No	No	Shandong Province	male	60	Hypertension	Arizona	Left inferior lobe inflammation, left pleural effusion	The spore-like particles were detected by subpulmonary leaf mass shadow biopsy. The sequence number of <i>Coccidioides immitis</i> detected by NGS was 981, and the relative abundance was 0.56 %.	Fluconazole	Improved

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Table 1 (continued)

ID	Author	Clinical presentation	Dissemination	Misdiagnosis/mistreatment	Provinces	Sex	Age	Past history	Exposure history	Imaging examination	Pathological results	Treatment	Prognosis
44	Case 2	Fever, cough and sputum	No	No	Shandong Province	male	22	None	California	Pulmonary nodule	Coccidioides immitis sequences detected by NGS was 4619	Fluconazole	Improved

Table 2

Results of blood routine test, Inflammatory parameter.

Parameters of detection	Case 1	Case 2	Reference range
Blood routine test			
White blood cell count (10 ⁹ /L)	17.58	10.03	3.5 –9.5
Neutrophil count (10 ⁹ /L)	13.77	7.14	1.8 –6.3
Lymphocyte count (10 ⁹ /L)	0.87	1.30	1.1 –3.2
Monocyte count (10 ⁹ /L)	1.18	0.76	0.1 –0.6
Eosinophil count (10 ⁹ /L)	1.70	0.79	0.02 –0.52
Basophil count (10 ⁹ /L)	0.06	0.04	0 –0.06
Percentage of neutrophil (%)	78.40	71.10	40 –75
Percentage of lymphocyte (%)	4.90	13.00	20 –50
Inflammatory parameter			
C-reactive protein(mg/L)	205.67	93.86	0 –5
Procalcitonin	0.16	0.10	< 0.05
Erythrocyte Sedimentation Rate(mm/h)	40.00	58.00	0 –15
Virus test results			
Influenza A virus Ig M	positive	positive	negative

coccidioidomycosis.

Materials and methods

We collected the medical records of two patients recently diagnosed with pulmonary Coccidioidomycosis complicated with organizing pneumonia (OP) at our hospital. We performed a comprehensive literature search using the MeSH terms "Coccidioidomycosis" and "pulmonary" combined with "China" on specific Chinese (e.g., CNKI, Wan Fang) and English (e.g., PubMed, Web of Science) databases to retrieve literature published between January 1, 1980, and February 29, 2024. Additionally, to access more resources, we contacted authors of relevant studies, reviewed the references of all full-text papers we retrieved, and performed citation searches. We collected demographic and clinical characteristics, which included clinical presentation, travel history, year of publication, imaging scans, histopathological findings, diagnosis and treatment, and clinical follow-up results. Finally, we compiled this information into a summary focusing on the clinical characteristics, geographical distribution, and growth trends of patients with primary pulmonary coccidioidomycosis and imported pulmonary coccidioidomycosis in China.

Results

Case report

In January 2024, two cases of pulmonary coccidioidomycosis complicated by organizing pneumonia (OP) were confirmed in our hospital. The clinical characteristics of the patients are shown in [Table 1](#). The two patients showed no obvious abnormality on physical examination. Their inflammatory parameters were increased and positive influenza A virus, among them, the first patient had an increased eosinophilic count (, negative sputum results culture and smears for acid-fast bacilli ([Table 2](#)). Chest CT showed ground glass opacities with consolidations ([Fig. 1 a-d](#)). The histopathological findings of the lung lower lobe tissue showed OP, eosinophilic infiltration and aggregation of foamy histiocytes, with special staining results showing tiny granular substances within the cytoplasm of the foamy histiocytes ([Fig. 2](#)). The results of Metagenomic Next-Generation Sequencing (mNGS) indicated the presence of CP and CI, respectively. Both patients received fluconazole antifungal treatment, while the former patient was given low-dose corticosteroids (8 mg methylprednisolone) for anti-inflammatory therapy. Follow-up showed significant improvement in symptoms, and chest CT showed improvement compared to previous images ([Fig. 1 c-d, g-h](#)).

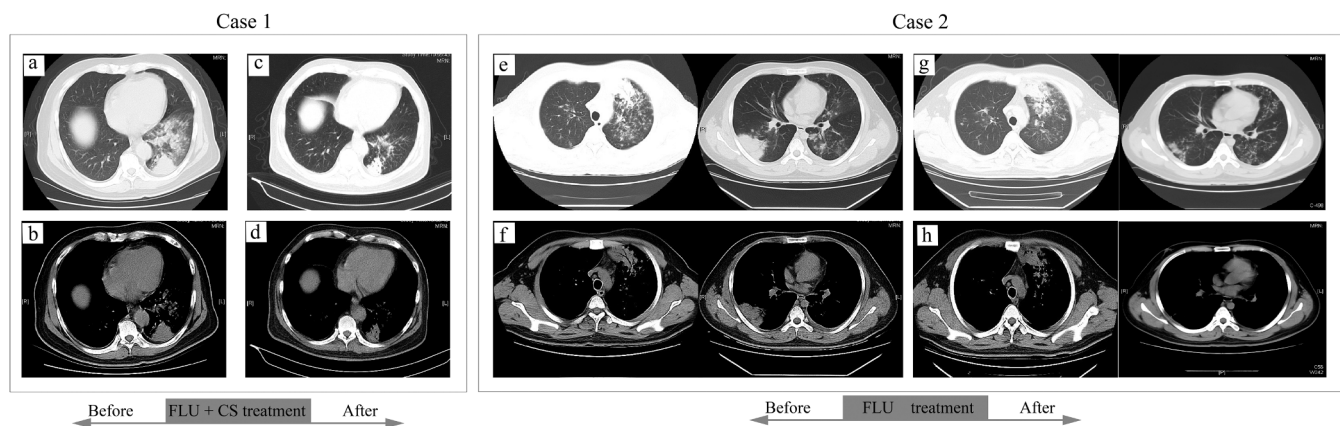


Fig. 1. Chest computed tomography (CT) scan images before and after treatment. Case 1, (a-b) Chest CT scan images showed multiple high-density shadows in the lower lobe of the left lung with indistinct margins, partial lung tissue consolidation, small amount of pleural effusion. (c-d) The consolidation had been resolved obviously after the treatment. Case 2, (e-f) Chest CT scan images show consolidation of the left upper lung and the right lower lung, in which the left upper lung shadow is distributed along the bronchial vascular bundle with uneven density. (g-h) After treatment, the consolidation of the lower right lung was obviously absorbed, and the consolidation of the upper left lung was slightly improved after the treatment. Abbreviations: FLU, fluconazole, CS, Corticosteroids.

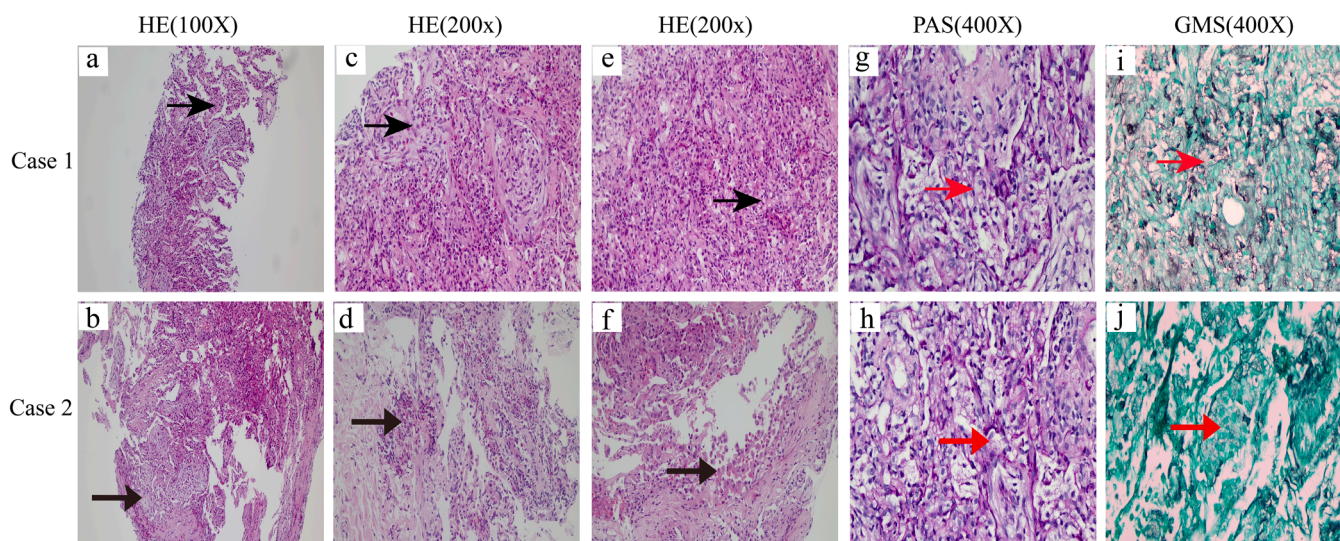


Fig. 2. Pathological H&E (Hematoxylin and Eosin) staining and special stains. (a-b) The image display widened alveolar septa, interstitial fibrosis, and focal areas of proliferative fibroblastic clusters within the alveolar spaces, indicating chronic organizing pneumonia (Black arrow) (c-d) There is significant eosinophilic infiltration in the pulmonary interstitial (Black arrow). (e-f) Aggregations of foamy histiocytes are seen in some regions, with microscopic granules present within the cells. (e-f) Regions containing aggregations of foamy histiocytes with microscopic granules in their cytoplasm are observed. (g-j) Special staining reveals tiny pink granular substances (PAS staining) and dark brown granular substances (GMS staining) within the cytoplasm of foamy histiocytes (Red arrow), suggestive of a Coccidioides infection. Abbreviations: PAS, Periodic Acid-Schiff; GMS, Grocott's Methenamine Silver.

Literature review

Demographic data and clinical characteristics

A total of 44 subjects were included in this analysis from 28 relatively complete reports, which includes the two cases we reported [4–31]. The average age of the 44 patients was 43.08 ± 3.03 years, with the oldest age being 81 years. The proportion of male was higher than that of female (34/44, 77.3%). 16 cases (37.2%) complicated by other site infection (such as bone and skin). Cough/sputum (81.8%) and fever (59.1%) were the most common symptoms, and 17 cases (38.6%) had other symptoms, such as lymphadenectasis, chest pain, chest tightness, etc. 12 cases (27.3%) were misdiagnosed and mistreated, among them, 5 cases (11.4%) were misdiagnosed as lung cancer, 4 cases (9%) were misdiagnosed as tuberculosis, and the remaining cases were misdiagnosed as bacterial pneumonia and interstitial pneumonia. 37 patients (84.1%) had a favorable prognosis. 27 patients (61.4%) had a

definite history of exposure in epidemic areas (Table 3).

To better understand the epidemiological characteristics of pulmonary coccidioidomycosis in Chinese patients, we analyzed the trends over time and their geographical distribution. Our findings indicate a gradual increase in Coccidioides spp. infections, from approximately 3–5 new cases each decade between 1980 and 2000. Notably, the period from 2010 to 2019 saw a doubling in the number of confirmed cases compared to the total of the previous three decades, with 22 cases versus 11. The majority of these cases were found in China's developed coastal regions, while fewer were reported inland. Specifically, Shanghai accounted for 9 cases (20.5%) (Fig. 3).

We divided the patients into two groups: epidemic area-exposed patients group and non-exposed patients group. We conducted a clinical characteristic analysis on both groups. Compared to the primary group, the imported group was relatively younger (41.63 ± 3.45 vs 45.59 ± 1.97 , $p < 0.05$). The proportion of males was higher in the

Table 3
Characteristics of the study population.

Characteristics	Cases	Percent
Sex		
Female	10	23.30 %
Male	34	76.70 %
Travel history		
NO	17	38.60 %
Yes	27	61.40 %
Dissemination, No.(%)		
NO	28	63.60 %
Yes	16	36.40 %
Misdiagnose, No.(%)		
NO	25	56.80 %
Yes	12	27.30 %
Unknown	7	15.90 %
Chief complaint		
Cough/sputum	36	81.80 %
Fever	26	59.10 %
Other symptoms	17	38.60 %
Treatment		
Pharmacotherapy	32	72.70 %
Surgical resection	4	9.10 %
Surgery+Pharmacotherapy	3	6.80 %
Unknown	5	11.40 %
Prognosis		
Recovery	37	84.10 %
Death	3	6.80 %
Unknown	4	9.10 %

imported group than in the primary group (88.9 % vs 58.8 %, $p = 0.021$), as well as the proportion of patients with disseminated pulmonary coccidioidomycosis (51.9 % vs 11.8 %, $p = 0.005$). There was no statistically significant difference in the proportion of misdiagnosis and prognosis between the two groups of patients ($p > 0.05$). 27 cases had a clear history of exposure to endemic areas, of which 24 (89 %) were from California and/or Arizona, and 11 (41 %) had a history of travel to Arizona (Fig. 4 and Table 4).

In the study, 30 cases (68.2 %) relied on histopathological findings or fungal culture for microbiological evidence of pulmonary coccidioidomycosis infection. 13 cases (29.5 %) were diagnosed with the help of new examination methods, such as matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS), NGS and PCR sequencing. Out of the 39 cases (88.6 %) of treated patients, 32 cases (72.2 %) received only drug therapy, 3 cases underwent a combination of surgery and drug therapy, and the status of subsequent drug therapy for the remaining 4 cases after surgery is unclear.

Discussion

The first documented case of the disease in China was reported by Wu et al. in 1985, involving a couple from Jiangxi Province, with no history of exposure to endemic areas, this is the first confirmed case of primary pulmonary coccidioidomycosis in China [31–33]. Despite existing case report sand reviews of coccidioidomycosis in China, there’s a notable gap in literature specifically addressing pulmonary coccidioidomycosis, the most commonly affected organ. This underscores the need for focused research in this area prevailing belief is that the spores primarily cause damage to the terminal and respiratory bronchioles, given that the spores typically range in size from 3 to 5 μm [34,35]. In recent years, economic development has led to increased trade and cultural exchanges between countries, potentially expanding the distribution of Coccidioides. This report highlights that patients with coccidioidomycosis in China are primarily found in coastal and developed regions, Coccidioides can survive in wet soil [36], has salt tolerance, and is better adapted to survive in coastal waters, which may be the reason why coastal residents are more susceptible to infection [37, 38]. In addition to that, Coccidioides has been found in eastern Washington State outside the historically defined epidemic range [39], but there has been one Washington State import among existing cases in China [40], this should draw the attention of public health agencies to monitor for new endemic epidemics.

The diagnosis of this disease relies on a combination of several diagnostic procedures. Cough and fever are the most common symptoms, but they are not specific for the diagnosis of Pulmonary Coccidioidomycosis. In China, the rate of misdiagnosis and mistreatment of pulmonary coccidioidomycosis remains around 27 %, this condition is often mistaken for tuberculosis or lung cancer [41]. The combination of imaging and pathology is crucial for the diagnosis of this disease. For instance, imaging studies suggest that fluid samples can be obtained by bronchoscopic alveolar lavage in the presence of parenchymal infiltration, caudal disease, or bronchopleural fistula, but not in isolated pulmonary nodules, The rapid diagnosis rate of the disease through Bronchoalveolar Lavage (BAL) obtained by bronchoscopy is 30 %–64 % [42–44]. Tissue biopsies of the two patients reported in this paper showed obvious OP, foam cells are a common phenomenon in OP [45], but obvious eosinophilic and plasma cell infiltration can be seen at the same time, which is not common in other pathogenic microbial infections. 25–30 % of patients have eosinophilia in peripheral blood white blood cells [46,47]. The presence of eosinophilia could aid in the diagnosis of pulmonary coccidioidomycosis, additionally, staining techniques such as GMS and PAS stain may show the presence of the fungus [48]. However, the effectiveness of these diagnostic methods

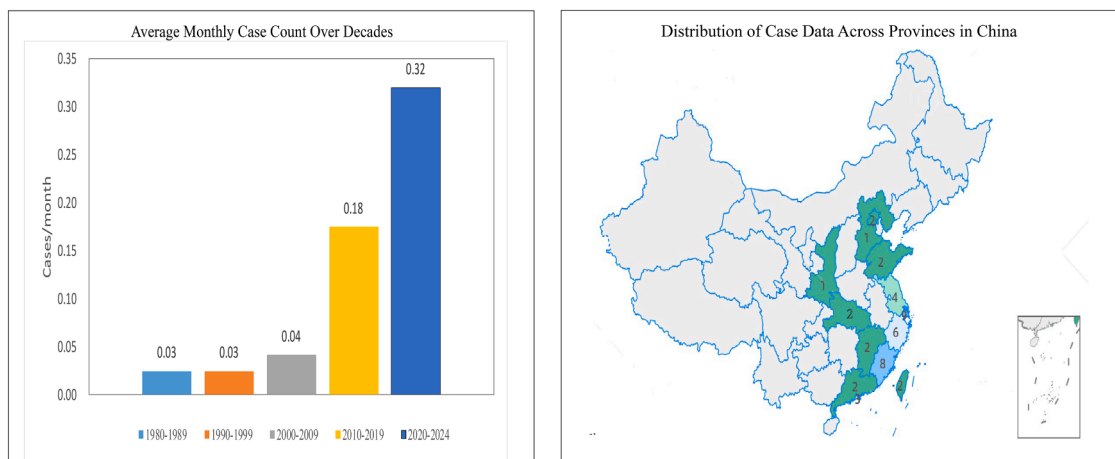


Fig. 3. Temporal and spatial distribution of pulmonary coccidioidomycosis patients in China. (a) Monthly incidence of pulmonary coccidioidomycosis patients in China. (b) Geographical distribution of pulmonary coccidioidomycosis patients in China.

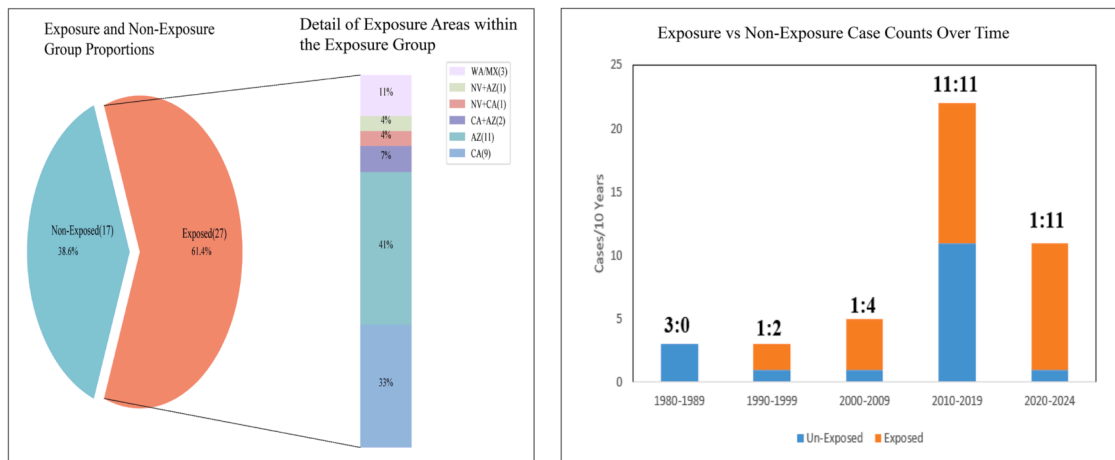


Fig. 4. Comparative Analysis of Exposed and Non-exposed Pulmonary Coccidioidomycosis Patients. (a) Proportional distribution of the number of patients in the two groups, with subgroup analyses of the origin of imported pulmonary coccidioidomycosis patients. (b) Proportional histogram of the number of two groups.

Table 4

Comparison of clinical characteristics between exposed and Non-exposed patients in an epidemic area.

Characteristics	Non-Exposed (n = 17)	Exposed (n = 27)	P Value
Age	45.29 ± 1.97	41.63 ± 3.45	0.001
Sex			0.021
Female	7(41.2 %)	3(11.1 %)	
Male	10(58.8 %)	24(88.9 %)	
Dissemination, No.(%)			0.007
NO	15(88.2 %)	13(48.1 %)	
Yes	2(11.8 %)	14(51.9 %)	
Misdiagnose, No.(%)			0.180
NO	10(58.8 %)	21(77.8 %)	
Yes	7(41.2 %)	6(22.2 %)	
Prognosis			0.879
Recovery	14(82.4 %)	23(85.2 %)	
Death	1(5.9 %)	2(7.4 %)	
Unknown	2(11.8 %)	2(7.4 %)	

largely depends on the experience of clinical and laboratory physicians, which poses a challenge for doctors in non-endemic areas.

With the development of new technologies, such as mNGS and MALDI-TOF are becoming more widely used in clinical microbiology. mNGS diagnoses pathogenic microorganisms at the genomic level. In our case study of two patients co-infected with the influenza A virus, mNGS showed its superiority in accurately detecting and identifying the causative pathogens [49]., NGS has become an important tool in the diagnosis of pulmonary coccidioidomycosis, especially in challenging cases where traditional culture methods may fail or provide delayed results. NGS enables rapid identification of fungal pathogens by detecting their genetic material directly from clinical specimens, offering a more sensitive and specific approach compared to traditional methods [50]. These pathogens were identified as CP and CI, respectively, where CP is identified as representative of the Arizona branch and CI is primarily found in the Central Valley of California. It is believed that CP's environmental range is relatively limited compared to the diverse populations present in Arizona [51,52]. This highlights the importance for clinicians to have a comprehensive understanding of a patient's travel history and to include detailed information about exposure to endemic areas in epidemiological reports. Such practices are crucial for improving the understanding of pulmonary coccidioidomycosis in China.

In terms of disease management, all symptomatic patients should receive antifungal treatment for a minimum of one year. In some cases, lifelong treatment may be necessary, particularly for those with severe or disseminated forms of the disease [53]. Certain patients may require

additional treatments alongside their antifungal treatment. Severe disseminated disease is rare in immunocompetent individuals [54], can lead to life-threatening conditions like acute respiratory distress syndrome (ARDS). Once developed, ARDS has a mortality rate approaching 100 % [55]., Azadeh's retrospective study suggests that short-term use of corticosteroids has no adverse effects on the early symptomatic treatment of acute coccidioidomycosis [56]. In our cases, Case 1 presented persistent fever symptoms. To reduce the inflammation, we considered the use of steroids as the benefits seemed to outweigh the infection, although corticosteroids have been used in the treatment of pulmonary coccidioidomycosis patients previously [57]. However, the application of pulmonary coccidioidomycosis with OP patients still needs to be further validated by prospective clinical trials in endemic areas. In addition, increased eosinophil count and pleural effusion might be one of the indications for corticosteroid application [58]. corticosteroid should be considered in patients with pulmonary coccidioidomycosis complicated with organizing pneumonia, prospective clinical trials in endemic areas are needed to validate their effectiveness and safety.

According to the CDC online database, about 200 deaths from coccidioidomycosis were reported annually in the United States from 1999 to 2019 [59,60], although the mortality rate has not changed much, the total number of cases is increasing and is dominated by an increase in the number of imported coccidioidomycosis cases. In addition, patients with no history of contact with infected areas may also be infected by Coccidioides-carrying cargo, for example, a patient from Hong Kong who had never travelled but had swept containers in a port was diagnosed with Coccidioidomycosis, suggesting that Coccidioidomycosis may also be transmitted by contaminated cargo [61], and this trend of an increase in the number of cases of patients with Coccidioides pneumophila in China is a cause for concern. The trend of increasing the cases of pulmonary coccidioidomycosis in China is noteworthy.

Our study has two limitations. Firstly, limited access to certain literature sources prevented us from obtaining complete detailed information [29]. However, our cases underwent thorough scrutiny. For example, different authors provided various perspectives on the same patient case [4,62], his emphasizes the crucial significance of detailed case reporting for future research. Secondly, we excluded the cases of pulmonary coccidioidomycosis in children and infants in this study, because the wide variability in age at diagnosis, which will have a great impact on the calculation of statistical results and cannot describe the whole.

Conclusion

Overall, the literature highlights the importance of considering pulmonary coccidioidomycosis in patients with relevant travel history and the potential role of eosinophilia on histopathology in aiding the diagnosis. It also emphasizes the need for careful management, including antifungal therapy and consideration of corticosteroid in complicated cases. Furthermore, the article submission explores the regional distribution and trends of pulmonary coccidioidomycosis cases. Given the evolving epidemiology of the disease, it is imperative for clinicians to be aware of the patient's travel history.

Patient perspective

They were grateful for the medical attention and detailed explanation provided by the healthcare team, which helped in managing the initial anxiety associated with the diagnosis. The clarity regarding the therapeutic process and the expected recovery trajectory provided comfort and reassured the patient about the effectiveness of the interventions.

Ethics

We acknowledge our responsibility to protect patient privacy and confidentiality, and all identifiable information has been appropriately de-identified or anonymized in this manuscript. We sincerely thank the patients for their participation and trust in allowing their medical information to be used in this research. Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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CRedit authorship contribution statement

Huanhuan Bi: Writing – review & editing, Writing – original draft, Data curation, Conceptualization. **Feng Hou:** Writing – review & editing, Writing – original draft, Data curation, Conceptualization. **Weizhong Han:** Writing – review & editing, Writing – original draft, Investigation. **JiaXing Sun:** Writing – review & editing, Investigation. **DunQiang Ren:** Writing – review & editing, Writing – original draft, Supervision. **Min Zhuang:** Writing – review & editing, Methodology. **Chunling Zhang:** Writing – review & editing, Writing – original draft, Supervision. **Hongmei Wang:** Writing – review & editing, Writing – original draft, Funding acquisition, Conceptualization.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Data Availability Statement

The original contributions presented in the study are included in the article Material, further inquiries can be directed to the corresponding authors.

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