

Pneumothorax in sarcoidosis

Katerina Manika¹, Ioannis Kioumis¹, Konstantinos Zarogoulidis¹, Ioanna Kougioumtzi², Georgios Dryllis³, Georgia Pitsiou¹, Nikolaos Machairiotis⁴, Nikolaos Katsikogiannis², Sofia Lampaki¹, Antonis Papaiwannou¹, Bojan Zaric⁵, Perin Branislav⁵, Haidong Huang⁶, Qiang Li⁶, Paschalis Steiropoulos⁷, Paul Zarogoulidis¹

¹Pulmonary Department, “G. Papanikolaou” General Hospital, Aristotle University of Thessaloniki, Thessaloniki, Greece; ²Surgery Department, University General Hospital of Alexandroupolis, Democritus University of Thrace, Alexandroupolis, Greece; ³Hematology Department, “Laiko” University General Hospital, Athens, Greece; ⁴Obstetric-Gynecology Department, “Thriassio” General Hospital of Athens, Athens, Greece; ⁵Institute for Pulmonary Diseases of Vojvodina, Clinic for Thoracic Oncology, Faculty of Medicine, University of Novi Sad, Serbia; ⁶Department of Respiratory Diseases Shanghai Hospital, II Military University Hospital, Shanghai 200433, China; ⁷Pulmonary Department, University General Hospital of Alexandroupolis, Democritus University of Thrace, Alexandroupolis, Greece

Correspondence to: Paul Zarogoulidis, MD, PhD. Pulmonary Department, “G. Papanikolaou” General Hospital, Aristotle University of Thessaloniki, Thessaloniki, Greece. Email: pzarog@hotmail.com.

Abstract: While sarcoidosis is a relatively common but often underdiagnosed disease, pneumothorax appears to be a rare clinical event observed mostly at the late stages of the disease course. The precise underlying mechanism of such complication is unclear and probably involves the formation of bullae due to bronchial obstruction and retraction-collapse of distracted lung tissue. Thoracoscopic bullectomy represent the preferred treatment option for recurrent pneumothoraces. The administration of corticosteroids for the treatment of pulmonary sarcoidosis may have a protecting effect for such recurrences, but remains a controversial issue.

Keywords: Sarcoidosis; pneumothorax; medical thoracoscopy

Submitted Aug 25, 2014. Accepted for publication Aug 26, 2014.

doi: 10.3978/j.issn.2072-1439.2014.09.11

View this article at: <http://dx.doi.org/10.3978/j.issn.2072-1439.2014.09.11>

Sarcoidosis is a relatively common inflammatory disease of unknown etiology, characterized by the formation of noncaseating granulomas (1). It affects all races and ethnic groups although significant differences both in incidence and in phenotype have been detected across the world (2). Sarcoidosis is considered to be a “great mimic” since it presents with an intriguing diversity of manifestations from literally all organs and systems. Despite this strong heterogeneity pulmonary manifestations typically predominate and abnormalities on chest radiographs are observed in approximately 90% of patients. In addition thoracic involvement accounts for most of the morbidity and mortality associated with the disease (3). The most characteristic radiologic findings are bilateral hilar lymphadenopathy and lung parenchymal infiltrates including reticular, reticulonodular and focal alveolar opacities (4). About 25% of patients exhibit atypical manifestations such

as cavities, pleural effusion, solitary pulmonary nodules, mycetomas, bullae and pneumothorax (5,6).

Bullae in sarcoidosis are considered different from the localized cystic airspaces which are often seen in stage IV disease, since they are larger and usually represent the cause of pulmonary function loss (7). The precise mechanism leading to bullae formation in sarcoidosis remains unclear. However, three distinct explanations have been proposed; (I) obstruction of bronchi or bronchioles due to endobronchial involvement, resulting in peripheral air trapping, distention and rupture, particularly during exercise of coughing (7-10). Nevertheless endobronchial involvement has not been detected in all cases where bronchial biopsy was performed (10); (II) retraction and collapse of surrounding pulmonary parenchyma leading to bullae formation. Granulomatous inflammation may lead to lung contraction and subsequent adjacent airspace enlargement (11); (III) tissue destruction

due to inflammatory alveolitis through by a variety of inflammatory mediators (11,12). It is also possible that all three mechanisms may participate in bullae formation (11).

The etiology of pneumothorax in sarcoidosis involves rupture of subpleural bullae or necrosis of subpleural granulomas (13). Pneumothorax occurs in 2% of patients with sarcoidosis and only few cases have been reported in the literature (11-15). Haemothorax or pleural effusion may coexist (16,17). Pneumothorax may present on both sides and different series have reported left (15) or right (12) predominance. Recurrent or bilateral pneumothorax seems to be common (16,18). Many authors have suggested that pneumothorax is usually observed as a complication of fibrosis or bullous disease late in the course of sarcoidosis (19-21). However pneumothorax can also be the presenting manifestation of the disease or occur as the first evidence of relapse (11,13-15).

The first case of bullous form of the sarcoidosis was presented by Zimmerman and Mann in 1949 (22). Bullous changes have been usually reported within 3-4 years of symptom presentation (12). Based on few published series, the age at diagnosis of bullous sarcoidosis ranges from 21 to 67 years (12) and no ethnic predominance was noted. The majority of patients present with an obstructive disorder in lung function which may be particularly severe (11). However, restrictive pattern and normal spirometry have also been reported (8,12,22,23). Bullae may involve the upper or lower lung zones equally (12).

Although both pneumothorax and bullous changes are considered to be rare manifestations of sarcoidosis it is conceivable that in fact they represent under-recognized forms of the disease. Due to nonspecific symptoms the diagnosis of sarcoidosis may not be suspected and symptoms may be attributed to bronchial asthma or COPD (11,12). This is particularly true in smokers with upper lobe bullae. In addition granulomatous lesions may not be noted along the walls of resected bullae, rendering biopsy of relatively spread lung tissue necessary in order to establish the diagnosis (12).

Keller *et al.* in their histopathological review have concluded that 37% of patients who underwent volume reduction surgery for emphysema presented with unsuspected findings such as fibrosis, granulomatosis, inflammation and neoplasia (24). More specifically noncaseating granulomatous changes were observed in 9 out of 80 cases and although mediastinal lymphadenopathy was noted in the majority of these cases, clinical characteristics of sarcoidosis were not present. Patients with another histopathological diagnosis in addition to emphysema had a

more complicated recovery after surgery in spite of similar radiologic and pulmonary function test preoperatively (24). Given the rarity of bullous sarcoidosis and the possibility of under-diagnosis a prospective study on the cases referred for bullectomy may be useful.

Treatment for pulmonary sarcoidosis remains controversial although most authors agree that corticosteroids are indicated when severe functional impairment exists at presentation or significant deterioration is observed during the course of the disease (25). The management of pneumothorax is even less clarified. Sharma suggested that early steroid treatment may be beneficial in pneumothorax relapse (19). In a more recent report a recurrence of pneumothorax was noted after discontinuation of prednisone (15). On the contrary Froudarakis *et al.* did not observe recurrence of pneumothorax in patients without treatment and concluded that steroids may be useful in patients with functional impairment (13). In this setting it seems reasonable to treat with corticosteroids in case of parenchymal abnormalities combined with loss in pulmonary function.

In pneumothorax complicating sarcoidosis, thorascopic bullectomy has been performed in case of recurrent pneumothorax (15) or when tube drainage was proved to be unsuccessful (14). Bullectomies have also been reported in cases of bullous sarcoidosis (9) since these patients may not respond to steroid treatment and rapidly progress to respiratory failure (11,12). The complication rate is higher in patient exhibiting underlying lung disease (24) and caution should be used in order to assure that the thoracic cavity (11,26-35) is filled with lung tissue after surgery (36-47).

In conclusion sarcoidosis is often under-recognized as a cause of recurrent spontaneous pneumothorax or bullae. Clinical clues that may help in this direction include young age, limited smoking history with severe obstruction and evidence of pulmonary or extrapulmonary sarcoidosis.

Acknowledgements

Disclosure: The authors declare no conflict of interest.

References

1. Statement on sarcoidosis. Joint Statement of the American Thoracic Society (ATS), the European Respiratory Society (ERS) and the World Association of Sarcoidosis and Other Granulomatous Disorders (WASOG) adopted by the ATS Board of Directors and by the ERS Executive Committee, February 1999. *Am J Respir Crit Care Med*

- 1999;160:736-55.
2. Grutters JC, Drent M, van den Bosch JMM. Sarcoidosis. *Eur Respir Mon* 2009;46:126-54.
3. Criado E, Sánchez M, Ramírez J, et al. Pulmonary sarcoidosis: typical and atypical manifestations at high-resolution CT with pathologic correlation. *Radiographics* 2010;30:1567-86.
4. Lynch JP, White ES. Pulmonary sarcoidosis. *Eur Respir Mon* 2005;32:105-29.
5. Hamper UM, Fishman EK, Khouri NF, et al. Typical and atypical CT manifestations of pulmonary sarcoidosis. *J Comput Assist Tomogr* 1986;10:928-36.
6. Verschakelen JA. Sarcoidosis: imaging features. *Eur Respir Mon* 2005;32:265-83.
7. Miller A. The vanishing lung syndrome associated with pulmonary sarcoidosis. *Br J Dis Chest* 1981;75:209-14.
8. Harden KA, Barthakur A. Cavitory lesions in sarcoidosis. *Dis Chest* 1959;35:607-14.
9. Pena CM, Cosgrove DM, Eng P, et al. Bullectomies for bullous sarcoidosis. *Cleve Clin J Med* 1993;60:157-60.
10. Zar HJ, Cole RP. Bullous emphysema occurring in pulmonary sarcoidosis. *Respiration* 1995;62:290-3.
11. Judson MA, Strange C. Bullous sarcoidosis: a report of three cases. *Chest* 1998;114:1474-8.
12. Jeebun V, Forrest IA. Sarcoidosis: an underrecognised cause for bullous lung disease? *Eur Respir J* 2009;34:999-1001.
13. Froudarakis ME, Bouros D, Voloudaki A, et al. Pneumothorax as a first manifestation of sarcoidosis. *Chest* 1997;112:278-80.
14. Omori H, Asahi H, Irinoda T, et al. Pneumothorax as a presenting manifestation of early sarcoidosis. *Jpn J Thorac Cardiovasc Surg* 2004;52:33-5.
15. Liu Y, Dai HP, Xu LL, et al. Recurrent pneumothorax as a presenting manifestation of active sarcoidosis: a case report and literature review. *Chin Med J (Engl)* 2010;123:1615-6.
16. Gomm SA. An unusual presentation of sarcoidosis--spontaneous haemopneumothorax. *Postgrad Med J* 1984;60:621-3.
17. Ravichander PR. Hydropneumothorax in sarcoidosis. *Respir Med* 1989;83:251-3.
18. Akelsson IG, Eklund A, Sköld CM, et al. Bilateral spontaneous pneumothorax and sarcoidosis. *Sarcoidosis* 1990;7:136-8.
19. Sharma OP. Sarcoidosis: unusual pulmonary manifestations. *Postgrad Med* 1977;61:67-73.
20. Flora G, Dostanic D, Jakovic R, et al. Pneumothorax in sarcoidosis. *Sarcoidosis* 1991;8:75-9.
21. Soskel NT, Sharma OP. Pleural involvement in sarcoidosis. *Curr Opin Pulm Med* 2000;6:455-68.
22. Zimmerman I, Mann N. Boeck's sarcoid; a case of sarcoidosis complicated by pulmonary emphysema and cor pulmonale. *Ann Intern Med* 1949;31:153-62.
23. Mireles-Cabodevila E, Sahi H, Farver C, et al. A young patient with a minimal smoking history presents with bullous emphysema and recurrent pneumothorax. *Chest* 2007;132:338-43.
24. Keller CA, Naunheim KS, Osterloh J, et al. Histopathologic diagnosis made in lung tissue resected from patients with severe emphysema undergoing lung volume reduction surgery. *Chest* 1997;111:941-7.
25. Grutters JC, van den Bosch JM. Corticosteroid treatment in sarcoidosis. *Eur Respir J* 2006;28:627-36.
26. Tsakiridis K, Mpakas A, Kesisis G, et al. Lung inflammatory response syndrome after cardiac-operations and treatment of lornoxicam. *J Thorac Dis* 2014;6 Suppl 1:S78-98.
27. Tsakiridis K, Zarogoulidis P, Vretzkakis G, et al. Effect of lornoxicam in lung inflammatory response syndrome after operations for cardiac surgery with cardiopulmonary bypass. *J Thorac Dis* 2014;6 Suppl 1:S7-20.
28. Argiriou M, Kolokotron SM, Sakellaridis T, et al. Right heart failure post left ventricular assist device implantation. *J Thorac Dis* 2014;6 Suppl 1:S52-9.
29. Madesis A, Tsakiridis K, Zarogoulidis P, et al. Review of mitral valve insufficiency: repair or replacement. *J Thorac Dis* 2014;6 Suppl 1:S39-51.
30. Siminelakis S, Kakourou A, Batistatou A, et al. Thirteen years follow-up of heart myxoma operated patients: what is the appropriate surgical technique? *J Thorac Dis* 2014;6 Suppl 1:S32-8.
31. Foroulis CN, Kleontas A, Karatzopoulos A, et al. Early reoperation performed for the management of complications in patients undergoing general thoracic surgical procedures. *J Thorac Dis* 2014;6 Suppl 1:S21-31.
32. Nikolaos P, Vasilios L, Efstratios K, et al. Therapeutic modalities for Pancoast tumors. *J Thorac Dis* 2014;6 Suppl 1:S180-93.
33. Koutentakis M, Siminelakis S, Korantzopoulos P, et al. Surgical management of cardiac implantable electronic device infections. *J Thorac Dis* 2014;6 Suppl 1:S173-9.
34. Spyrtos D, Zarogoulidis P, Porpodis K, et al. Preoperative evaluation for lung cancer resection. *J Thorac Dis* 2014;6 Suppl 1:S162-6.
35. Porpodis K, Zarogoulidis P, Spyrtos D, et al. Pneumothorax and asthma. *J Thorac Dis* 2014;6 Suppl 1:S152-61.

36. Panagopoulos N, Leivaditis V, Koletsis E, et al. Pancoast tumors: characteristics and preoperative assessment. *J Thorac Dis* 2014;6 Suppl 1:S108-15.
37. Visouli AN, Darwiche K, Mpakas A, et al. Catamenial pneumothorax: a rare entity? Report of 5 cases and review of the literature. *J Thorac Dis* 2012;4 Suppl 1:17-31.
38. Zarogoulidis P, Chatzaki E, Hohenforst-Schmidt W, et al. Management of malignant pleural effusion by suicide gene therapy in advanced stage lung cancer: a case series and literature review. *Cancer Gene Ther* 2012;19:593-600.
39. Papaioannou M, Pitsiou G, Manika K, et al. COPD Assessment Test: A Simple Tool to Evaluate Disease Severity and Response to Treatment. *COPD* 2014;11:489-95.
40. Boskovic T, Stanic J, Pena-Karan S, et al. Pneumothorax after transthoracic needle biopsy of lung lesions under CT guidance. *J Thorac Dis* 2014;6 Suppl 1:S99-107.
41. Papaiwannou A, Zarogoulidis P, Porpodis K, et al. Asthma-chronic obstructive pulmonary disease overlap syndrome (ACOS): current literature review. *J Thorac Dis* 2014;6 Suppl 1:S146-51.
42. Zarogoulidis P, Porpodis K, Kioumis I, et al. Experimentation with inhaled bronchodilators and corticosteroids. *Int J Pharm* 2014;461:411-8.
43. Bai C, Huang H, Yao X, et al. Application of flexible bronchoscopy in inhalation lung injury. *Diagn Pathol* 2013;8:174.
44. Zarogoulidis P, Kioumis I, Porpodis K, et al. Clinical experimentation with aerosol antibiotics: current and future methods of administration. *Drug Des Devel Ther* 2013;7:1115-34.
45. Zarogoulidis P, Pataka A, Terzi E, et al. Intensive care unit and lung cancer: when should we intubate? *J Thorac Dis* 2013;5 Suppl 4:S407-12.
46. Hohenforst-Schmidt W, Petermann A, Visouli A, et al. Successful application of extracorporeal membrane oxygenation due to pulmonary hemorrhage secondary to granulomatosis with polyangiitis. *Drug Des Devel Ther* 2013;7:627-33.
47. Zarogoulidis P, Kontakiotis T, Tsakiridis K, et al. Difficult airway and difficult intubation in postintubation tracheal stenosis: a case report and literature review. *Ther Clin Risk Manag* 2012;8:279-86.

Cite this article as: Manika K, Kuhajda I, Zarogoulidis K, Kougioumtzi I, Dryllis G, Pitsiou G, Machairiotis N, Katsikogiannis N, Lampaki S, Papaiwannou A, Zaric B, Branislav P, Huang H, Li Q, Steiropoulos P, Zarogoulidis P. Pneumothorax in sarcoidosis. *J Thorac Dis* 2014;6(S4):S466-S469. doi: 10.3978/j.issn.2072-1439.2014.09.11