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# Spinal Cord Ischemia Secondary to Epidural Metastasis from Small Cell Lung Carcinoma

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Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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**Conflict of interest:** None declared

**Patient:** Male, 56
**Final Diagnosis:** Small cell lung carcinoma
**Symptoms:** Back pain • paralysis
**Medication:** —
**Clinical Procedure:** MRI
**Specialty:** Pulmonology

**Objective:** Unusual clinical course

**Background:** Spinal cord ischemia is an uncommon event that is mainly caused by dissociation of the ascending aorta as a complication after aortic surgery. Spinal arteries can develop collateral circulation; therefore, the frequency of spinal infarction is about 1% of that in the brain. Few cases of spinal cord ischemia developing in the course of lung cancer have been reported.

**Case Report:** We presented the case of a 56-year-old man with small cell lung carcinoma, cT4N2M1a (stage IV). He was treated with irradiation and 2 courses of platinum and etoposide combination chemotherapy. He complained of back pain followed by quadriplegia and sensory disturbance after cessation of chemotherapy. With a diagnosis of spinal cord metastasis, steroids were administered. However, diaphragmatic paralysis appeared a few hours later. He was started on palliative care and died after 6 days. Autopsy showed epidural metastasis and spinal ischemia at the C5 level.

**Conclusions:** Epidural metastasis can compress the spinal artery and cause circulatory disorders. Spinal cord ischemia should be considered in patients with rapid paralysis in the course of lung cancer.

**MeSH Keywords:** Epidural Neoplasms • Small Cell Lung Carcinoma • Spinal Cord Ischemia • Spinal Cord Neoplasms

**Full-text PDF:** http://www.amjcaserep.com/abstract/index/idArt/902813

## Background

Infarction of the spinal cord is an uncommon but well-known complication of thoracic aortic surgery and aortic cross-clamping, with disruption of segmental arterial supply to the cord [1]. Spinal arteries can develop collateral circulation; therefore, the frequency of developing spinal infarction is only about 1% of that in the brain [2]. Infarction of the cervical cord may present with pain, paralysis, dissociated sensory loss, and autonomic deficit [3,4]. Metastasis to the nervous system, such as spinal epidural metastasis (SEM), is one of the most important differential diagnosis of spinal cord infarction. Lung cancer, especially small cell lung carcinoma (SCLC), accounts for most cases of SEM [5]. We encountered a rare case of spinal cord ischemia with concomitant SEM from SCLC.

## Case Report

A 56-year-old Japanese man was referred because of a left lung tumor on chest radiograph. He had been experiencing chronic cough and chest pain for 3 weeks. His past medical history included hypertension and hypothyroidism, which were treated with amlodipine, doxazosin mesylate, and levothyroxine. His annual checkup 2 months before was normal on chest X ray. He had smoked a pack of cigarettes per day for 35 years and did not have any notable family history of cancer. On physical examination, his left lung sound was decreased without rales, but other findings were normal. A chest computed tomography (CT) scan showed a 57-mm × 27-mm tumor at the hilum of the left upper lobe, with an accessory nodule on the left lower lobe, enlarged hilar and station #7 mediastinal lymph nodes, and mild pleural effusion (Figure 1A). Serum C-reactive protein (CRP) (2.72 mg/dL) and lactase dehydrogenase (LDH) (497 U/L)

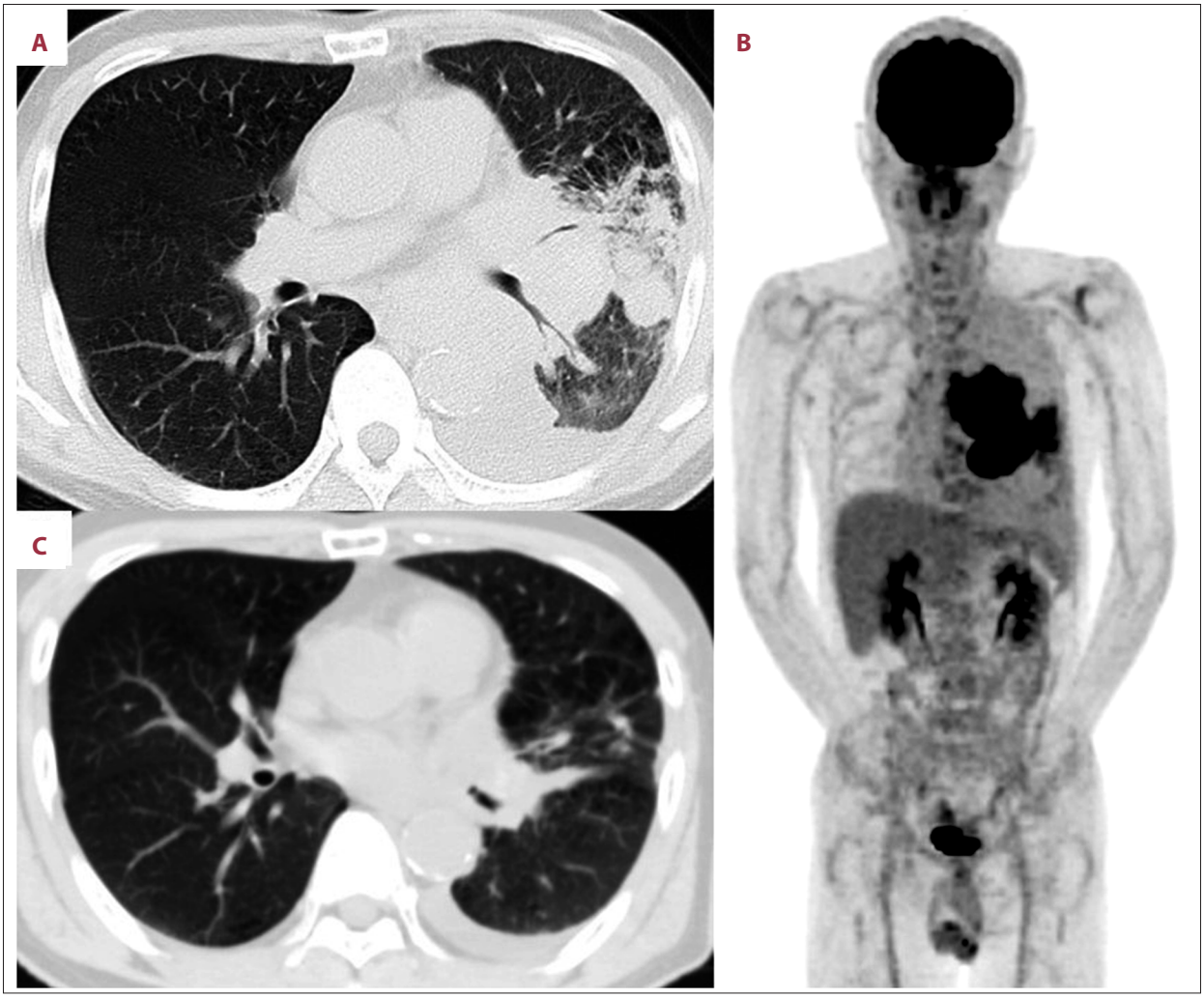


**Figure 1.** CTs and PET/CT images before and after chemoradiotherapy. (**A**) CT scan at the first visit shows a primary lesion at left hilar area, enlarged mediastinal lymph nodes, and pleural effusion. (**B**) PET/CT scan does not show any distant metastasis before chemoradiotherapy. (C) CT scan after chemoradiotherapy shows primary lesion and lymph nodes shrinking.

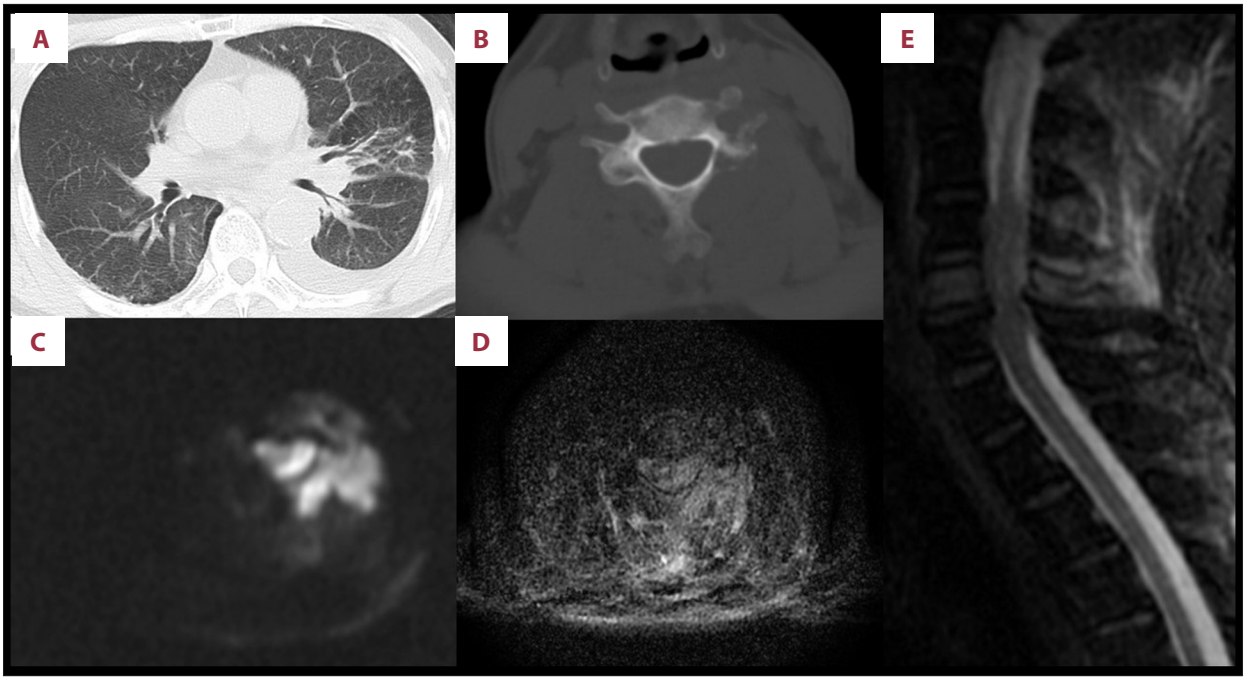


**Figure 2.** CT and MRI images at the emergency room. (**A**) CT scan at the emergency room shows no progression of the chest lesions, (**B**) but an osteolytic lesion at the left part of the C5 vertebral body is seen. (**C, D**) Diffusion-weighted and fat suppression T2-weighted MRI show a hyperintense lesion at the paravertebral soft tissue. (**E**) Sagittal section of fat suppression T2-weighted MRI shows spinal cord enlargement, but the abnormal signal is unclear.

were slightly elevated. Neuron-specific enolase (NSE) was elevated at 157.3 ng/mL (normal range <10 ng/mL), but carcinoembryonic antigen (CEA), cytokeratin fragment (CYFRA), and pro-gastrin releasing peptide (pro-GRP) were within normal limits. Bronchoscopy was performed, but biopsy and cytology were negative due to difficulty in reaching the tumor through the narrowed bronchus. Pathologic evaluation of pleural effusion cell block led to a diagnosis of SCLC. A positron emission tomography/computed tomography (PET/CT) scan and cranial magnetic resonance imaging (MRI) excluded distant metastases (Figure 1B, 1C). Finally, he was diagnosed as having SCLC, cT4N2M1a (stage IV), limited disease (LD), in accordance with the 7th edition of the General Rule for Clinical and Pathological Record of Lung Cancer from the Japan Lung Cancer Society.

Concurrent chemoradiotherapy (CRT) with cisplatin and etoposide was started at 20 days after the first visit. Cisplatin was changed to carboplatin at the second course due to grade 1 renal dysfunction. CT showed decrease in the size of the primary lesion and lymph nodes; this was evaluated as response evaluation criteria in solid tumors (RECIST) partial remission (PR) after CRT. Serum NSE decreased to within the normal range (9.3 ng/mL). The patient elected to stop carboplatin and etoposide after 2 courses. Twenty days after completion of radiation therapy, he noted severe pain in his neck and left shoulder. Two weeks after, he developed paraplegia, paresthesia, and vesicorectal dysfunction, followed by quadriplegia within 2 days. He was then brought in for emergency hospitalization.

On physical examination, he could only move his right elbow weakly in manual muscle testing (MMT) 2/5, and his neck and face were normal. He had pansensory loss below his neck. Blood CRP (0.83 mg/dL), LDH (293 mg/dL), and NSE (29.8 pg/mL) were elevated. CT revealed osteolytic lesion at the left part of the C5 vertebral body. There was no intracranial lesion or any signs of progression of the primary lesion and lymph nodes on CT (Figure 2A, 2B). MRI of the spine showed focal hyperintense signals on fat suppression T2-weighted images and diffusion-weighted images at the C5 vertebral body and surrounding soft tissue, including the *erector spinae*. Sagittal section fat suppression T2-weighted MRI showed spinal cord enlargement around the C5 level, but abnormal signals were unclear (Figure 2C–2E). Therefore, we diagnosed spinal cord metastasis from SCLC and started steroids upon hospitalization. However, the next day, he was noted to have paradoxical breathing and severe respiratory discomfort, both of which were attributed to diaphragmatic paralysis. He was started on palliative care and died 6 days after hospitalization.

An autopsy was performed to determine the cause of the unusually rapid progression of paralysis from lung cancer metastasis. The primary lesion comprised a sheet of formatted small round tumor cells with necrosis and fibrosis; immunostaining was

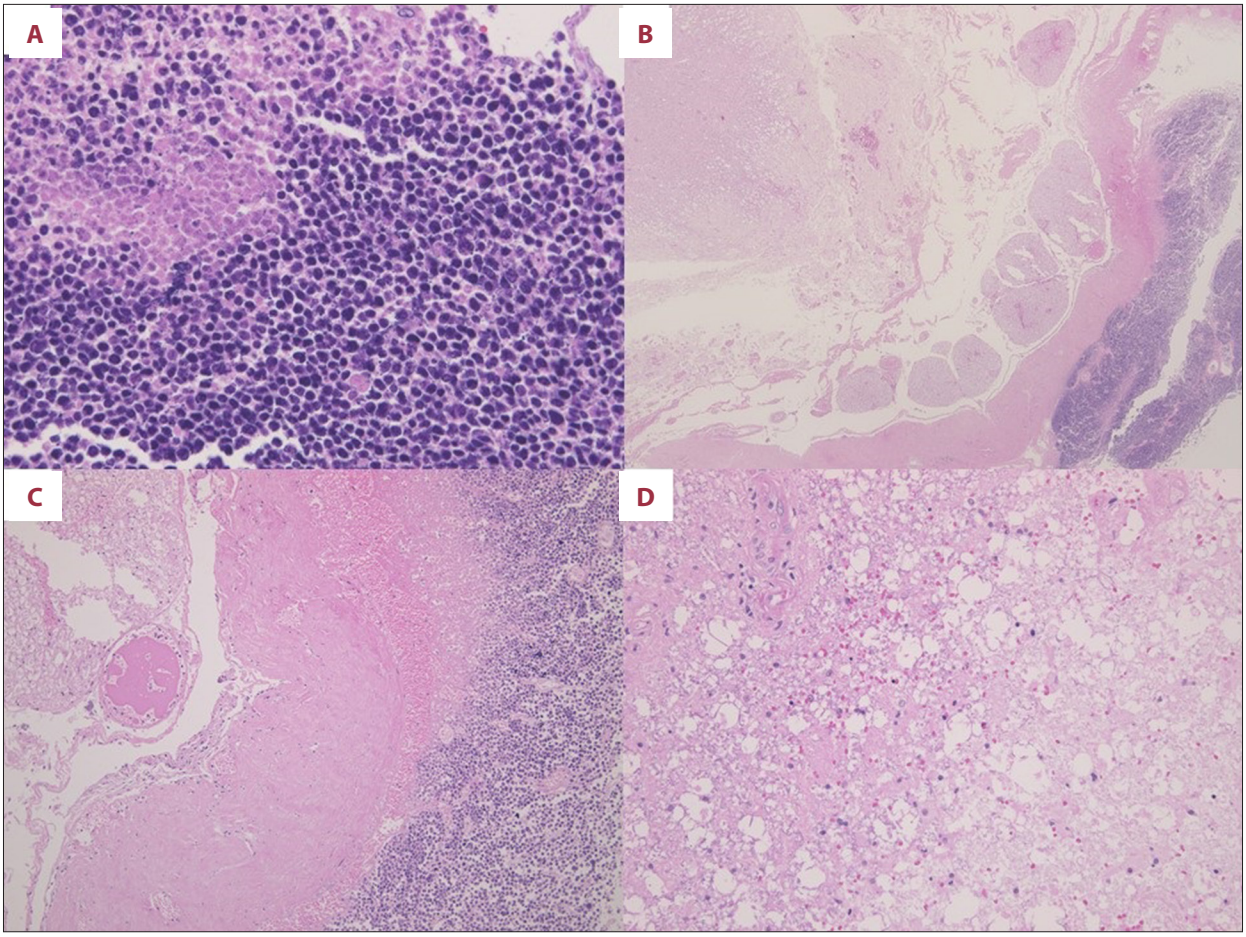


**Figure 3.** Autopsy images. (**A**) The primary lesion shows hyperchromatic atypical cells with high N/C ratio. The bulk of the tumor shows coagulation necrosis due to treatment (hematoxylin-eosin stain, 400×). (**B**) Cervical metastasis shows epidural invasion, but not intradural or spinal cord invasion (hematoxylin-eosin stain, 40×). (**C**) Epidural metastasis and fibrin thrombus in the spinal small vessel (hematoxylin-eosin stain, 200×). (**D**) Spinal cord shows colliquative necrosis (hematoxylin-eosin stain, 200×).

positive for CD56, synaptophysin, and chromogranin (Figure 3A). There were metastases to the C5 vertebrae and peripheral tissue, with invasion of the dura mater, but without subdural or spinal cord infiltration. The neck and upper thoracic spinal cord showed colliquative necrosis and demyelination with fibrin thrombus in the small subdural vessels, indicating spinal cord infarction (Figure 3B–3D). The other organs did not show indications of being in a hypercoagulable state, such as Trousseau's syndrome and thrombotic thrombocytopenic purpura. There were metastases to the lumbar spine, left pleura, and liver. The brain did not have any metastasis or other lesions. Pneumonia with massive sputum was found. The cause of the death was breathing muscle paralysis due to spinal cord infarction and pneumonia.

## Discussion

Lung cancer commonly metastasizes to certain organs, such as the contralateral lung (49.4%), liver (42.2%), bone (39.1%), adrenals (26.3%), and brain (22.8%). On the other hand, it has been reported that spinal cord metastasis accounts for only 3.2% of lung cancer metastases [6]. SEM, a common type of spinal metastasis, causes neuropathy by spinal cord compression; it ranks second to the brain as a cause of neurologic dysfunction caused by metastasis. Most patients with epidural involvement have associated vertebral metastasis, usually at the thoracic level (70%), followed by the lumbar region (20%) and cervical region (10%). There are 3 modes by which metastatic tumors can reach the epidural space. In approximately 85% of patients, the tumor reaches the spinal cord indirectly from an initial hematogenous spread to the vertebral body, followed by growth in the bone and spread into the epidural space, eventually causing secondary compression of the spinal cord. A less common mode is by direct invasion of a paravertebral tumor into the spinal canal through an intervertebral foramen, which compresses the spinal cord. The least common mode of metastasis is direct hematogenous spread to the spinal epidural space, dura, or spinal cord [7]. In our case,

the lung tumor reached the epidural space through the intervertebral foramen.

Spinal cord ischemia is extremely uncommon and occurs mostly in the anterior spinal artery territory. Unlike cerebral infarction, spinal cord ischemia lacks conclusive epidemiologic data. Infarction of the cervical segment of the spinal cord is unusual and the number of reported cases in the medical literature remains small. An extensive literature search for lung cancer with spinal cord ischemia in PubMed generated 4 published reports: 1) spinal cord ischemia following air embolism after CT-guided lung biopsy, 2) thoracotomy without epidural anesthesia, 3) adjuvant chemotherapy with tegafur, gimeracil and oteracil, and 4) intercostal nerve neurolysis secondary to alcohol and thoracic epidural steroid injections. In all these cases, the lesions were mainly located in the thoracic level; the air embolism case included an additional cerebellar lesion [8–11].

In the present case, we identified on autopsy dura mater invasion of the cervical spinal metastasis via the intervertebral foramen and spinal cord ischemia at the same level. A possible cause of spinal cord ischemia might have been that the small vessels around the spinal cord epidural metastasis were compressed or otherwise affected. Spinal cord ischemia at the cervical level and its pathophysiology are extremely rare and unclear. This case demonstrates the possibility of an association between lung cancer and spinal cord ischemia.

## Conclusions

In SCLC patients with metastasis around the spinal cord, we should consider not only spinal cord metastasis, but also other complications, such as spinal cord ischemia.

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