Int J Clin Exp Pathol 2014;7(12):8637-8646
www.ijcep.com /ISSN:1936-2625/IJCEP0002836

Original Article

Cryptogenic organizing pneumonia associated with invasive pulmonary aspergillosis: a case report and review of the literature

Shuanshuan Xie[1], Changxing Shen[1], Yunfeng Zhang[2], Kun Lu[1], Feng Hu[3], Min Tan[1], Haiyan Lin[1], Lei Xu[1], Qing Yuan[1], Xiaolian Song[1], Changhui Wang[1]

[1]Department of Respiratory Medicine, Shanghai Tenth People's Hospital, Tongji University, Shanghai 200072, PR China; [2]Department of Respiratory Medicine, Shanghai Liqun Hospital, Putuo District, Shanghai 200072, PR China; [3]Department of Respiratory Medicine, Shanghai St.Lukes Hospital, Shanghai 200072, PR China

Received September 28, 2014; Accepted November 26, 2014; Epub December 1, 2014; Published December 15, 2014

Abstract: Background: Concomitant occurrence of invasive pulmonary aspergillosis (IPA) with cryptogenic organizing pneumonia (COP) is scarce. Here, we report a case where COP was a presenting feature in a patient with diagnosed IPA, and review additional 58 COP patients reported in the literature from 1988 through 2013. Case outline: The study was reviewed and approved by the Institutional Ethics Committee of Shanghai Tenth People's Hospital of Tongji University and was conducted in compliance with the Helsinki Declaration. Written informed consent was obtained from patient. A 56-year-old man presenting with productive cough for several weeks and unremitting high fever for a week was hospitalized with an initial clinical diagnosis of pneumonia, for which antibiotics were prescribed but did not work. Seeing that the condition progressed both clinically and radiographically, bronchoscopy, bronchoalveolar lavage and lung biopsy were performed, and the diagnosis of cryptogenic organizing pneumonia (COP) and invasive pulmonary aspergillosis (IPA) co-existence was made. Initially, the patient responded to steroid pulse therapy and voriconazole treatment, and his condition was partially improved. However, the patient's condition deteriorated progressively 5 months after the disease onset and the patient died during the third admission due to respiratory failure and the adverse reactions of coriaceous hormone therapy. Conclusion: The diagnosis of cryptogenic organizing pneumonia (COP) and invasive pulmonary aspergillosis (IPA) co-occurrence depends on clinical, radiological and histological presentations. Similarities with other disease processes could lead to a delayed diagnosis or misdiagnosis. The present case suggests that clinicians should be alert to this disease in their clinical practices.

Keywords: Cryptogenic organizing pneumonia, invasive pulmonary aspergillosis, bronchiolitis obliterans organizing pneumonia

Introduction

Cryptogenic organizing pneumonia (COP) is an interstitial lung disease characterized by intra-alveolar buds of connective tissue. The characteristic clinical features of COP are usually non-specific and include constitutional symptoms with flu-like illness, followed by progressive cough, dyspnea, fever, elevation of biological inflammatory markers, patchy infiltrates on chest radiography and chest computed tomography (CT), and a restrictive spirometric pattern with diffusion impairment. As COP can be idiopathic or associated with a known underlying disease, delayed diagnosis or misdiagnose is likely to occur.

In this case report, we present a 56-year-old man with co-occurrence of COP and IPA. IPA remains a significant cause of morbidity and mortality. The spectrum of disease related to Aspergillus spp. within the lung is variable. The exact nature of any association of Aspergillus spp. either in the development or progression of COP remains unexplored.

To the best of our knowledge, this is a scarce case report of COP and IPA co-occurrence.

Case presentation

The study was reviewed and approved by the Institutional Ethics Committee of Shanghai

Table 1. Clinical features of the patient during the in-hospital treatment period

Variable	First-time admission		Second-time admission			Third-time admission		
Time	07-21	08-08	08-24	08-27	08-30	11-09	11-18	11-27
WBC (× 10^9/l)	4.19	4.26	5.33	5.91	12.7↑	6.38	4.17	1.73↓
Neut (%)	49.5↓	46.2↓	74.6↑	80.5↑	90.0↑	76.0↑	85.6↑	68.0
Hb (g/L)	136	123↓	124↓	119↓	114↓	89↓	100↓	102↓
PLT (× 10^9/l)	112	218	250	258	333↑	55↓	56↓	82↓
CRP (mg/l)	16.5 ↑	23.8↑	119.0↑	136↑	40.3↑		148.8↑	> 214↑
K (mmol/L)	3.56	4.19	4.56	3.90		3.09↓	5.22↑	4.98
Ca (mmol/L)	ND	2.16	2.16			2.02↓	2.38	2.23
BUN (mmol/L)	2.7	5.1	4.8			13.4↑	15.3↑	16.9
Creat (mg/L)	67.3	74.6	70.6			45.9↓	56.3↓	72.6
Glu (ummol/L)	4.5	ND	ND			7.9↑		
SGOT (U/L)	18.4	14.8	ND	55.6	62.5↑	82.5↑	67.1↑	25.9
SGPT (U/L)	35.4	23.1	107.4↑	97.1↑	101.8↑	25.8	16.9	56.5↑
γ-GT (U/L)	23.8	26.8	ND	215.4↑		92.9↑	114.4↑	150.8↑
Protein (g/L)	69	66	61↓		49↓	43↓	40	66
Albumin (g/L)	41	34	32↓	26↓	25↓	28↓		24↓

Abbreviations: WBC, white blood count; Hb, Hemoglobin B; PLT, Platelets; CRP, C Reactive Protein; K, kalium; Ca, calcium; BUN, Blood Urea Nitrogen; SGOT, serum glutamic-oxaloacetic transaminase; SGPT, Serum Glutamic Pyruvic Transaminase; γ-GT, γ-glutamyltransferase. ↑: Increase (compare with normal data); ↓: Decrease (compare with normal data).

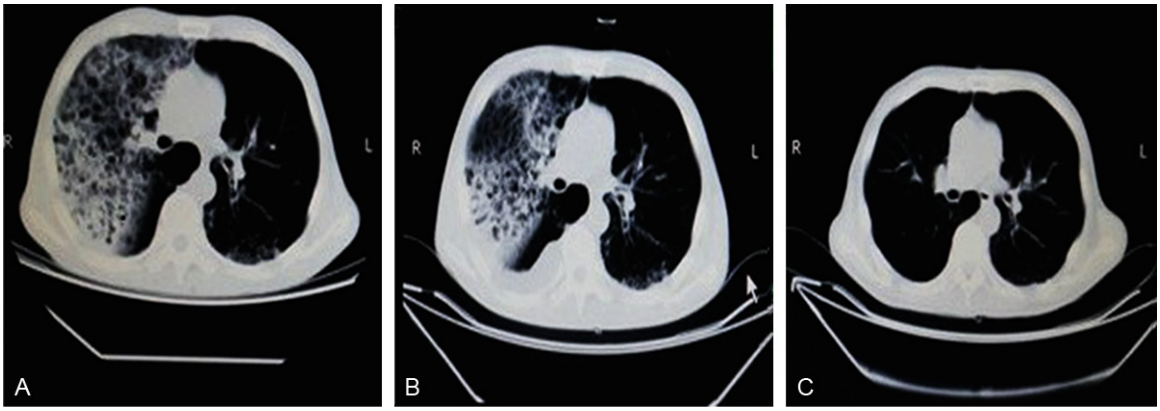

Figure 1. Chest computed tomographies (CT). A: Upon first admission, diffuse infiltrating lesions were evident in right lobe; B: one week after ceftriaxon was initiated, a slight decrease of the lesions can be observed; C: Chest computed tomographies (CT) showed hydropneumothorax after lung biopsy in second admission.

Tenth People's Hospital of Tongji University and was conducted in compliance with the Helsinki Declaration. Written informed consent was obtained from patient. A 56-year-old man came to our hospital for medical consultation because of productive cough for several weeks and unremitting high fever (39°C) in a recent week. Before admission, the patient had experienced a one-year history of expectoration with white bubble sputum, cough and shortness of breath. The patient reported no exposure to musty or dusty conditions that may have instigated or exacerbated the symptoms, nor did he have a history of alcohol abuse or smoking.

Physical examination on admission showed that the patient looked acutely ill and emaciated. Laboratory test results showed that the blood profiling, hepatic and renal functions were outside the normal ranges. The results of arterial blood gas and electrolyte tests are shown in **Table 1**. The results of HIV (human immunodeficiency virus), HBV (hepatitis B virus), sputum smear and cultures for bacilli and mycobacteria were negative.

Bacteriological analysis did not reveal any pathogenic agent. Bronchoalveolar lavage fluid (BAL) showed numerous hyphae of Aspergillus.

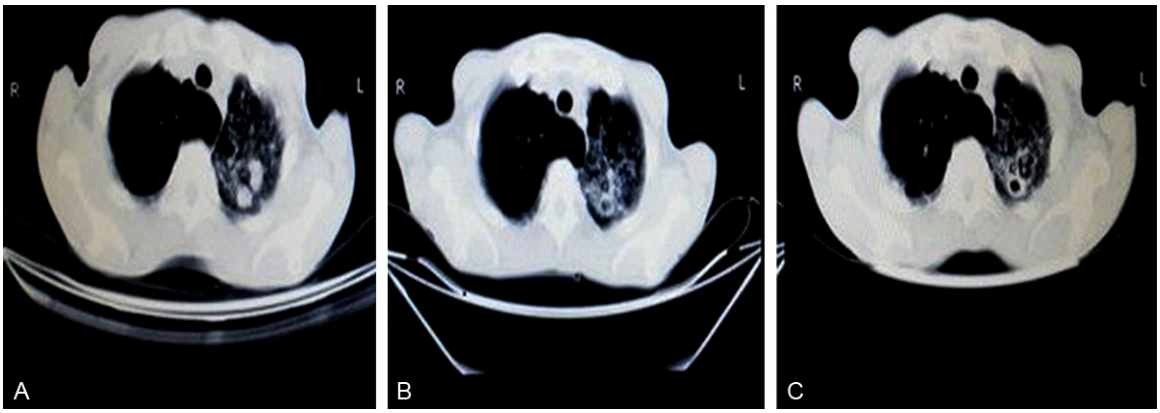

Figure 2. Chest computed tomographies (CT). A: Upon second admission, the diagnosis of invasive pulmonary aspergillosis (IPA): Multiple lesions were present in left lungs, including: cavity, bronchiolitis associated with thicken edbronchial walls; B: After 45 mg/day prednisone treatment in second admission; C: lesions were relapse in left lobe of third-time admission.

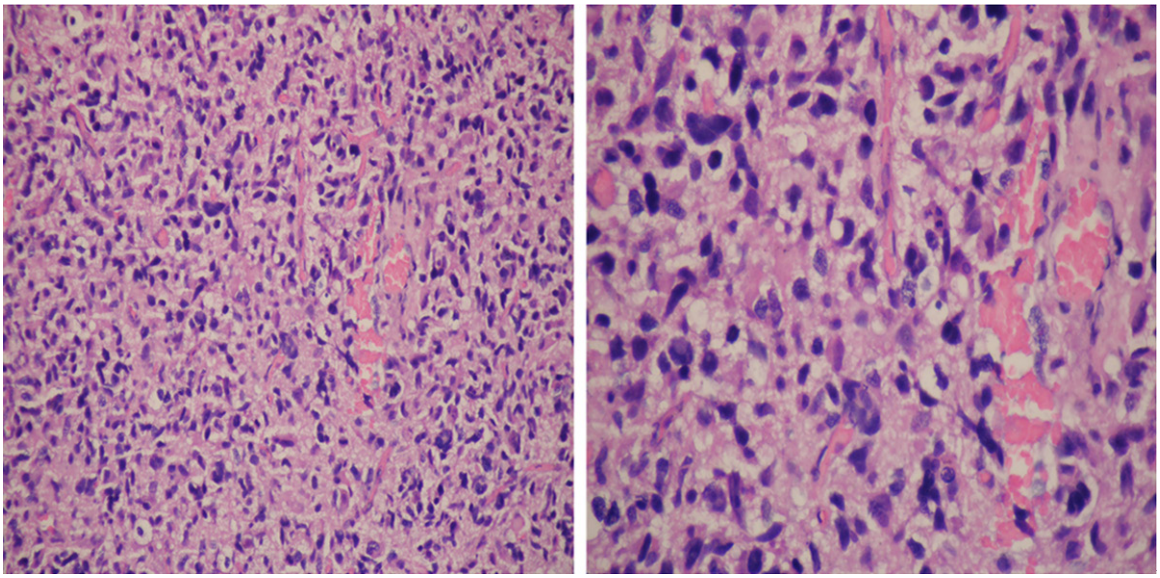

Figure 3. Histopathological. Pathological observation confirmed the diagnosis of cryptogenic organizing pneumonia (COP): numerous capillary channels, plump endothelial cells, and stromal cells with foamy clear cytoplasm. (left Hematoxylin and eosin (H&E) × 200, right Hematoxylin and eosin (H&E) × 400).

Aspergillus was detected in the sputum of the patient. Pulmonary function presented restrictive ventilatory functional disturbance.

First treatment

Based on the initial diagnosis of bilateral pneumonia as shown by CT and laboratory parameters (**Figure 1A** and **Table 1**), ceftriaxone was initiated. As no improvement was observed in the symptoms and pulmonary infiltrates as detected by CT seven days after the first admission and antibiotic therapy (**Figure 1B**), the diagnosis of IPA was made based upon the patient's failure to respond to the empirical treatment, the further imaging findings, and the culture-positive Aspergillus fumigatus detected in the fiberoptic bronchoscopy anti-pollution brush sample. An antifungal regimen using intravenous voriconazole (0.2 q12 h after 0.3 q12 h) was immediately initiated. One week later, the patient's general appearance improved throughout the antifungal treatment, and the patient's temperature returned to a normal level. The patient was discharged and converted to oral voriconazole (200 mg once every 12 h).

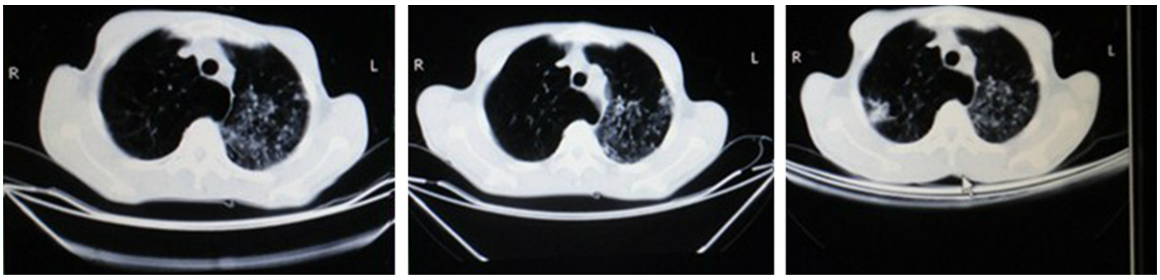

Figure 4. Chest computed tomographies (CT). Upon third admission. After Glucocorticoid therapy, CT reexamination demonstrated no obvious focal absorption.

Second treatment

Two weeks after discharge, the patient was re-admitted to the hospital with one day remittent high fever. Supposing that the patient had not got rid of the fungal infection completely, he was put on oral voriconazole and intravenous moxifloxacin again after the second admission. At day 7 after admission, the patient's condition deteriorated progressively, and CT scan showed bilateral patchy opacities (**Figure 2A**). To clarify the diagnosis, CT-guided percutaneous lung biopsy was performed. Histology revealed centrilobular emphysema, activated alveolar cells, and granulated polyps in the terminal bronchioli and alveolar ducts (**Figure 3**). Fibrin and foam cells were found in the alveoli. These findings were consistent with the diagnosis of COP. However, the patient developed hydropneumothorax, mediastinal emphysema and subcutaneous emphysema after lung biopsy, and therefore closed drainage of thoracic cavity and high-flow oxygen inhalation were administered for a week. CT scan revealed that the hydropneumothorax was absorbed and the chest tube was withdrawn (**Figure 1C**).

After the diagnosis of COP, 45 mg/day prednisone was administered but the symptoms were not relieved (**Figure 2B**). Methylprednisolone I.V (intravenous drip) therapy (80 mg daily) was initiated instead, with the dosage tapering from 10 mg to 40 mg daily, and then to oral methylprednisolone (40 mg daily). During the 10-day follow-up period, the patient remained well, with no other symptoms.

Third treatment

Three months after the second admission, CT reexamination demonstrated no obvious focal absorption (**Figure 2C**, **Figure 4**). Glucocorticoid therapy-related complications including osteoporosis, lower-extremity skin infection, hypoalbuminemia and glucose metabolic disorder were observed in company with COP and IPA. Consequently, the patient's condition deteriorated, and the patient develop acute respiratory failure requiring mechanical ventilation. Despite our unremitting efforts, the patient died in the hospital.

Literature review

Cryptogenic organizing pneumonia used to be known as bronchiolitis obliterans organizing pneumonia (BOOP) in the past few decades. But as no specific cause can be detected in most cases, it is often considered idiopathic because organizing pneumonia is the major histological criterion without the presence of bronchiolitis obliterans in some cases. Despite its relative rarity, a common disorder that was especially gratifying for the clinician due to its prompt improvement under corticosteroid treatment.

Because of the limited published literature on this topic and limited information on the outcome of COP, we reviewed a total of 53 case reports involving 58 patients with COP or BOOP diagnosed from 1988 through 2013 published in PubMed, EMBASE, and Cochrane databases (**Table 2**). The 58 patients included 36 males and 22 females who ranged in age from 14 to 75 years with a mean of 50 years. Of them, 11 patients were reported to have HIV, 6 patients have ID (idiopathic), 6 have cancer, 4 have RA (rheumatoid arthritis), 2 have UC (ulcerative colitis), 2 have SS (Sjogren syndrome), and 2 have SLE (systemic lupuserythematosus). The remaining 25 patients were reported to have other different causes (**Table 2**). Of the 58 patients reported in the published literature,

Table 2. Literature review of reported cases of COP

Studies	Year	Mean Age (yr)	No. of Patients M/F	Associated conditions	Pulmonary Function Results*	Mean Dose of Prednisone Daily	Duration of Therapy	Type of Biopsy	Outcome
Swinburn *et al.* [1]	1988	20	0/1	UC	NA	40 mg	NA	OLBX	R = 1
Allen *et al.* [2]	1989	40	1/0	HIV	NA	80 mg	5 mo	OLBX	C = 1
Camus *et al.* [3]	1989	70	2/0	Acebut or amio	NA	40 mg	17 mo	TBBX = 1 OLBX = 1	R = 1 C = 1
Patel *et al.* [4]	1989	56.6	0/2	ID = 2	NA 2) 2.44	NA	NA	OLBX = 1 TBBX = 1	R = 2
Liote *et al.* [5]	1990	39	1/0	HIV	NA	NA	NA	OLBX	C = 1
Garcia-Vicuna *et al.* [6]	1990	67	1/0	RA	NA	7.5 mg and 10 mg MTX	8 mo	OLBX	C=1
Matteson *et al.* [7]	1990	52	1/0	SS	NA	400 mg	3 mo	OLBX	R = 1
Carey *et al.* [8]	1991	56	1/0	CnI	NA	NA	> 3 mo	OLBX	R = 1
Anonymous *et al.* [9]	1991	68	1/0	ID = 1	1) 1.31 2) 1.46 4) 59	60 mg	7 mon	TBBX	R = 1
Laguna *et al.* [10]	1991	28	1/0	VIDS	NA	1 mg/kg	11 mo	OLBX	C = 1
Thiel *et al.* [11]	1991	75	1/0	RA	1) 1.64 2) 2.53	80 mg	18 mo	OLBX	R = 1
Peramaki *et al.* [12]	1991	60	1/0	Parainf 3 virus	1) 1.02 2) 2.85	60 mg	NA	OLBX	C = 1
Kaufman *et al.* [13]	1991	26	0/1	VIDS	1) 2.94 2) 3.66	60 mg	"Few mo"	OLBX	R=1
Gammon *et al.* [14]	1992	41	1/1	SLE	1) 1.68 2) 2.11 3) 64	60 mg	3 mo	OLBX	R = 1 D = 1
Thirman *et al.* [15]	1992	37	1/0	BMT	1) 3.9 2) 4.11	120 mg	> 1 yr	TBBX	C = 1
Usui *et al.* [16]	1992	69	0/1	SS	1) 1.2 2) 1.52	1,000 mg	2 d	Autopsy	D = 1
Robinson *et al.* [17]	1992	71	1/0	PAN=1	NA	NA	1 wk	OLBX	D = 1
Romero *et al.* [18]	1992	58	0/1	ML	1) 0.9 2) 1.15	60 mg	10 mo	TBBX	C = 1
Rutherford *et al.* [19]	1992	48	1/0	MGN	NA	500 mg IV	8 mo	OLBX	R = 1
Domingo *et al.* [20]	1993	54	1/0	ID=1	3) 100 4) 107	1 mg/Kg	12 mo	OLBX	R = 1
Hsue *et al.* [21]	1993	36	0/1	PM	2) 2.32	60 mg	> 1 yr	OLBX	C = 1
Ippolito *et al.* [22]	1993	68	0/1	RA	NA	60 mg	> 5 mo	OLBX	R = 1
Reich *et al.* [23]	1993	68	1/0	ID = 1	NA	No treament		TBBX	R = 1
Schwarz *et al.* [24]	1993	45	0/1	ID = 1	NA	2 gm IV	> 5 mo	OLBX	R = 1
Yale *et al.* [25]	1993	64	0/1	PVM	NA	60 mg	9 mo	OLBX	R = 1
Zackrison *et al.* [26]	1993	63	1/0	EMC	NA	80 mg	"Several months"	OLBX	C = 1

Leo *et al.* [27]	1994	35	1/0	HIV	NA	20-30 mg	9 mo	TBBX	C = 1
Garcia *et al.* [28]	1994	32	1/0	HIV	NA	NA	14 mo	autopsy	D = 1
Watson *et al.* [29]	1995	30	0/1	Nodular sclerosing hodgkin's diease	NA	NA	4 mo	TBBX	R = 1
Joseph *et al.* [30]	1995	30	1/0	HIV	NA	NA	NA	TBBX	C = 1
Sanito *et al.* [31]	1995	47	1/0	NA	NA	60	15 mo	TBBX	C = 1
Pohl *et al.* [32]	1996	26	0/1	NA	Idiopathic CD4+depletion	NA	14	OLBX	C = 1
Zahraa *et al.* [33]	1996	14	1/0	HIV	NA	40	15 mo	OLBX	D = 1
Diaz *et al.* [34]	1997	26	1/0	HIV	NA	60	10 mo	OLBX	D = 1
Ghidini *et al.* [35]	1999	27	0/1	HIV	NA	40 mg	6 mo	OLBX	C = 1
Alleman *et al.* [36]	2002	43	1/0	NA	restriction.	high-dose	6 mo	OLBX	C = 1
Koinuma *et al.* [37]	2002	60	0/1	NA	NA	12.5 mg	8 mo	TBBX	R = 1
Song *et al.* [38]	2003	61	1/0	BAC	NA	1 mg/kg	7 mo	TBBC	C = 1
Khater *et al.* [39]	2004	64	1/0	AIDS+CHF	NA	50 mg	> 4 mo	TBBX	D = 1
Kaushik *et al.* [40]	2004	70	1/0	RA	NA	250 mg	4 week	TBBX	C = 1
Guerriero *et al.* [41]	2005	71	0/1	Breast cancer	NA	60 mg	NA	clinically	R = 1
Verma *et al.* [42]	2006	56	1/0	Pneumocystis carinii	NA	NA	NA	OLBX	C = 1
Carreno *et al.* [43]	2007	56	0/1	PCKD	NA	60 mg	> 2 mo	fiberbronchos-copy	C = 1
Fenton *et al.* [44]	2008	71	0/1	Nitrofurantoin	1) 1.33 2) 1.53 3) 57 4) 47	40 mg	11 mo	TBBX	C = 1
Bissoli *et al.* [45]	2008	71	0/1	Breast cancer	NA	NA	1 week	biopsies bronchoscopy	C = 1
Miladinovic-Djukanovic *et al.* [46]	2009	57	1/0	NA	3) 69 4) 61.8	60 mg	15 mo	OLBX	C = 1
Wantke *et al.* [47]	2008	46	0/1	SRP positive necrotising myositis	1) 1.96 2) 2.81 3) 61 4) 72	0.75 mg/kg	33 mo	OLBX	R = 1
Park *et al.* [48]	2009	45	0/1	ADM/Breast cancer	NA	20 mg	> 2 mo	TBBX	D = 1
Ponnuswamy *et al*. [49]	2009	50	1/0	NA	1) 2.14 2) 2.65 3) 100 4) 93	NA	> 2 mo	OLBX	C = 1
Hua *et al.* [50]	2010	33	1/0	KFD	NA	45 mg	3 mo	TBBX	R = 1
Sato *et al.* [51]	2011	32	0/1	AOSD	NA	30 mg	> 1 mo	TBLB	R = 1
Aydogdu *et al.* [52]	2012	57	1/0	UC/Air leak syndrome	NA	1 mg/kg (60 mg)	> 1 mo	TBBX	C = 1
Hiraki *et al*. [53]	2012	72	3/0	Lung cancer	NA	NA	NA	NA	D = 3

Abbreviations: NA, not available; R, recovery; C, chronic; D, death; OLBX, open lung biopsy; TBBX, trans-bronchial biopsy; UC, ulcerative colitis; ID, idiopathic; RA, rheumatoid arthritis; MTX, methotrexate; SS, Sjogren syndrome; Cni, Cryptococcus Normanna infection; VIDS, variable immunodeficiency syndrome; SLE, systemic lupuserythematosus; PAN, polyesterification; M, malignant lymphoma; MGN, mesangiocapillary glomerulo nephritis; PM-DM, Polymyositis-dermatornyositis; PVM, plasmodium vivax malaria; EMC, essential mixed cryoglobulinemia; ADM, Amyopathic dermatomyositis; AOSD, adult onset Still's disease; BAC, Bronchioloalveolar Carcinoma; KFD, Kikuchi Fujimoto disease; NM, necrotising myositis; PCKD, polycystic kidney disease; SRP, Signal recognition particle; *: 1) FEV1; 2) FVC; 3) FEV1%P; 4) FVC%P.

30 patients were diagnosed by OLBX (open lung biopsy), 19 by TBBX (trans-bronchial biopsy), 2 by autopsy, and 2 by other types of biopsy. TBBX failed to make a correct diagnosis in 6 patients, in whom OLBX was required. Pulmonary function tests showed a restrictive pattern in most patients and a combined restrictive and obstructive pattern in one case. Generally, patients recovered completely at a dose of 20-1,000 mg/d prednisone. The usual duration was 3-4 months. A standardized therapeutic protocol allowed a reduction in prednisone doses without adversely affecting the outcome and relapse rate. Of the 58 patients, 22 (37.9%) patients resolved completely, 25 (43.1%) patients improved but had residual abnormalities, and 11 (19%) patients died.

Discussion

This article reports a 56-year-old male patient who was diagnosed with IPA and COP, and reviews additional 58 COP patients reported in the literature during the period from 1988 through 2013. COP and IPA were suspected mostly because of TBBX, histopathology, and radiological findings. The simultaneous presence of these two diseases is scare and has never been reviewed so many literatures before.

Interestingly, both COP and IPA are predominantly air space and present similar radiological features. Co-existence of COP and IPA makes both diagnosis and treatment difficult and challenging. Firstly, some authors have demonstrated that long-term systemic corticosteroid therapy with underlying chronic lung conditions is a risk factor for IPA. Secondly, it is also worth considering whether anti-fungal agents are a risk factor for COP. IPA is a life-threatening fungal infection that predominantly affects fungal infection that predominantly affects severely immunocompromised patients [54, 55], particularly those with prolonged neutropenia or organ transplantation. Other predisposing factors, such as prolonged systemic corticosteroid therapy and HIV infection, have also been recognized. Thirdly, the case of COP in our patient responded to corticosteroids but relapse occurred when the corticosteroid dosage was tapered off. This patient died of the adverse reactions of corticosteroids. Therefore, in such patients, and specially diagnosis of COP and IPA should be considered significant by further investigations to rapidly confirm the diagnosis.

To avoid delayed diagnosis and therapeutic pitfalls, clinicians should maintain a high index of suspicion for IPA and COP: 1) COP is not responsive to antibiotic therapy and is associated with pathogens on bronchioloalveolar lavage or lung biopsy. 2) Amphotericin-B is the drug of choice for the treatment of IPA. The combination of amphotericin-B and flucytosine not only offers a synergistic effect but helps reduce the dosage and the toxic effect of amphotericin-B. 3) The disease is usually responsive to corticosteroid treatment. However, relapse can occur when steroids are tapered or discontinued. Long-term use of corticosteroids is often associated with complications in diverse organs and systems, and therefore the importance of limiting corticosteroid prescriptions at the lowest possible dose should be addressed [56, 57]. We feel that the strategy should aim at minimizing the adverse effects of corticosteroids and avoiding over-treatment to obtain a well-equilibrated balance between using an efficient treatment protocol and minimization of the adverse effects of corticosteroids by using low doses and short treatment durations.

Conclusion

This is a scarce report of COP and IPA. In the presence of pulmonary disease, the detection of fungi and COP should prompt additional diagnostic efforts. In addition, preventive methods should be established as soon as possible. This case report suggests that waiting for positive results of routine microbiological analyses runs the risk of a fatal delay in diagnosis. Heightened surveillance with endotracheal cultures, HRCT scan and lung biopsy must be considered early in the management of such patients for the sake of avoiding a delay in appropriate treatment. Voriconazole or amphotericin-B or both should currently be considered the drug of choice in the management of COP and IPA.

Acknowledgements

We thank all the histology technologists at the tenth people of Shanghai for their technical support. This study was funded by the National Natural Science Foundation of China (No. 81172229, 81100018). The funders had no

role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Xiaolian Song or Dr. Changhui Wang, Department of Respiratory Medicine, Shanghai Tenth People's Hospital, Tongji University, 301 Yanchang Rd (M), Shanghai 200072, PR China. E-mail: song-xiao-lian@hotmail.com (XLS); wang-chang-hui@hotmail.com (CHW)

References

[1] Swinburn CR, Jackson GJ, Cobden I, Ashcroft T, Morritt GN, Corris PA. Bronchiolitis obliterans organizing pneumonia in a patient with ulcerative colitis. Thorax 1988; 43: 735-36.

[2] Allen JN, Wewers MD. HIV-associated bronchiolitis obliterans organizing pneumonia. Chest 1989; 96: 197-98.

[3] Camus P, Noel-Lombard J, Perrichon M, Piard F, Guérin JC, Thivolet FB, Jeannin L. Bronchiolitis obliterans organizing pneumonia in patients taking acebutolol or amiodarone. Thorax 1989; 44: 711-15.

[4] Patel U, Jenkins PF. Bronchiolitis obliterans organizing pneumonia. Respir Med 1989; 83: 241-44.

[5] Liote H, Porte JM, Postal Mj, Postal MJ, Martin de Lassalle E, Derenne JP. Bronchiolitis obliterans, pneumocystosis and HIV infection. Rev Mal Respir 1990; 7: 603-6.

[6] Garcia-Vicuna R, Diaz-Gonzale F, Castaneda S, Arranz M, López-Bote JP. Rheumatoid disease resembling lung neoplasia. J Rheumatol 1990; 17: 1686-88.

[7] Matteson EL, Ike RW. Bronchiolitis obliterans organizing pneumonia and Sjogren's syndrome. J Rheumatol 1990; 17: 676-79.

[8] Carey CF, Mueller L, Fotopoulos CL, Dall L. Bronchiolitis obliterans organizing pneumonia asscociated with Cryptococcus neoformans infection (letter). REV infect Dis 1991; 13: 1253-54.

[9] Anonymous: Case records of the Massachusetts General Hospital. Weekly clinicopathological exercises. Case 17-1991. A 68-year-old man with diffuse, patchy pulmonary infiltrates. N Engl J Med 1991; 324: 1195-205.

[10] Laguna del Estal P, Martin T, Martin F, López E. Obliterating bronchiolitis in a patient with human immunodeficiency virus infection. Med Clin (Barc) 1991; 97: 638.

[11] Van Thiel RJ, van der Burg S, Groote AD, Nossent GD, Wills SH. Bronchiolitis obliterans-organizing pneumonia pneumonia and rheumatoid arthritis. Eur Respir J 1991; 4: 905-11.

[12] Perämäki E, Salmi I, Kava T, Romppanen T, Hakkarainen T. Unilateral bronchiolitis obliterans organizing pneumonia and bronchoaveolar lavage neutrophilia in a patient with parainfluenza 3 virus infection. Respir Med 1991; 85: 159-61.

[13] Kaufman J, Komorowski R. Bronchiolitis obliterans organizing pneumonia in common variable immunodeficiency syndrome. Chest 1991; 100: 552-53.

[14] Gammon RB, Bridges TA, al-Nezir H, Alexander CB, Kennedy JI Jr. Bronchiolitis obliterans organizing pneumonia asscociated with systemic lupus erythematosus. Chest 1992; 102: 1171-74.

[15] Thirman MJ, Devine SM, O'Toole K, Cizek G, Jessurun J, Hertz M, Geller RB. Bronchiolitis obliterans organizing pneumonia as a complication of allogeneic bone marrow transplantion. Bone Marrow Transplant 1992; 10: 307.

[16] Usui Y, Kimula Y, Miura H, Kodaira Y, Takayama S, Nakayama M, Kataoka N. A case of bronchiolitis obliterans organizing pneumonia associated with primary Sjogren's syndrome who died of superimposed diffuse alveolar damage. Respir 1992; 59: 122-24.

[17] Robinson BW, Sterrett G. Bronchiolitis obliterans organizing pneumonia associated with polyarteritis nodosa. Chest 1992; 102: 1895-97.

[18] Romero S, Martin C, Massuti B, Aranda I, Hernandez L. Malignant lymphoma in a patient with relapsing bronchiolitis obliterans organizing pneumonia. Chest 1992; 102: 1895-97.

[19] Rutherford PA, Veale D, Ashcroft T, Morley AR, Gibson GJ, Wilkinson R. Mesangiocapillary glomerulonephritis as the presenting feature of cryptogenic organizing pneumonitis. Nephrol Dial Transplant 1992; 7: 1043-46.

[20] Domingo JA, Perez-Calvo J, Carretero JA, Ferrando J, Cay A, Civeira F. Bronchiolitis obliterans organizing pneumonia. An unusual cause of solitary pulmonary nodule. Chest 1993; 103: 1621-23.

[21] Hsue YT, Paulus HE, Coulson WF. Bronchiolitis obliterans organizing pneumonia in polymyositis. A case report with long term survival. J Rheumatol 1993; 20: 877-79.

[22] Ippolito JA, Palmer L, Spector S, Kane PB, Gorevic PD. Bronchiolitis obliterans organizing pneumonia and rheumatoid arthritis. Semin Arthritis Rheum 1993; 23: 70-78.

[23] Reich J, Scott D. Levitating lung lesions due to bronchiolitis obliterans organizing pneumonia. Chest 1993; 103: 623-24.

[24] Schwarz MI. Diffuse pulmonary infiltrates and respiratory failure following 2 weeks of dys-

pnea in a 45-year old woman. Chest 1993; 104: 927-29.
[25] Yale SH, Adlakha A, Sebo TJ, Ryu JH. Bronchiolitis obliterans organizing pneumonia caused by plasmodium vivax malaria. Chest 1993; 104: 1294-96.
[26] Zackrison LH, Katz P. Bronchiolitis obliterans organizing pneumonia associated with essential mixed cryoglobulinemia. Arthritis Rheum 1993; 36: 1627-30.
[27] Leo YS, Pitchon HE, Messler G, Meyer RD. Bronchiolitis obliterans organizing pneumonia in a patient with AIDS. Clin Infect Dis 1994; 18: 921-4.
[28] Garcia Rio F, Garcia Satue JL, Prados C, Casadevall J, Gómez L, Pino JM. 3 nonidiopathic forms of bronchiolitis obliterans organizing pneumonia. Arch Bronconeumol 1994; 30: 263-5.
[29] Watson D, Fadem JJ Jr. Bronchiolitis obliterans organizing pneumonia cured by standard dose inhaled triamcinolone:the first documented case. South med J 1995; 88: 980-3.
[30] Joseph J, Harley RA, Frye MD. Bronchiolitis obliterans with organizing pneumonia in AIDS. N Engl J Med 1995; 332: 273.
[31] Sanito NJ, Morley TF, Condoluci DV. Bronchiolitis obliterans organizing pneumonia in an AIDS patient. Eur Respir J 1995; 8: 1021-1024.
[32] Pohl W. A patient with idiopathic bronchiolitis obliterans with organizing pneumonia and idiopathic CD4 t T-lymphocytopenia. Wien Klin Wochenschr 1996; 108: 473-477.
[33] Zahraa J, Herold B, Abrahams C, Johnson D. Bronchiolitis obliterans organizing pneumonia in a child with acquired immunodeficiency syndrome. Pediatr Infect Dis J 1996; 15: 448--451.
[34] Diaz F, Collazos J, Martinez E, Mayo J. Bronchiolitis obliterans in a patient with HIV infection. Respir Med 1997; 91: 171-173.
[35] Ghidini A, Mariani E, Patregnani C, Marinetti E. Bronchiolitis obliterans organizing pneumonia in pregnancy. Obstet Gynecol 1999; 94: 843.
[36] Alleman T, Darcey DJ. Case report: bronchiolitis obliterans organizing pneumonia in a spice process technician. J Occup Environ Med 2002; 44: 215-6.
[37] Koinuma, D, Miki, M, Ebina, M, Tahara M, Hagiwara K, Kondo T, Taguchi Y, Nukiwa T. Successful treatment of a case with rapidly progressive bronchiolitis obliterans organizing pneumonia (BOOP) using cyclosporin A and corticosteroid. Intern Med 2002; 41: 26-9.
[38] Song J, Gorgan L, Corkey R, Kwa SL. An unusual case of bronchiolitis obliterans organizing pneumonia concomitant with bronchioloalveolar carcinoma. Respiration 2004; 71: 95-7.
[39] Khater FJ, Moorman JP, Myers JW, Youngberg G, Sarubbi FA. Bronchiolitis obliterans organizing pneumonia as a manifestation of AIDS: case report and literature review. J Infect 2004; 49: 159-164.
[40] Kaushik P, Cooper ES, Banda VR, Vatsavai SR, Kaushik R. Bronchiolitis obliterans with organizing pneumonia in rheumatoid arthritis-a fatal case and short review of literature. Rheumatol Int 2005; 25: 391-393.
[41] Guerriero G, Battista C, Montesano M, Carino R, Primavera A, Costantino S, Spoto S, D'Angelillo RM, Altomare V. Unusual complication after radiotherapy for breast cancer bronchiolitis obliterans organizing pneumoniacase report and review of the literature. Tumori 2005; 91: 421-423.
[42] Verma N, Soans B. Cryptogenic organizing pneumonia associated with Pneumocystis carinii infection and sirolimus therapy in a renal transplant patient. Australas Radiol 2006; 50: 68-70.
[43] Carreño CA, Gadea M. Case report of a kidney transplant recipient converted to everolimus due to malignancy: resolution of bronchiolitis obliterans organizing pneumonia without everolimus discontinuation. Transplantation Proceedings 2007; 39: 594-595.
[44] Fenton ME, Kanthan R, Cockcroft DW. Nitrofurantoin-associated bronchiolitis obliteran organizing pneumonia: report of a case. Can Respir J 2008; 15: 311-312.
[45] Bissoli L, Di Francesco V, Valbusa F, Zivelonghi A, Fantin F, Zamboni M. Case of bronchiolitis obliterans organising pneumoniae (BOOP) after nine months post-operative irradiation for breast cancer. Age Ageing 2008; 37: 235.
[46] Miladinovic-Djukanovic N, Djokovic J, Torbica N, Popević M. Cryptogenic Organizing Pneumonia Case Report. Srp Arh Celok Lek 2009; 137: 681-3.
[47] Wantke F, Kneussl M, Hubner M, Derfler K, Brücke T, Schmaldienst S. Signal recognition particle (SRP) positive myositis in a patient with cryptogenic organizing pneumonia (COP). Rheumatol Int 2010; 30: 1361-1365.
[48] Park SH, Kum YS, Kim KC, Choe JY, Park SH, Kim SK. Pneumomediastinum and subcutaneous emphysema secondary to amyopathic dermatomyositis with cryptogenic organizing pneumonia in invasive breast cancer: a case report and review of literature. Rheumatol Int 2009; 29: 1231-1235.
[49] Ponnuswamy A, Mediratta N, Lyburn ID, Finnerty JP. False positive diagnosis of malignancy in a case of cryptogenic organising pneumonia presenting as a pulmonary mass with mediastinal nodes detected on fluorodeoxyglucose-positron emission tomography: a case report. J Med Case Rep 2009; 14; 3: 124.
[50] Hua F, Zhu L. Kikuchi Fujimoto disease associated with cryptogenic organizing pneumonia:

case report and literature review. BMC Infect Dis 2010; 10: 64.
[51] Sato H, Yokoe I, Nishio S, Onishi T, Takao T, Kobayashi Y, Haraoka H. A case of adult onset Still's disease complicated with cryptogenic organizing pneumonia. Intern Med 2011; 50: 247-251.
[52] Aydoğdu M, Gürsel G, Özyilmaz E, Akyürek N, Memış L. A case of ulcerative colitis complicated with bronchiolitis obliterans organizing pneumonia (BOOP) and air leak syndrome. Turk J Gastroenterol 2012; 23: 590-5.
[53] Hiraki T, Gobara H, Kato K, Toyooka S, Mimura H, Kanazawa S. Bronchiolitis obliterans organizing pneumonia after radiofrequency ablation of lung cancer: report of three cases. J Vasc Interv Radiol 2012; 23: 126-30.
[54] Codish SD, Tobias JS, Hannigan M. Combined amphotericin-B-flucytosine therapy in aspergillus pneumonia. J Am Med Assoc 1979; 241: 2418-2419.
[55] von Eiff M, Roos N, Schulten R, Hesse M, Zühlsdorf M, van de Loo J. Pulmonary aspergillosis:early diagnosis improves survival. Respiration 1995; 62: 341-347.
[56] Epler GR. Heterogeneity of bronchiolitis obliterans organizing pneumonia. Curr Opin Pulm Med 1998; 4: 93-97.
[57] King TE. Bronchiolitis. In: Schwarz MI and King TE, editors. Interstitial Lung Disease. 3rd edition. Hamilton, ON, Canada: B.C. Decker; 1998. pp. 645-684.