Silent Neoplastic Cardiac Invasion in Small Cell Lung Cancer: A Case Report and Review of the Literature

Ngoc Pham
Mark D. Bonnen
Yohannes T. Ghebre

Corresponding Authors: Yohannes T. Ghebre, e-mail: yohannes.ghebre@bcm.edu and Mark D. Bonnen, e-mail: mark.bonnen@bcm.edu

Conflict of interest: None declared

Source of support: YTG was an awardee of the Stanford University School of Medicine Dean’s fellowship (grant number 1049528-149-KAVFB), Stanford SPARK Translational Research Program, the Tobacco-Related Disease Research Program (TRDRP) of the University of California (grant number 20FT-0090), the Houston Methodist Research Institute, and the Caroline Weiss Law Fund for Research in Molecular Medicine at Baylor College of Medicine. He is currently supported by AHA (17GRNT33460159), NIH (grant numbers K01HL118683; R01HL137703), and by intramural funding from BCM

Patient: Female, 66
Final Diagnosis: Small cell lung cancer
Symptoms: Impaired memory
Medication: —
Clinical Procedure: Chest X-ray • computed tomography • magnetic resonance imaging • electrocardiogram
Specialty: Oncology

Objective: Rare co-existence of disease or pathology

Background: Secondary malignant tumor of the heart is one of the most life-threatening complications of lung cancer. Several published case reports have documented non-small cell lung cancer (NSCLC) patients with neoplastic cardiac invasion. However, the number of reported cases of small cell lung cancer (SCLC) with neoplastic cardiac invasion is limited.

Case Report: We present a rare case of advanced SCLC in a patient with asymptomatic neoplastic cardiac invasion. We also discuss radiation therapy modalities that should be considered in SCLC patients with cardiac invasion.

Conclusions: Clinicians should be vigilant about cases of SCLC with asymptomatic intra-cardiac invasion and practice caution when diagnosing, as well as treating with radiation as a monotherapy.

MeSH Keywords: Lung Neoplasms • Neoplasm Metastasis • Radiation • Small Cell Lung Carcinoma

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/908374

This work is licensed under Creative Common Attribution-NonCommercial-NoDerivatives 4.0 International (CC BY-NC-ND 4.0)
Background

Neoplastic cardiac invasion is one of the morbid complications of lung cancer. Autopsy reports have demonstrated that up to 7% of all cancer cases have cardiac metastases and up to 10% of bronchogenic tumors have atrial invasion [1]. However, the literature shows limited reports of small cell lung cancer (SCLC) patients with neoplastic cardiac invasion [2–7]. In addition to cardiac invasion, brain metastasis is another fatal complication that occurs in up to 70% of SCLC patients with advanced disease [8]. Some of the tumor- and treatment-related symptoms in these cases include dysregulated secretion of antidiuretic hormone, peripheral neuropathy, and encephalopathy.

A significant proportion of SCLC patients with cardiac metastases have atrial invasion, which may lead to systemic embolization and/or outflow obstruction [9,10]. In such cases, aggressive local treatment is important regardless of overall prognosis. Given the life-threatening nature of the disease, the current criterion standard treatment for neoplastic cardiac invasion is surgical resection. However, treatment decision is complicated when the patient is not a suitable candidate for surgery due to comorbidities (e., thrombocytopenia, refractory diabetes, and poor pulmonary function) or performance status. In such cases, radiotherapy is an alternative local treatment option. Recent studies reported the use of radiotherapy in non-small cell lung cancer (NSCLC) invaded into the heart [1,2]. Treatment outcomes were very promising and treatment-related cardiac complications are not common. Despite these favorable outcomes in NSCLC, there are only limited reports on the use of high-dose radiotherapy as the definitive monotherapy for cardiac invasive tumors from SCLC. Tumor cells in SCLC are responsive to chemotherapy and radiotherapy. In our experience, we often observed tumor shrinkage on cone beam computed tomography shortly after the initiation of radiation therapy. One of the challenges, however, is the uncertainty of how radiation therapy will affect the structure and function of the heart after the tumor is treated. Here, we present a rare case of asymptomatic cardiac invasion from lung cancer in a patient with stage IV SCLC. We also discuss radiation therapy modalities that should be considered in SCLC patients with cardiac invasion.

Case Report

A 66-year-old woman with a 30-pack-year smoking history presented to the Emergency Department for cognitive impairment with memory loss. On admission, she received a chest X-ray that showed a large left lung mass. A follow-up chest computed tomography (CT) and magnetic resonance imaging (MRI) tests showed a 7.7×8.5×7.4 cm necrotic mass arising from the right lower lobe to invade the left atrium via the inferior left pulmonary vein and extend into the left ventricle (Figure 1). On electrocardiogram (ECG), there was also evidence of the left atrial mass prolapsing through the mitral annulus with partial mitral valve obstruction. The ECG reports showed normal sinus rhythm, and routine laboratory tests, including metabolic panel and complete blood count, were normal with the exception of low platelet count (120 000 per microliter). Further work-up with MRI brain, in the presence or absence of contrast, revealed a 4.5×2.8×3.2 cm hemorrhagic temporal occipital lesion. Subsequently, the patient received craniotomy with gross total resection of the brain tumor and...
the pathology report revealed poorly differentiated carcinoma with immunohistochemical stains confirming strongly re-
active tumor cells for CD56, consistent with neuroendocrine differentiation. In addition, bronchoscopy-based biopsy of the 
right lower lung lobe confirmed similar pathology to that of 
the brain specimen. Accordingly, she was diagnosed with stage 
IV, T4NMX1, SCLC of the right lower lung lobe. The post-oper-
avative course was significant for worsening thrombocytopenia 
with a sharp drop in platelet count to as low as 19,000 per 
microliter. Thoracic surgery and medical oncology teams rec-
nommended against surgery or chemotherapy. The radiation 
oncology team was further consulted for treatment options 
and offered a course of palliative radiotherapy treatment to 
the thorax and whole brain. Unfortunately, the patient died of 
an unknown cause before the planned radiotherapy regi-
men could be delivered. At the family’s request, an autopsy 
was not performed.

Discussion

Here, we report a case of asymptomatic neoplastic cardiac in-
vasion in a patient with stage IV SCLC. This report is in line 
with the limited number of SCLC cases that involved intra-car-
diac invasion [3–7]. However, our patient, despite being stage 
IV SCLC, showed no symptoms of cardiac invasion and her ECG 
was normal. The pathogenesis of cardiac invasion in SCLC is 
thought to be hematologic or lymphatic spread, or direct in-
vasion from a nearby tumor. Due to fatal outcomes of intra-
atrial tumors, the standard treatment of choice in such cas-
es is complete en bloc resection of the primary tumor and left 
atrium with or without the great vessels [1]. However, when a 
patient does not qualify for surgery, as in this case, there is a 
compelling need for alternate treatment such as radiotherapy.

The use of radiation as the local monotherapy for cardiac le-
sions is currently underutilized, even for non-surgical patients, 
primarily due to the concern of radiation-induced heart disease 
(RIHD), which is a relatively common complication when the 
heart receives a large dose of radiation [11]. At doses above 
30 Gy, RIHD may become apparent within the first 2 years of 
exposure and the risk increases, with accelerated manifes-
tations, at higher radiation doses. High-dose irradiation of a 
large volume of the heart can seriously damage vital compo-
nents of the heart, including the valves, arteries, and conduct-
ing systems. Acutely, the pericardium may be severely inflamed 
(pericarditis), while the long-term complications include cardi-
ac fibrosis and coronary artery disease. Collectively, these com-
plications are responsible for significant cardiovascular mor-
bidity and mortality, particularly in patients with underlying 
major adverse cardiovascular events.

Modern radiation oncology techniques, such as intensity-mod-
ulated radiotherapy (IMRT) or stereotactic body radiotherapy 
(SBRT), can overcome the aforementioned risks by substan-
tially reducing the radiation dose to the heart. The increased 
accuracy and precision of contemporary radiotherapy treat-
ment planning algorithm and technology allows for a sharp 
dose fall-off to the normal heart and a smaller margin used 
for daily set-up error and internal organ motion. In particular, 
strategies such as deep inspiratory breath hold [12] or respi-
atory gating [13] can significantly reduce the risk of pericar-
dial disease and coronary artery disease. Lee et al. recently 
employed IMRT to deliver 50 Gy in 20 fractions to the meta-
static cardiac lesion from NSCLC, with the maximum dose to 
the intra-atrial lesion reaching 55.8 Gy and a mean dose of 
23 Gy to the uninvolved heart [1]. The patient had no acute 
complications from radiation, and in fact had complete reso-
lution of her intra-cardiac disease within 3 months. Similarly, 
Li et al. reported the use of SBRT to deliver a 40 Gy total dose 
in 10 fractions for an atrial tumor thrombus from NSCLC [2]. 
A complete response was achieved within 12 months and no 
cardiac toxicity was noted. A study by Orcurto et al. reported 
a right heart metastasis from a small cell lung cancer [5]. The 
patient was treated with chemotherapy (6 cycles of cisplatin 
etoposide) followed by radiotherapy (total dose of 60 Gy) 
to the lung mass, nodes, and cardiac metastasis. Radiation 
treatment technique and fractionation schedule was not dis-
cussed in the paper. Patient had complete response on restag-
ing PET/CT at 2 months.

The positive outcomes of these recent reports suggest that ra-
diation can be safely used to treat neoplastic involvement of 
the atria. Regrettfully, our patient died before treatment could 
be delivered.

Conclusions

Clinicians should be vigilant about cases of SCLC with asymp-
tomatic intra-cardiac invasion and practice caution when di-
agnosing, as well as treating with radiation as a monotherapy.

References:

1. Lee P, Kishan AU: Radiotherapy is effective for a primary lung cancer in-
vading the left atrium. BMJ Case Rep, 2012; 2012: pii: bcr2012006667
2. Li Y, Lou J, Qiu S et al: Stereotactic radiotherapy for the treatment of lung 
cancer with a giant left atrial tumor thrombus: A case report and literature 
review. Oncol Lett, 2016; 11: 2229–32
3. Duncan MD, Swinburne AI, Sahni S et al: Small cell lung cancer presenting 
as a cardiac mass with embolic phenomena. Am J Med, 2017;130: e55–57
4. Nahapetian R, Luraschi-Monjagatta C: Medical image of the week: Extensive 
small cell lung cancer with cardiac invasion. Southwest J Pulm Crit Care, 
2013; 6: 143–44
5. Orcurto MV, Delaloye AB, Letovanec I et al: Detection of an asymptomatic right-ventricle cardiac metastasis from a small-cell lung cancer by f-18-fdg pet/ct. J Thorac Oncol, 2009; 4: 127–30
6. Shah R, John E, Fan TH et al: A patient with metastatic small-cell lung cancer and giant right ventricular mass. Echocardiography, 2016; 33: 491–93
7. Bussani R, De-Giorgio F, Abbate A, Silvestri F: Cardiac metastases. J Clin Pathol, 2007; 60: 27–34
8. van Oosterhout AG, van de Pol M, ten Velde GP, Twijnstra A: Neurologic disorders in 203 consecutive patients with small cell lung cancer. Results of a longitudinal study. Cancer, 1996; 77: 1434–41
9. Sadat U, Noor N, See TC, Varty K: Peripheral arterial ischemia by a primary lung tumour invading left atrium. Lung cancer, 2007; 57: 237–39
10. Woodring JH, Bognar B, van Wyk CS: Metastatic chondrosarcoma to the lung with extension into the left atrium via invasion of the pulmonary veins: Presentation as embolic cerebral infarction. Clin Imaging, 2002; 26: 338–41
11. Yusuf SW, Sami S, Daher IN: Radiation-induced heart disease: A clinical update. Cardiol Res Pract, 2011; 2011: 317659
12. Remouchamps VM, Vicini FA, Sharpe MB et al: Significant reductions in heart and lung doses using deep inspiration breath hold with active breathing control and intensity-modulated radiation therapy for patients treated with locoregional breast irradiation. Int J Radiat Oncol Biol Phys, 2003; 55: 392–406
13. Becker-Schiebe M, Stockhammer M, Hoffmann W et al: Does mean heart dose sufficiently reflect coronary artery exposure in left-sided breast cancer radiotherapy?: Influence of respiratory gating. Strahlenther Onkol, 2016; 192(9): 624–31