Spontaneous pneumothorax as an early manifestation of pulmonary sarcoidosis: a case-based review

Arif Kodza[1*], Bana Hadid[2], Sumatha Suresh[3], Iqra Aftab[4], Elif Yakut[5], Aleksander Feoktistov[6], Eugeniya Golub[6]

European Journal of Medical Case Reports
Volume 8(5):99–103
DOI: 10.24911/ejmcr.173-1684354133

ABSTRACT

Background: Sarcoidosis is a multisystem inflammatory disorder characterized by non-caseating granulomas with predominantly lung manifestations that can cause restrictive or, less commonly, obstructive lung disease. Rarely is pneumothorax a manifestation of sarcoidosis; it has been reported as an early finding in sarcoidosis, but it is typically attributed to ruptured bullae, cysts, or pleural granulomas.

Case Presentation: We present a unique case of spontaneous pneumothorax attributed to biopsy-proven sarcoid disease in a patient with no prior history of pulmonary complications. The patient's rapid development of novel pulmonary sequelae necessitates treatment of sarcoidosis early in the disease course.

Conclusion: We recommend a treatment plan of appropriate chest tube placement in the affected lung(s) and prompt steroid therapy for patients with sarcoidosis presenting with a pneumothorax. We also review the literature for the etiology, pathophysiology, and presentation of pneumothorax in sarcoidosis, treatment of this sequela, and pulmonary function test findings in these patients.

Keywords: Sarcoidosis, pneumothorax, bullous disease, restrictive lung disease, steroid therapy.

Received: 17 May 2023 **Accepted:** 10 February 2024 **Type of Article:** CASE REPORT **Specialty:** Rheumatology

Correspondence to: Arif Kodza
*Department of Internal Medicine, New York University Langone Hospital, Brooklyn, NY.
Email: arif.kodza@nyulangone.org
Full list of author information is available at the end of the article.

Background

Sarcoidosis is a multisystem inflammatory disorder characterized by non-caseating granulomas with predominantly lung manifestations. Pulmonary function tests (PFTs) can show restrictive or, less commonly, obstructive lung disease. Rarely is pneumothorax a manifestation of sarcoidosis; it is noted in only 2%-4% of cases and is frequently seen as a late-presenting complication secondary to ruptured bullae, cysts, or pleural granulomas [1-4]. Still, pneumothorax has been reported as an early finding in sarcoidosis [5-7]. Here, we present a unique case of spontaneous pneumothorax attributed to biopsy-proven sarcoid disease in a patient with no prior history of pulmonary complications.

Case Report

A 60-year-old Black woman presented to the Emergency Department after a syncopal episode in which she sustained trauma to her left flank. She denied trauma to the head and no alteration in consciousness before or after the episode. A review of systems was only remarkable for shortness of breath associated with dull left-sided chest pain on exertion for several days. A week before the presentation, she underwent an uncomplicated ureteral stent placement for a ureterovesical stone and hydronephrosis of the right kidney. Her past medical history is remarkable for thyroid cancer treated with thyroidectomy. Her only medication is levothyroxine. She has no history of tobacco or inhaled substance use.

The patient's presenting vitals were stable, and her initial oxygen saturation was 95% on room air. Her oxygen saturation briefly decreased to 92%, which subsequently improved to 98% with the administration of supplemental oxygen via nasal cannula at a rate of 2 l/minute flow. The initial physical examination was most notable for decreased breath sounds in the upper and lower lung fields relative to the right side. Neurological and musculoskeletal examinations demonstrated no abnormalities. No skin changes were noted over the left flank, and there was no tenderness to palpation over the ribs at the site of injury.

Initial studies included an electrocardiogram, which demonstrated normal sinus rhythm and rate. Her basic metabolic panel was significant for a calcium level elevated to 11.0 mg/dl (normal range: 8.4-10.4 mg/dl). Follow-up serum testing to assess the cause of hypercalcemia

revealed an elevated Angiotensin-Converting Enzyme level, a normal Parathyroid Hormone level, and a 1,25-dihydroxy-Vitamin D/25-hydroxy-Vitamin D ratio greater than 4.0, suggesting active granulomatous disease. A venous blood gas revealed a mild respiratory acidosis with a normal lactate level. Diagnostic two-view chest radiographs demonstrated a novel moderate left-sided pneumothorax measuring up to 2.8 cm anteriorly and bilateral hilar prominence. These images did not show rib fractures or bullae, indicating that the pneumothorax was not caused by the puncturing of the pleura by a rib fragment at the time of her flank trauma. The hilar prominence noted on the radiograph prompted further exploration with computerized tomography (CT) of the chest, which additionally demonstrated diffuse pulmonary micronodules in a perilymphatic distribution (Figures 1 and 2).

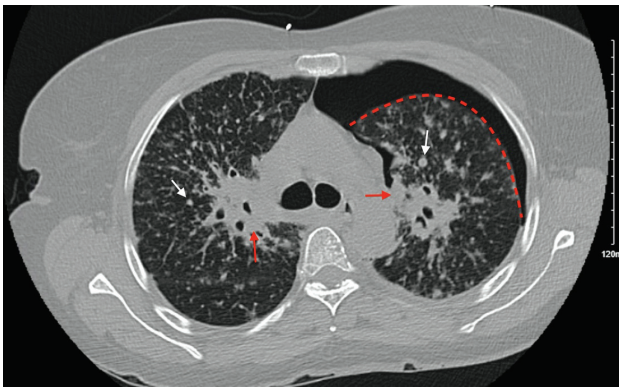

Figure 1. *CT image of the chest revealing moderate left pneumothorax measuring up to 2.8 cm anteriorly (contour of collapsed lung demarcated by red dashed line). Bilateral hilar lymphadenopathy is noted (red arrows). Diffuse bilateral pulmonary micronodules (white arrows) in a perilymphatic distribution are also noted.*

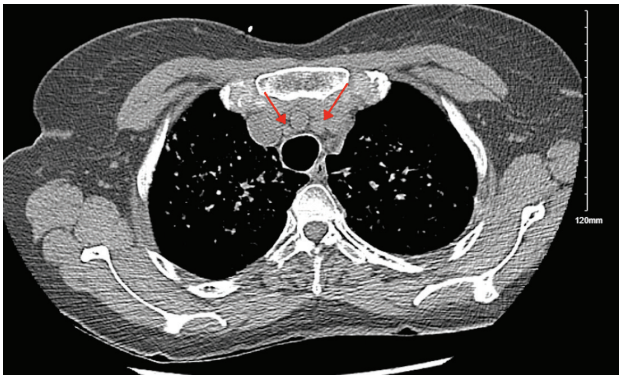

Figure 2. *CT image of the chest revealing mediastinal lymphadenopathy (red arrows).*

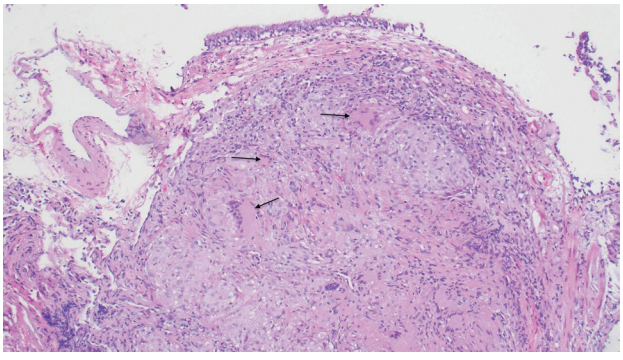

Figure 3. *Hematoxylin & eosin staining of transbronchial lung biopsy (low power). Non-necrotizing granulomas (black arrows) are formed by histiocytes, lymphocytes, and multinucleated giant cells with bronchial epithelial cells at the top.*

The finding of a pneumothorax led to chest tube placement through the left chest wall to allow re-expansion of the left lung. Subsequently, the patient's work of breathing improved, and her oxygen saturation eventually increased to 100% on room air. However, the patient's abnormal calcium studies and imaging findings suggested a novel diagnosis of an underlying sarcoid disease which instigated the pneumothorax. To confirm this suspicion, an endobronchial ultrasound bronchoscopy was performed to garner biopsy-level evidence of sarcoidosis. Diffuse lymphadenopathy was visualized, and pathological analysis of the biopsies revealed non-caseating granulomas with no evidence of dysplasia (Figure 3), thus implicating sarcoidosis as the most likely etiology of her presentation rather than lymphoma or metastatic disease. Subsequent PFT demonstrated a forced expiratory volume/forced vital capacity equal to 34% of the predicted value and a diffusing capacity of the lungs for carbon monoxide equal to 64% of the predicted value, consistent with a severe obstructive ventilatory defect.

The combination of a spontaneous pneumothorax, hypercalcemia, and the recent history of a ureteral stone, in the setting of confirmed sarcoid disease, led us to initiate an oral prednisone course starting at 20 mg daily for 2 weeks, then 10 mg daily for 2 weeks. At the 1-month follow-up, the patient reported significant improvement in her shortness of breath and exercise tolerance. In addition, follow-up serum testing revealed an improvement in her serum calcium to 9.8 ng/dl. Her sarcoidosis remained in remission with no further complications at the time of procurement of the manuscript.

Discussion and Review

Our case involves the finding of a spontaneous pneumothorax in a 60-year-old Black woman with biopsy-proven sarcoidosis. Sarcoidosis is an inflammatory, multisystemic disorder of unknown etiology. In combination with genetic factors, it is thought that there is an environmental trigger of the disease in susceptible individuals that results in the characteristic non-caseating granulomatous inflammation with a predominance of T-helper cell lymphocytes [8]. Macrophages autonomously express the enzyme 1-alpha-hydroxylase, resulting in the overproduction of 1,25-OH-vitamin D, and thus leading to hypercalcemia and hypercalciuria [9]. Pulmonary manifestations are seen in more than 90% of cases, and typical symptoms include cough and dyspnea

[10]. The disease can affect any area of the respiratory tract, from the oral mucosa and vocal cords to the terminal bronchioles and visceral pleura [11].

Diagnosis is made through a combination of findings from imaging, PFTs, and bronchoscopy with biopsy. Classic findings on chest CT are bilateral hilar lymphadenopathy and perilymphatic nodules along interlobular septa [12]. However, the results of these modalities can be discordant. The anatomic abnormalities (e.g., extrinsic compression, luminal stenosis, mucosal involvement, or airway distortion) caused by the granulomatous inflammation, even when severe on imaging, may or may not result in symptoms or PFT changes [13,14]. Also, renal involvement is likely underreported, and the specific manifestations are not elucidated [9].

Pneumothorax is a rare manifestation of sarcoidosis, thought to occur in 2% to 4% of patients [2-4]. The scant literature on this topic reports that pneumothorax is typically a manifestation of late sarcoid disease [2]. However, it can be the presenting sign of sarcoidosis or occur early in the disease course [5,6,15]. Recurrent or bilateral pneumothorax has also been reported [6,16,17].

The etiology of pneumothorax in sarcoidosis appears to be secondary to the rupture of a subpleural bulla or necrosis of a subpleural granuloma [2,3,5,18]. The exact mechanism of bullae development in sarcoidosis remains unclear but it is likely due to a combination of several proposed mechanisms. Bronchiolar obstruction by endobronchial lesion involvement leads to peripheral air-trapping and distension of airspaces which are prone to rupture [1,19,20]. Retraction mechanisms such as regression or fibrosis of the surrounding diseased pulmonary parenchyma may also lead to airspace enlargement and the formation of bullae [19,21]. It is also possible that cytokine release by granulomas drives alveolitis and air-trapping adjacent to diseased regions [19,22]. Bullae rupture is likely instigated by overdistension of the airspace or with increased exertional pressure, such as during exercise or with coughing.

The age of diagnosis of bullous sarcoidosis ranges from 21 to 67 years of age, and these changes in sarcoidosis are usually reported within 3-to-4 years of symptom presentation [22]. Our patient uniquely experienced a quick onset of pulmonary sarcoid disease leading to pneumothorax despite having no known prior history of such disease. A ruptured bulla may have caused the pneumothorax, but chest imaging did not reveal any other bulla in both lungs. The likelihood is higher that necrosis of a subpleural granuloma may have led to the development of the pneumothorax. Our patient's presentation suggests that these pulmonary sequelae may occur early in the disease course and may lead to rapid deterioration of pulmonary function if the sarcoid disease is not appropriately treated.

Most authors agree that corticosteroid therapy for pulmonary sarcoidosis is indicated when severe functional impairment is present or significant deterioration is noted [1]. Oral prednisone improves pulmonary lesions and lung function and may even prevent recurrent pneumothorax [6]. Discontinuation of prednisone therapy may cause sarcoid disease remission, thus instigating recurrent pneumothorax [6]. However, Froudarakis et al. [2] did not observe a recurrence of pneumothorax in the absence of systemic therapy, concluding that steroids may be only helpful for patients with impaired lung function. The pneumothorax is managed with chest tube insertion until the afflicted lung demonstrates appropriate function.

Our patient's PFT finding of severe obstructive ventilatory defect suggests a rare manifestation of pulmonary sarcoidosis. Sarcoidosis is generally regarded as a restrictive airway disease, but it can cause obstructive disease because it affects the entire respiratory tree [14,23]. According to one retrospective analysis of 164 patients presenting with newly diagnosed pulmonary sarcoidosis, the percentage of patients presenting with an obstructive lung defect was 23.2% [24]. Moreover, there were no differences in smoking status or diagnosis of asthma or chronic obstructive pulmonary disease between the obstructive and restrictive groups [24]. Patients with obstructive pulmonary sarcoid disease patterns were significantly older than those with restrictive patterns [24]. Obstructive airway disease is more common in African American patients with sarcoidosis than white European or American and Japanese patients [25].

It is essential to recognize that Black patients, especially Black females, have been found to have the worst prognosis and have been shown to have more rapidly progressing pulmonary disease [26]. They also historically tend to have obstructive findings on PFTs [25], though there is evidence suggesting this is not the case [24]. However, to the best of our knowledge, there is no literature reporting the difference in the prevalence of pneumothorax in sarcoid disease amongst different races. Given that Black patients may have more severe pulmonary disease, it can be postulated that they are more likely to experience pneumothoraxes, and further research is needed to explore this topic.

Conclusion

In summation, this interesting case suggests that patients with sarcoidosis may develop a pneumothorax early in the disease course. A pneumothorax may even be the first pulmonary sequela of sarcoidosis. A purely obstructive ventilatory defect without restriction does not preclude the development of pneumothorax. Chest tube placement in the afflicted lung(s) and prompt steroid therapy should be considered in patients with sarcoidosis presenting with pneumothorax.

List of Abbreviations

CT computerized tomography
PFT pulmonary function test

Conflicts of interest

The authors declare that there is no conflict of interest regarding the publication of this case report.

Funding

None.

Consent for publication

Written consent was received from the patient.

Ethical approval

Ethical approval is not required at our institution to publish an anonymous case report.

Author details

Arif Kodza[1], Bana Hadid[2], Sumatha Suresh[3], Iqra Aftab[4], Elif Yakut[5], Aleksander Feoktistov[6], Eugeniya Golub[6]

1. Department of Internal Medicine, New York University Langone Hospital, Brooklyn, NY
2. Department of Internal Medicine, Columbia University Irving Medical Center, New York NY
3. Department of Internal Medicine, State University of New York Downstate Health Sciences University, Brooklyn, NY
4. AtlantiCare Physician Group - Rheumatology, Egg Harbor Township, NJ
5. Department of Pathology, NYC Health and Hospitals/Kings County Hospital Center, Brooklyn, NY
6. Department of Rheumatology, NYC Health and Hospitals/Kings County Hospital Center, Brooklyn, NY

References

1. Manika K, Kioumis I, Zarogoulidis K, Kougioumtzi I, Dryllis G, Pitsiou G, et al. Pneumothorax in sarcoidosis. J Thorac Dis. 2014 Oct;6 Suppl 4:S466–9.
2. Froudarakis ME, Bouros D, Voloudaki A, Papiris S, Kottakis Y, Constantopoulos SH, et al. Pneumothorax as a first manifestation of sarcoidosis. Chest. 1997 Jul;112(1):278–80. https://doi.org/10.1378/chest.112.1.278
3. Riley EA. Boeck's sarcoid; a review based upon a clinical study of fifty-two cases. Am Rev Tuberc. 1950 Sep;62(3):231–85.
4. Sharma OP. Sarcoidosis: unusual pulmonary manifestations. Postgrad Med. 1977 Mar;61(3):67–73. https://doi.org/10.1080/00325481.1977.11712149
5. Omori H, Asahi H, Irinoda T, Itabashi T, Saito K. Pneumothorax as a presenting manifestation of early sarcoidosis. Jpn J Thorac Cardiovasc Surg. 2004 Jan;52(1):33–5. https://doi.org/10.1007/s11748-004-0059-2
6. Liu Y, Dai HP, Xu LL, Li X. Recurrent pneumothorax as a presenting manifestation of active sarcoidosis: a case report and literature review. Chin Med J (Engl). 2010 Jun;123(12):1615–6.
7. Rastogi R, Joon P. Pneumothorax - a rare presenting sign of sarcoidosis. J Gen Pract (Los Angel). 2016;4(256):2. https://doi.org/10.4172/2329-9126.1000256
8. Baughman RP, Field S, Costabel U, Crystal RG, Culver DA, Drent M, et al. Sarcoidosis in America. Analysis based on health care use. Ann Am Thorac Soc. 2016 Aug;13(8):1244–52. https://doi.org/10.1513/AnnalsATS.201511-760OC
9. Bergner R, Löffler C. Renal sarcoidosis: approach to diagnosis and management. Curr Opin Pulm Med. 2018 Sep;24(5):513–20. https://doi.org/10.1097/MCP.0000000000000504
10. Baughman RP, Lower EE, Gibson K. Pulmonary manifestations of sarcoidosis. Presse Med. 2012 Jun;41(6 Pt 2):e289–302. https://doi.org/10.1016/j.lpm.2012.03.019
11. Baughman RP, Lower EE, Tami T. Upper airway. 4: sarcoidosis of the upper respiratory tract (SURT). Thorax. 2010 Feb;65(2):181–6. https://doi.org/10.1136/thx.2008.112896
12. Raoof S, Amchentsev A, Vlahos I, Goud A, Naidich DP. Pictorial essay: multinodular disease: a high-resolution CT scan diagnostic algorithm. Chest. 2006 Mar;129(3):805–15. https://doi.org/10.1378/chest.129.3.805
13. Polychronopoulos VS, Prakash UB. Airway involvement in sarcoidosis. Chest. 2009 Nov;136(5):1371–80. https://doi.org/10.1378/chest.08-2569
14. Danila E, Jurgauskiene L, Malickaite R. BAL fluid cells and pulmonary function in different radiographic stages of newly diagnosed sarcoidosis. Adv Med Sci. 2008;53(2):228–33. https://doi.org/10.2478/v10039-008-0014-z
15. Fein A, Gupta R, Goodman P. Spontaneous pneumothorax as a presenting pulmonary manifestation of early sarcoidosis. Chest. 1980 Mar;77(3):455–6. https://doi.org/10.1378/chest.77.3.455b
16. Akelsson IG, Eklund A, Sköld CM, Tornling G. Bilateral spontaneous pneumothorax and sarcoidosis. Sarcoidosis. 1990 Sep;7(2):136–8.
17. Gomm SA. An unusual presentation of sarcoidosis-spontaneous haemopneumothorax. Postgrad Med J. 1984 Sep;60(707):621–3. https://doi.org/10.1136/pgmj.60.707.621
18. Younes I, Elkattawy S, Hammad W, Kotys J, Dhanoa P, Remolina C. Secondary spontaneous pneumothorax in a patient with sarcoidosis treated with endobronchial valve. Chest. 2021;160(4):A2008. https://doi.org/10.1016/j.chest.2021.07.1779
19. Judson MA, Strange C. Bullous sarcoidosis: a report of three cases. Chest. 1998 Nov;114(5):1474–8. https://doi.org/10.1378/chest.114.5.1474
20. Sawahata M, Yamaguchi T. Imaging findings of fibrosis in pulmonary sarcoidosis. Sarcoidosis Vasc Diffuse Lung Dis. 2022;39(2):e2022018.
21. Higuchi H, Okuzumi S, Kakimoto T, Hamabe K, Morinaga S, Minematsu N. Long-term findings in bullous sarcoidosis: a case report and literature review. Intern Med. 2023 Aug;62(16):2395–400. https://doi.org/10.2169/internalmedicine.1130-22
22. Jeebun V, Forrest IA. Sarcoidosis: an underrecognised cause for bullous lung disease? Eur Respir J. 2009 Oct;34(4):999–1001. https://doi.org/10.1183/09031936.00084609
23. Morgenthau AS, Teirstein AS. Sarcoidosis of the upper and lower airways. Expert Rev Respir Med. 2011 Dec;5(6):823–33. https://doi.org/10.1586/ers.11.66
24. Thillai M, Potiphar L, Eberhardt C, Pareek M, Dhawan R, Kon OM, et al. Obstructive lung function in sarcoidosis may be missed, especially in older white patients. Eur Respir J. 2012 Mar;39(3):775–7. https://doi.org/10.1183/09031936.00103811

25. Sharma OP, Johnson R. Airway obstruction in sarcoidosis. A study of 123 nonsmoking black American patients with sarcoidosis. Chest. 1988 Aug;94(2):343–6. https://doi.org/10.1378/chest.94.2.343

26. Hena KM. Sarcoidosis epidemiology: race matters. Front Immunol. 2020 Sep;11:537382. https://doi.org/10.3389/fimmu.2020.537382

Summary of the case

1	**Patient (gender, age)**	F, 60
2	**Final diagnosis**	Sarcoidosis
3	**Symptoms**	Shortness of breath, syncope
4	**Medications**	Prednisone
5	**Clinical procedure**	Chest-tube insertion, endobronchial ultrasound bronchoscopy
6	**Specialty**	Internal medicine, rheumatology, pulmonology, pathology