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【 CASE REPORT 】

Pulmonary Sarcoidosis Presenting with Acute Respiratory Failure: A Report of a Case Diagnosed by Endobronchial Ultrasound-guided Transbronchial Needle Aspiration on Ventilation after Intubation

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Abstract:

Sarcoidosis is a multisystem granulomatous disease of unknown etiology and is pathologically characterized by non-caseating granulomas in the organs involved. We herein report a case of sarcoidosis in a Japanese woman with acute respiratory failure, diagnosed using endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) on the ventilator after intubation. Only a few cases of previously undiagnosed sarcoidosis presenting acute respiratory failure have been reported. It is important to be aware that undiagnosed sarcoidosis may present with acute respiratory failure. Therefore, EBUS-TBNA under mechanical ventilation may be useful for the immediate diagnosis of patients.

Key words: sarcoidosis, acute respiratory failure, endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA)

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Introduction

Sarcoidosis is a multisystem granulomatous disease of unknown etiology. It most commonly affects the mediastinal lymph nodes, lungs, skin, liver, and eyes (1). It may also affect the heart, central nervous system, spleen, and upper respiratory tract.

The progress of pulmonary diseases is typically slow, and some do not progress. The progress of pulmonary sarcoidosis leads to chronic interstitial lung disease accompanied by dyspnea, cough, and fatigue (2). Acute respiratory disorders are rare and usually occur in advanced sarcoidosis based on previous respiratory infectious diseases, like pneumonia or, more specifically, bronchospasm, in cases where the airways are hyperresponsive due to granulomatous inflammation or are injured due to fibrocystic pulmonary sarcoidosis (3). An acute initial presentation with respiratory failure in a previously undiagnosed patient is rare, and only a few cases have been reported (4-11).

A sarcoidosis diagnosis is based on the compatible clinical and radiologic findings supported by histological findings in one or more organs of noncaseating epithelioid cell granulomas while excluding other similarly developing diseases (1). For patients with parenchymal lung disease or apparent mediastinal adenopathy, flexible bronchoscopy with bronchoalveolar lavage (BAL), an endobronchial biopsy, and a transbronchial biopsy (TBLB) are the traditional methods for a minimally invasive diagnosis of sarcoidosis. Recent reports have confirmed the diagnostic value of endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) for a mediastinal lymph node biopsy in patients with suspected sarcoidosis (12, 13). Compared to a transbronchial biopsy, TBNA of the mediastinal nodes by endobronchial or esophageal ultrasound results in a higher diagnostic yield, is less invasive, and is safer (14, 15). However, there have been no reported cases of sarcoidosis diagnosis by EBUS-TBNA on the ventilator after intubation, and there are very few case reports of sarcoidosis presenting with acute respiratory failure.

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Table. Laboratory Tests.

Arterial blood gas (Room air)		Biochemistry		Bronchoalveolar lavage	
pH	7.472	TP	7.0 g/dL	Cell count	175,000 /mL
$PaCO_2$	35.8 mmHg	Alb	2.9 g/dL	Neutrophils	16.0 %
PaO_2	51.6 mmHg	T-bil	0.6 mg/dL	Lymphocytes	73.0 %
HCO_{3-}	25.8 mEq/L	AST	20 U/L	Macrophages	11.0 %
Base excess	2.8 mEq/L	ALT	20 U/L	CD4/CD8 ratio	18.2
Lactate	0.9 mg/dL	LD	193 U/L		
Glucose	136 mg/dL	CK	50 U/L	Urinary antigen test	
		ALP	349 U/L	*Streptococcus pneumoniae*	negative
Hematology		γ-GTP	84 U/L	*Legionella pneumophila*	negative
WBC	8,400 /μL	Na	137 mEq/L		
Neutro	76.8 %	K	4.1 mEq/L	Rapid antigen test	
Eosino	1.4 %	Cl	100 mEq/L	Influenza A	negative
Baso	0.6 %	Ca	9.1 mg/dL	Influenza B	negative
Mono	9.1 %	P	3.7 mg/dL	*Mycoplasma pneumoniae*	negative
Lymph	12.1 %	BUN	12 mg/dL		
Atypical-Lymph	0 %	sCr	0.53 mg/dL		
RBC	387×10^4 /μL	eGFR	82.85 mL/min/1.73m^2		
Hb	12.7 g/dL	CRP	12 mg/dL		
Ht	39.2 %	BNP	11.6 pg/mL		
Plt	36.1×10^4 /μL	IGRA	negative		
		β-D-glucan	<5 pg/mL		
Blood coagulation		ACE	10.5 U/L		
PT-INR	1.1	KL-6	195 U/mL		
APTT	30.1 sec	sIL-2R	1,728 U/mL		
D-dimer	1.5 μg/mL				

WBC: white blood cells, Neutro: neutrophils, Eosino: eosinophils, Baso: basophils, Mono: monocytes, Lymph: lymphocytes, RBC: red bell cells, Hb: hemoglobin, Ht: hematocrit, Plt: platelets, PT-INR: prothrombin time-international normalized ratio, APTT: activated partial thromboplastin time, TP: total protein, Alb: alubumin, T-bil: total-bilirubin, AST: aspartate transaminase, ALT: alanine transaminase, LD: lactate dehydrogenase, CK: creatine kinase, ALP: alkaline phosphatase, γ-GTP: γ-glutamyltransferase, BUN: blood urine nitrogen, sCr: serum creatinine, eGFR: estimated glomerular filtration rate, CRP: C-reactive protein, BNP: brain natriuretic peptide, IGRA: interferon gamma releasing assay (QuantiFERON®-TB Gold Plus), ACE: angiotensin-converting enzyme, KL-6: krebs von den Lungen-6, sIL-2R: soluble interleukin-2 receptor, CD4/CD8 ratio: cluster of differentiation 4/cluster of differentiation 8 ratio

We herein report a case of sarcoidosis with severe acute respiratory failure that was successfully treated using corticosteroid therapy after a successful diagnosis by EBUS-TBNA on the ventilator after intubation.

Case Report

A 76-year-old Japanese woman was admitted to the hospital with general malaise and dyspnea for the past week. On chest auscultation, fine crackles were detected in both the lungs, and her percutaneous oxygen saturation (SpO_2) level was 85% (room air). Chest computed tomography (CT) revealed bilateral diffuse irregular thickening of the bronchovascular bundles and ground glass opacification with mediastinal lymphadenopathy. Previous doctors suspected bacterial pneumonia and prescribed antibiotics (Ceftriaxone 2 g/day + Azithromycin 500 mg/day). However, her respiratory status worsened, leading to her transfer to our hospital on the day of admission.

She had a medical history of hypertension and mild dementia and was taking donepezil and amlodipine. She had not started any new drugs or supplements recently. Chest radiography, performed at our hospital one year ago, had revealed no abnormalities. She had no history of smoking or alcohol abuse and did not have any familial history of connective tissue or hematological diseases.

Upon admission, her blood pressure was 154/67 mmHg, and her heart rate was 102 beats/min. The oxygen saturation level was 85% (room air), respiratory rate was 20 breaths/min, and her body temperature was 36.0 °C. Fine crackles were detected in both lower lungs, but there were no cardiac murmurs/rubs/gallops, jugular venous distention, or edema suggesting heart failure. She also had no history or any physical examination results indicative of connective tissue or hematological diseases.

Laboratory tests showed Type 1 respiratory failure and elevated C-reactive protein and sIL-2R levels (Table). Chest radiography showed diffuse reticular and ground-glass opacities in the bilateral lungs with mediastinal widening. Chest CT demonstrated bilateral thickening of bronchovascular bundles and septum predominantly in the upper lobes with bilateral hilar and mediastinal lymphadenopathies as well as pleural effusion (Fig. 1A-C).

Because we considered community-acquired pneumonia

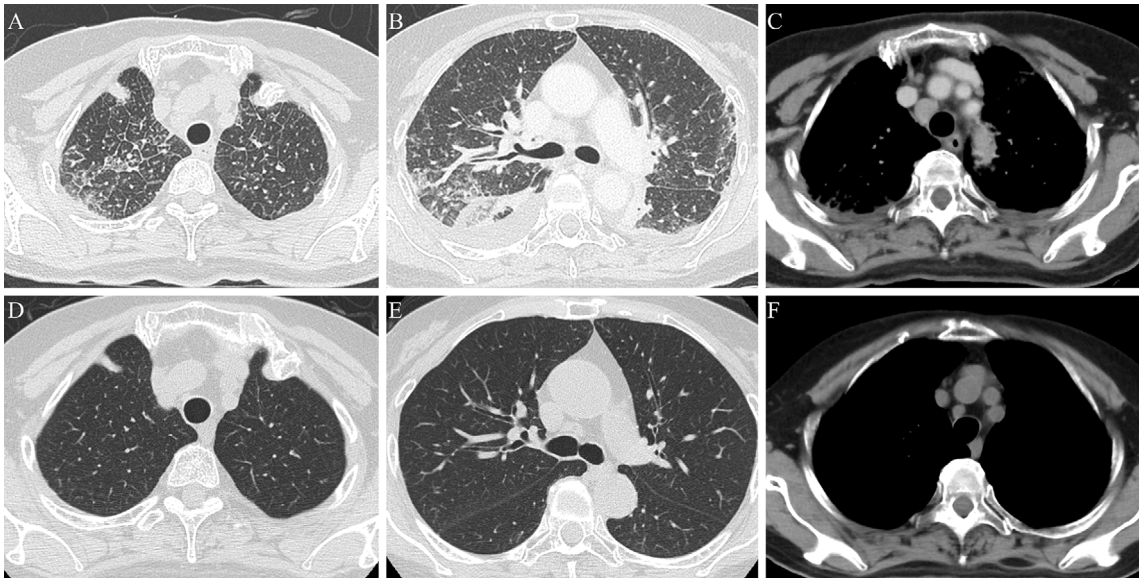

Figure 1. **CT findings on admission (A-C) and three months after treatment (D-F). Plain and contrast-enhanced CT of the chest revealed septal thickening with ground-glass opacities (A), thickening of the bronchovascular bundles with bilateral pleural effusion (B), and hilar and mediastinal lymphadenopathies (C). The septal thickening with ground-glass opacities in the bilateral lung, thickening of the bronchovascular bundles with bilateral pleural effusion were improved (D, E). The lymph nodes had shrunk (F). CT: computed tomography**

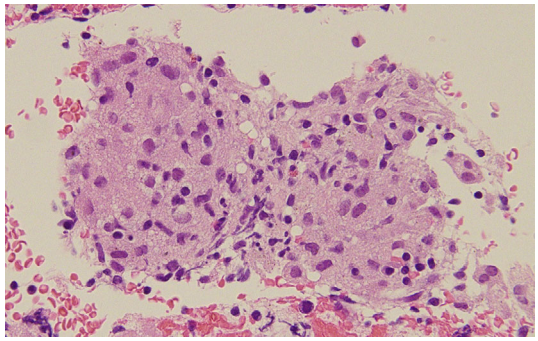

Figure 2. **EBUS-TBNA of a lymph node (4R: right lower paratracheal lymph node) revealed noncaseating granuloma with the accumulation of inflammatory cells, including monocytes, macrophages, and lymphocytes. The results of tissues smear, culture, and polymerase chain reaction for acid fast bacilli were negative. EBUS-TBNA: endobronchial ultrasound-guided transbronchial needle aspiration (Hematoxylin and Eosin staining, ×40)**

as a differential diagnosis, we continued her antibiotics treatment (Ceftriaxone 2 g/day + Azithromycin 500 mg/day). Under strict informed consent from the patient and her family, on day 2, we performed BAL and EBUS-TBNA on the ventilator after intubation in the intensive-care unit. Fentanyl (0.1 mg), propofol (80 mg), and rocuronium (50 mg) were used for intubation. After intubation, the patient was attached to a ventilator [pressure-limited assist control mode, respiratory rate of 20 breaths/minute, applied positive end-expiratory pressure (PEEP) of 8 cmH_2O, fraction of inspired oxygen 1.0, inspiratory pressure level of 10 cmH_2O]. Propofol (150 mg/h) and fentanyl (20 μg/h) were used for sedation and pain relief, respectively. We performed EBUS-TBNA on the right lower paratracheal lymph node (4R) and BAL on the right middle lobe.

Bronchoscopy was successfully performed without any complications, and she was extubated on day 3. BAL revealed lymphocytosis and an elevated CD4-to-CD8 ratio (Table). Random skin and bone-marrow biopsies performed on day 2 showed no evidence of malignant lymphoma. BAL fluid cultures were negative, and the BAL cytology was negative. A lymph node (4R) biopsy by EBUS-TBNA revealed noncaseating granuloma with an accumulation of macrophages, indicating sarcoidosis (Fig. 2). On day 5, we diagnosed her condition as sarcoidosis based on the clinical, radiological, and pathological results and initiated the administration of prednisolone (30 mg/day: 0.75 mg/kg ideal body weight).

After starting therapy, her respiratory status improved, and she did not require any further oxygen administration. Transthoracic echocardiography on day 5 revealed no apparent abnormal findings that indicated sarcoidosis or heart failure, with a preserved ejection fraction [left ventricular ejection fraction (LVEF): 71%]. Furthermore, we detected no asymmetric septal hypertrophy, no focal areas of akinesis or dyskinesis, no wall thinning or thickness, no aneurysm, and no valve regurgitation or stenosis. There was no ocular involvement either. Her general and respiratory conditions improved gradually, and she was discharged on day 13. Prednisolone was gradually tapered, and her CT findings had improved by three months after starting the treatment (Fig. 1D-F).

Discussion

We showed here that sarcoidosis could be diagnosed clinically and histologically via EBUS-TBNA in a patient with acute respiratory failure on a mechanical ventilator. This case has two important implications.

First, we should be aware that patients with sarcoidosis can present with acute respiratory failure. The clinical picture of sarcoidosis can be diverse in terms of its presentation, time span, affected organs, and severity. Lung involvement is observed in 86-92% of cases based on chest X-ray, either alone or, for approximately 50% of cases, in association with extra-pulmonary disease (16). The most common respiratory symptom is a chronic dry cough. Dyspnea and respiratory failure are uncommon and usually associated with advanced pulmonary fibrosis (17). Pleural effusion is also very rare, but sarcoidosis with acute respiratory failure sometimes involves pleural effusion (4, 5, 11). The acute presentation of sarcoidosis is well recognized as Lofgren's syndrome, which is characterized by hilar adenopathy, erythema nodosum, and arthritis (18, 19). However, even in cases of Lofgren's syndrome, sarcoidosis does not generally lead to acute pulmonary symptoms. Our patient showed acute respiratory failure without any clinical signs of Lofgren's syndrome. The pathophysiological mechanism of acute pulmonary disease in sarcoidosis is unknown.

Second, EBUS-TBNA may be useful for diagnosing patients with sarcoidosis with acute respiratory failure. For a definitive diagnosis of sarcoidosis, a biopsy is needed in order to detect the noncaseating granuloma in addition to the pertinent clinical manifestations. Biopsies should be performed on the most accessible organs that appear to be involved. If the patient does not appear to have any involvement at the body surface, the next option is to perform a biopsy or fine-needle aspiration of radiographically enlarged intrathoracic lymph nodes or the lung parenchyma. Recent reports have described EBUS-TBNA as being less invasive and safer than a TBLB (12-15).

However, although EBUS-TBNA is a safe procedure, some complications may occur (20, 21). A systematic review of 190 studies that examined EUS-guided fine-needle aspiration and EBUS-TBNA reported severe adverse events in 0.14% and minor adverse events in 0.22% of cases. Common complications include barotrauma, such as pneumothorax. Pneumomediastinum is a very rare complication but can be serious if it does occur (22). Therefore, it is important to minimize these complications by performing appropriate patient selection, an adequate evaluation of the risk-benefit in high-risk patients, and strict adherence to safety procedures. Mechanical ventilation is a well-known risk factor of pulmonary barotrauma (23). Although not a true barotrauma, direct injury such as that suffered by a TBLB or TBNA in the alveolar or pleural space in certain mechanically ventilated patients may result in the escape of air into the surrounding tissue spaces (24). In our case, we considered a TBLB to be a high-risk procedure that might have led to pneumothorax, as the patient could not stop breathing while on mechanical ventilation. Therefore, we performed EBUS-TBNA of an enlarged lymph node (4R), which facilitated the successful diagnosis of her condition as sarcoidosis without any complications.

In conclusion, it is important to be aware that undiagnosed sarcoidosis may present with acute respiratory failure. EBUS-TBNA under mechanical ventilation may be useful for the immediate diagnosis of a patient.

The authors state that they have no Conflict of Interest (COI).

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