Acute Hypoxemic Respiratory Failure in Sarcoidosis: A Case Report and Literature Review

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Introduction

Sarcoidosis, a multisystem granulomatous disorder of unknown etiology, is characterized by depression of cutaneous delayed-type hypersensitivity and a heightened helper T cell type 1 immune response in the affected organs.[1] Sarcoidosis occurs worldwide and affects young and middle-age adults of both sexes. Many patients remain asymptomatic, and spontaneous remission is common. Sarcoidosis usually follows a chronic course, sometimes leading to substantial deterioration in lung function.[2]

Acute respiratory failure (ARF) is the most common admitting diagnosis in respiratory intensive care units, and the most common cause is ARDS.[3] Apart from the usual causes of ARDS,[4] there is a group of diffuse noninfectious parenchymal lung diseases that can mimic ARDS and present in an acute fashion and fulfill all or most of the clinical, physiologic, and radiographic criteria for ARDS.[5] Sarcoidosis, however, is not a listed cause of ARF. We describe a patient with ARF who was finally proven to have sarcoidosis on surgical lung biopsy. We discuss the literature on similar cases.

Case Summary

A 40-year-old man was admitted to the respiratory intensive care unit with history of breathlessness over the week prior to admission. He also complained of fever, cough, fatigue, malaise, and weight loss of about 7 kg in the preceding 3 weeks. There was no hemoptysis. He had had no exposure to dusts or fumes, either at work or at home. He was a surgeon by occupation. He had a history of intravenous pentazocine abuse and a smoking history of 20 pack-years. Prior to seeing us he had received multiple antibiotics, without substantial response. Radiograph showed bilateral peripheral reticulonodular shadows (Fig. 1), and he was started on anti-tuberculosis treatment 7 days prior to admission at our institute. On examination, he was febrile (38.4° C) and had a heart rate of 106 beats/min, a respiratory rate of 36 breaths/min, and normal blood pressure. There was central cyanosis. Auscultation revealed bilateral basal crackles. S_{pO_2} on room air was 80%, which improved to 92% with oxygen (F_{IO_2} 0.4) via air-entrainment mask. Arterial blood gas analysis showed a P_{aO_2} of 63 mm Hg (P_{aO_2}/F_{IO_2} 157 mm Hg). Electrocardiogram revealed sinus tachycardia but no other abnormalities. Echocardiogram was normal.

Table 1 shows the results of investigations. Tuberculin skin testing with one tuberculin unit purified protein derivative showed no erythema or induration after 72 hours. High-resolution computed tomogram showed bilateral patchy ground-glass opacity, areas of peribronchovascular thickening, interlobular septal thickening, and septal nodules (Fig. 2). Contrast-enhanced computed tomogram did not reveal any lymph nodes (Fig. 3). Flexible bronchoscopy was deferred because of his hypoxemia, and he underwent surgical lung biopsy, with no complications. Histology revealed multiple compact noncaseating granulomas in the interstitium. Staining for acid-fast bacilli and periodic acid-Schiff stain for fungi were negative (Fig. 4). There were occasional giant cells with asteroid bodies. The overall picture was consistent with sarcoidosis, and our final diagnosis was sarcoidosis with ARF. He was started on intravenous methylprednisolone, 1 g daily for 3 days, followed by oral prednisolone (40 mg/d). The respiratory failure rapidly improved, and he was discharged within a week of starting glucocorticoids. Radiograph at 3 months showed clearing of the opacities (Fig. 5), and he remains well.

Discussion

The initial diagnoses we considered in this patient with ARF and pulmonary opacities (ARDS mimic) were hy-

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The authors have disclosed no conflicts of interest.

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DOI: 10.4187/respcare.01174

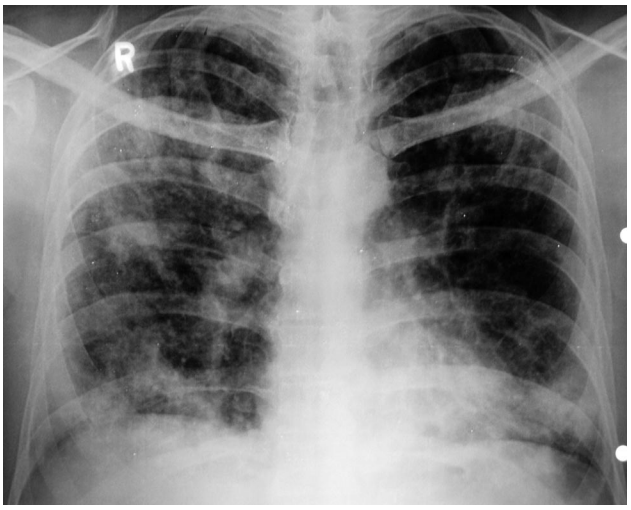

Fig. 1. Chest radiograph shows bilateral reticulonodular opacities.

Table 1. Summary of Investigations

Complete Blood Count	
Hemoglobin (gm/dL)	12.8
Total leucocytes (cells/μL)	10,800
Neutrophils (%)	64
Lymphocytes (%)	34
Eosinophils (%)	1
Basophils (%)	1
Platelets (cells/μL)	180,000
Coagulation profile	
Prothrombin time (s)	12 (normal 11–13)
Activated partial thromboplastin time (s)	36 (normal 32–38)
Biochemistry	
Sodium/potassium (mEq/L)	138/4.1
Serum creatinine (mg/dL)	0.8
Aspartate transaminase (IU/mL)	34 (normal 0–40)
Alanine transaminase (IU/mL)	36 (normal 0–40)
Alkaline phosphatase (U/L)	120 (normal 40–128)
Calcium/phosphate (mmol/L)	9.6/3.4
Others	
HIV-1 and HIV-2 antibodies	Non-reactive
Antinuclear factor	Negative
Anti-neutrophilic cytoplasmic antibody	Negative
Angiotensin-converting enzyme (U/L)	71 (normal 8–65)

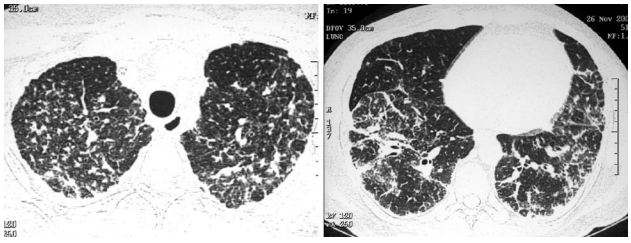

Fig. 2. High-resolution computed tomogram shows peribronchovascular thickening, interlobular septal thickening, and septal nodules.

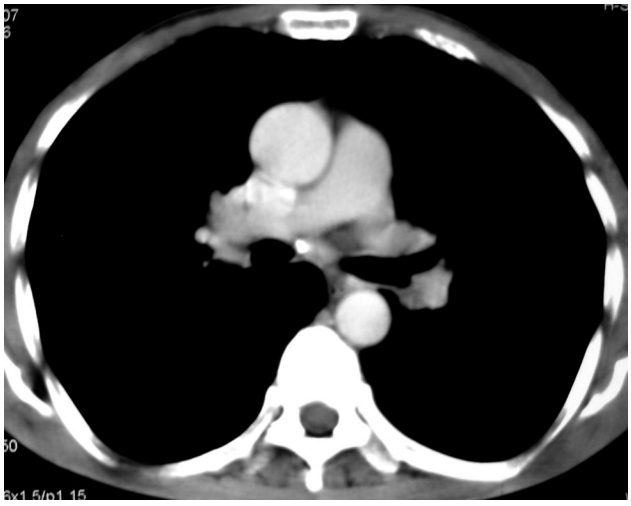

Fig. 3. Computed tomogram shows no hilar/mediastinal lymphadenopathy.

persensitivity pneumonitis, bronchiolitis obliterans with organizing pneumonia, acute eosinophilic pneumonia, tuberculosis with ARDS, and acute interstitial pneumonia, in that order. The diagnosis of sarcoidosis was a surprise only because of the rarity of sarcoidosis presenting as ARF. Our systematic literature search with the search terms "sarcoidosis" and "acute respiratory failure, acute respiratory distress syndrome, acute lung injury, ARDS, ALI" revealed only 5 cases of pulmonary sarcoidosis presenting with ARF (Table 2) in the world literature.[6–10] In retrospect, the computed tomogram finding of nodular interlobular septal thickening does suggest sarcoidosis. Another interesting feature was the absence of lymphadenopathy, because sarcoidosis is often initially suspected when lymphadenopathy is prominent. Though the lungs are almost always involved in sarcoidosis, the presentation is usually not as fulminant as it was in our patient. Another feature was the elevated serum angiotensin-converting enzyme, which is produced by the epithelioid cells of sarcoid granulomas. Measurement of serum angiotensin-converting enzyme was introduced as a promising diagnostic test in the mid-1970s,[11] but its overall sensitivity and specificity are about 55% and 90%, respectively; many other disorders (eg, diabetes mellitus, cirrhosis, acute hepatitis, chronic renal disease, silicosis, Gaucher disease, leprosy, asbestosis, and berylliosis) also have elevated angiotensin-converting enzyme.[12]

ARF in sarcoidosis can occur in situations other than pulmonary parenchymal involvement, but these are also very rare. Patients with cardiac sarcoidosis can present with acute pulmonary edema, which can lead to ARF.[13] Neurologic involvement can present with polyradiculoneuropathy and ventilatory failure akin to Guillain-Barré

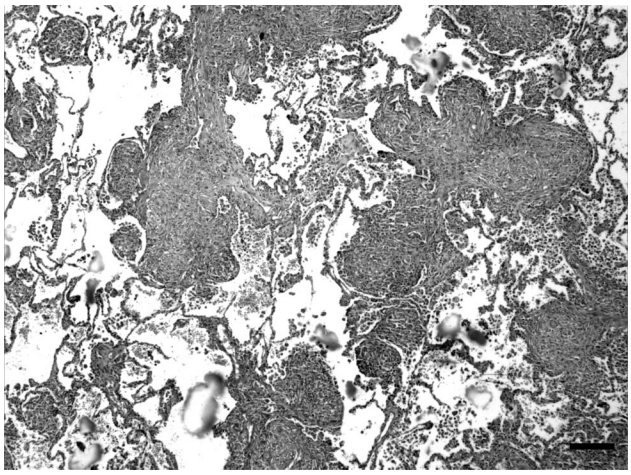

Fig. 4. Lung biopsy (hematoxylin and eosin stain) shows multiple compact noncaseating granulomas in the interstitium. Stain for acid-fast bacilli was negative. The scale bar represents 50 μm.

syndrome.[14] Laryngeal sarcoidosis with acute upper-airway obstruction can present with ARF.[15]

Teaching Points

• Sarcoidosis can occasionally present with hypoxemic respiratory failure and should figure in the differential diagnosis, even when lymphadenopathy is absent. In a large series of 274 confirmed cases of pulmonary sarcoidosis, pulmonary involvement without hilar/mediastinal lymphadenopathy was encountered in only 8% of cases.[16]

• The present case highlights the potential value of biopsy in a patient with ARF. Without a surgical lung biopsy the diagnosis of sarcoidosis could easily have been missed and he would have received antibiotics and glucocorticoids. We think such misdiagnosis could cause underreporting of ARF in sarcoidosis, because many such patients might receive steroids in the management of idiopathic ARF, and the diagnosis is often not confirmed following improvement with therapy. In a recent study surgical lung biopsy in patients with ARDS led to a change in management in the majority of patients, with the addition

Table 2. Reported Cases of Pulmonary Sarcoidosis That Presented as Acute Respiratory Failure

First Author	Year	Age	Sex	Duration of Dyspnea	P_{aO_2} (mm Hg on F_{IO_2} 0.21)	Serum Angiotensin-Converting Enzyme	Radiograph Findings	Computed Tomography Findings	Demonstration of Granuloma	Time to Improvement With Steroids
Sabbagh[7]*	2002	50	Male	3 weeks	52	Not stated	Bilateral air-space disease	No computed tomography	Bronchoscopic lung biopsy	6 days
Leiba[8]*	2004	41	Female	1 week	S_{pO_2} 70%	Elevated	Bilateral pulmonary opacities	Ill-defined reticulonodular densities Mediastinal lymphadenopathy	Mediastinoscopic lymph node biopsy	Few days
Chirakalwasan[6]*	2005	33	Male	1 week	43	Elevated	Bilateral pulmonary opacities	No pulmonary opacities at the time of computed tomography Subcarinal lymph node involvement	Bronchoscopic lung biopsy	3 days
Suyama[9]†	1990	55	Male	10 days	32	Elevated	Bilateral nodular opacities, minimal pleural effusions, bilateral hilar adenopathy	No computed tomography	Bronchoscopic lung biopsy Liver and bone-marrow biopsy	Not stated
Shibata[10]†	2007	66	Male	Not stated	Not stated	Elevated	Not stated	Bilateral ground-glass opacity and pleural effusion	Skin biopsy	Not stated

* English literature (data from case reports)
† Non-English literature (data from abstracts)

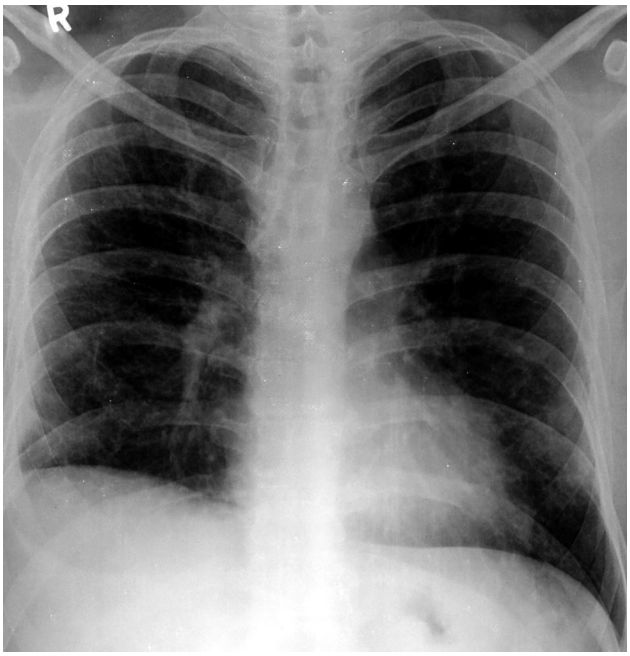

Fig. 5. Follow-up radiograph at 3 months shows complete resolution of the opacities.

of therapies in 60% and the withdrawal of therapies in 37%.[17]

• This case demonstrates the chameleon-like presentation of sarcoidosis. Sarcoidosis should be considered in the evaluation of a patient with ARF of uncertain etiology. The diagnosis is established when clinical and radiologic findings are supported by histological evidence of noncaseating granulomas and the exclusion of other possible causes.

REFERENCES

1. Iannuzzi MC, Rybicki BA, Teirstein AS. Sarcoidosis. N Engl J Med 2007;357(21):2153-2165.
2. Gupta D, Sharma OP. Sarcoidosis. In: Jindal SK, Shankar PS, Raoof S, Gupta D, Aggarwal AN, Agarwal R, editors. Textbook of pulmonary & critical care medicine. Volume 2. New Delhi: Jaypee Brothers Medical Publishers; 2011:1174-1202.
3. Aggarwal AN, Agarwal R, Gupta D, Jindal SK. Nonpulmonary organ dysfunction and its impact on outcome in patients with acute respiratory failure. Chest 2007;132(3):829-835.
4. Agarwal R, Aggarwal AN, Gupta D, Behera D, Jindal SK. Etiology and outcomes of pulmonary and extrapulmonary acute lung injury/ARDS in a respiratory ICU in North India. Chest 2006;130(3):724-729.
5. Schwarz MI, Albert RK. "Imitators" of the ARDS: implications for diagnosis and treatment. Chest 2004;125(4):1530-1535.
6. Chirakalwasan N, Dallal MM. Pulmonary sarcoidosis presenting with acute respiratory failure. South Med J 2005;98(3):382-384.
7. Sabbagh F, Gibbs C, Efferen LS. Pulmonary sarcoidosis and the acute respiratory distress syndrome (ARDS). Thorax 2002;57(7):655-656.
8. Leiba A, Apter S, Leiba M, Thaler M, Grossman E. Acute respiratory failure in a patient with sarcoidosis and immunodeficiency–an unusual presentation and a complicated course. Lung 2004;182(2):73-77.
9. Suyama T, Satoh H, Inoue T, Noguti Y, Ohtsuka M, Yosizawa Y, et al. [A case of sarcoidosis presenting with high fever and acute respiratory failure]. Kekkaku 1990;65(12):811-819. *Article in Japanese.*
10. Shibata S, Saito K, Ishiwata N, Ieki R. [A case of sarcoidosis presenting with high fever and rash progressing to acute respiratory failure]. Nihon Kokyuki Gakkai Zasshi 2007;45(9):691-697. *Article in Japanese.*
11. Lieberman J. Elevation of serum angiotensin-converting-enzyme (ACE) level in sarcoidosis. Am J Med 1975;59(3):365-372.
12. Studdy PR, Bird R. Serum angiotensin converting enzyme in sarcoidosis–its value in present clinical practice. Ann Clin Biochem 1989;26Pt 1):13-18.
13. Kong HH, Sheldon H. Acute breathlessness, heart block and sudden death in a 66-year-old man. Can Med Assoc J 1982;127(8):689-693.
14. Miller R, Sheron N, Semple S. Sarcoidosis presenting with an acute Guillain-Barré syndrome. Postgrad Med J 1989;65(768):765-767.
15. Davis C, Girzadas DV Jr. Laryngeal sarcoidosis causing acute upper airway obstruction. Am J Emerg Med 2008;26(1):114.e1-e3.
16. Jindal SK, Gupta D, Aggarwal AN. Sarcoidosis in developing countries. Curr Opin Pulm Med 2000;6(5):448-454.
17. Patel SR, Karmpaliotis D, Ayas NT, Mark EJ, Wain J, Thompson BT, et al. The role of open-lung biopsy in ARDS. Chest 2004;125(1):197-202.