ISSN 1941-5923 © Am J Case Rep. 2015: 16: 912-915 DOI: 10.12659/AJCR.895276

Department of Pulmonary, Critical Care, and Sleep Medicine, University of Tennessee Health Science Center, College of Medicine at Memphis, Memphis, TN,



Received: 2015.07.08 Accepted: 2015.09.24 Published: 2015.12.30

Authors' Contribution:		
Study Design	А	
Data Collection	В	
Statistical Analysis	С	
Data Interpretation	D	
Manuscript Preparation	Е	
Literature Search	F	
Funds Collection	G	

Pleural Small Cell Lung Carcinoma: An Unusual **Culprit in Pleural Effusion**

U.S.A.

- Oluwaseyi D. Adejorin EF Amik Sodhi EF
- **BEF** Felicia A. Hare
- **EF** Arthur S. Headley
- EF Luis C. Murillo
- Dipen Kadaria BEFG

Corresponding Author: Conflict of interest:

Dipen Kadaria, e-mail: dkadaria@uthsc.edu None declared

Patient:	Male, 77
Final Diagnosis:	Pleural small cell carcinoma
Symptoms:	Chest pain • shortness of breath
Medication:	-
Clinical Procedure:	Thoracocentesis
Specialty:	Pulmonology
Objective:	Rare disease
Background:	Small cell lung carcinoma (SCLC) usually presents as lung or mediastinal lesions. It is very rare for SCLC to pres- ent primarily as an isolated pleural effusion with no lung or mediastinal lesions.
Case Report:	We report the case of a 77-year-old white male with a 60-pack year history of smoking, chronic obstructive pul- monary disease (stage IV), and asbestos exposure who presented with shortness of breath and left lateral chest pain for 7 days. On physical examination, he was very short of breath, with a prolonged expiratory phase on chest auscultation. Laboratory results were normal except for leukocytosis and chest radiograph revealing left- sided pleural effusion. Computerized tomography (CT) scanning of the chest with IV contrast showed left-sid- ed pleural effusion without any lung or mediastinal lesions. Thoracentesis was performed and fluid was sent for analysis. Repeat CT chest/abdomen/pelvis, done immediately following thoracocentesis, did not show any masses or lymphadenopathy. Fluid analysis, including cytology and immunostain pattern, was consistent with
Conclusions:	small cell carcinoma. Small cell lung cancer presenting as an isolated pleural effusion is extremely rare. It requires close attention to cytology and immunohistochemistry of pleural fluid samples. It also has implications for management and should be managed as limited-stage SCLC.
MeSH Keywords:	Pleural Effusion • Pleural Effusion, Malignant • Small Cell Lung Carcinoma
Full-text PDF:	http://www.amjcaserep.com/abstract/index/idArt/895276
	761 10 5 16



Background

SCLC usually presents as a lung lesion or mediastinal lymphadenopathy. It can be classified as limited disease (confined to 1 lung with/without lymph nodes on the same side, which can potentially be treated within 1 radiation port) or extensive disease (in the contralateral lung, lymph nodes on the contralateral side and/or distant metastasis). It is very rare for SCLC to present as a pleural effusion only with no lung or mediastinal lesion [1–3]. We present the case of a patient with pleural effusion due to small cell carcinoma without any evidence of lung lesions.

Case Report

A 77-year-old white male with a 60-pack year history of smoking, chronic obstructive pulmonary disease (stage IV), and asbestos exposure presented with shortness of breath and left lateral chest pain for 7 days. Admission vitals were: Temp: 99°F, BP: 110/70 mmHg, HR: 100/min RR: 18/min. On physical examination he was very short of breath, with a prolonged expiratory phase on chest auscultation. Laboratory results showed leukocytosis and a chest radiograph showed left-sided pleural effusion (Figure 1). CT chest with IV contrast showed a leftsided pleural effusion without any lung lesions or mediastinal lymphadenopathy. Thoracentesis was performed and fluid was sent for analysis. The fluid re-accumulated within 24 hours and a repeat thoracentesis was performed. Repeat CT chest/abdomen/pelvis, done immediately following thoracocentesis, did not show any masses or lymphadenopathy (Figures 2, 3).

The fluid was found to have tumor cells positive for synaptophysin, weakly positive for CD56, and negative for chromogranin and CD45 (Figures 4, 5). The immunostaining pattern, in conjunction with the cytomorphology, was consistent with small cell carcinoma.

The patient was referred to oncology service. However, due to his poor functional status (stage IV COPD with oxygen dependence and limited mobility) and patient preference, he was referred for hospice care.

Discussion

Lung cancer is the leading cause of malignant pleural effusion, seen in about 7–15% of all lung cancer at some time during the course of the illness [4–6]. Pleural effusions occur most frequently with adenocarcinoma [7].

SCLC occurs most commonly in heavy smokers and usually presents as a mass in the central airways, such as near the hilum of the lung, or as a mediastinal lesion with accompanying



Figure 1. Chest X- ray at presentation.



Figure 2. CT chest after thoracocentesis (mediastinal window).

adenopathy [8,9]. It has particular propensity to spread to the liver, adrenal glands, bone, bone marrow, and brain [9]. It can also present as a paraneoplastic syndrome, including Lambert-Eaton syndrome, SIADH, or Cushing's syndrome [9]. Extrapulmonary small cell carcinomas are rare [10,11]. However, there have been reports of it in the esophagus, salivary glands, gastrointestinal tract, pancreas, cervix, uterus, urinary bladder, prostate, and skin [10–12]. Small cell carcinoma originating from the pleura or metastasizing to the pleura is very rare [1,13]. In 1 series, less than 3% of patients with SCLC had significant pleural effusion (requiring thoracocentesis) [1]. In another series, 2–7% of patients with SCLC had pleural effusions, but the number of isolated pleural effusions was not



Figure 3. CT chest after thoracocentesis (lung window).



Figure 4. Tumor cells in pleural fluid.

reported [8]. There are some reported cases of pleural masses, biopsy of which showed small cell carcinoma [14]

In addition to recognition of SCLC cells in pleural effusion cytology based on morphology, immunohistochemistry has been proven to be very helpful in diagnosis [2]. Chromogranin and synaptophysin are the markers commonly used to identify neoplastic cells of neuroendocrine origin. TTF-1 is also a sensitive marker for SCLC, with more than 90% reactivity [2]. It may sometimes be difficult to morphologically differentiate neoplastic cells from lymphocytes, and immunohistochemistry can be invaluable in such instances [1].

References:

- 1. Chhieng DC, Ko EC, Yee HT et al: Malignant pleural effusion due to smallcell lung carcinoma: A cytologic and immunocytochemical study. Diagn Cytopathol, 2001; 25(6): 356–60
- Smith R, Nguyen GK: Unusual cytologic manifestation of small cell lung cancer in associated pleural effusion. Diagn Cytopathol, 2004; 30: 266–67



Figure 5. Tumor cells in pleural fluid; Synaptophysin immunoperoxidase stain.

Despite being a rare presentation, survival of patients with SCLC presenting with isolated pleural effusion without any lung or mediastinal lesion is comparable to other patients with limited disease SCLC [3,15]. Patients with limited disease SCLC are treated with combination chemotherapy (usually Cisplatin and Etoposide) and concurrent thoracic radiotherapy [16]. However, treatment remains challenging because of SCLC's rapid growth, development of drug resistance during the course of the disease, and short disease-free duration following first-line chemotherapy [8].

In our case, the patient presented with a left pleural effusion and no lung or mediastinal primary site was found. As mentioned above, this is extremely rare. Pleural fluid cytology and immunostaining pattern were suggestive of small cell lung carcinoma.

Conclusions

Primary small cell lung cancer limited to the pleura and presenting as a pleural effusion without any underlying lung lesions is extremely rare. The present case underscores the importance of a good cytological examination along with advanced immunohistochemical markers on the pleural fluid. It also has implications for management, and isolated SCLC pleural effusion should be managed as limited-stage SCLC.

- Dearing MP, Steinberg SM, Phelps R et al: Outcome of patients with SCLC: Effects of changes in staging procedures and imaging technology on prognostic factors over 14 years. J Clin Oncol, 1990; 8(6): 1042–49
- 4. Emerson GL, Emerson MS, Sherwood GE: The Natural history of carcinoma of the lung. J Thoracic Surg, 1959; 37: 291–304

- 5. Cohen S, Hossain S: Primary carcinoma of the lung: a review of 417 histologically proved cases. Dis Chest, 1966; 49: 626–29
- Johnston WW: The malignant pleural effusion: A review of cytopathological diagnoses of 584 specimens from 472 consecutive patients. Cancer, 1985; 56; 905–9
- Porcel JM, Esqueda A, Vives M, Bielsa S: Etiology of pleural effusions: analysis of more than 3000 consecutive thoracenteses. Arch Broncopneumol, 2014; 50(5): 161–65
- Kallianos A, Rapti A, Zarogoulidis P et al: Therapeutic procedure in SCLC. J Thoracic Dis, 2013; Suppl 4: S420–24
- 9. Argiris A, Murren JR: Staging and clinical prognostic factors for small-cell lung cancer. Cancer J, 2001; 7: 437–47
- Ochsenreither S, Marnitz-Schultze S, Schneider A et al: Extrapulmonary small cell carcinoma (EPSCC): 10 years' multi-disciplinary experience at Charité. Anticancer Res, 2009; 29(8): 3411

- 11. Wong YN, Jack RH, Mak V et al: The epidemiology and survival of extrapulmonary small cell carcinoma in South East England, 1970–2004. BMC Cancer, 2009; 9: 209
- Brennan SM, Gregory DL, Stillie A et al: Should extrapulmonary small cell cancer be managed like small cell lung cancer? Cancer, 2010; 116(4): 888–95
- 13. Schinkewitch P, Gasser B, Wihlm JM et al: Small cell carcinoma of the pleura. A case report. Lung Cancer, 1996; 16(1): 87–94
- 14. Satoh H, Ishikawa H, Ohtsuka M, Sekizawa K: Small cell carcinoma of the pleura. South Med J, 2002; 95(10): 1221
- Livingston RB, McCracken JD, Trauth CJ, Chen T: Isolated pleural effusion in small cell lung carcinoma: Favorable prognosis. A review of the southwest oncology group experience. Chest, 1982; 81: 208–11
- Fukuoka M, Furuse K, Saijo N et al: Randomized trial of cyclophosphamide, doxorubicin, and vincistrine versus cisplatin and etoposide versus alternation of these regimens in small cell lung cancer. J Natl Cancer Inst, 1991; 83(12): 855–61