CASE REPORT

A Resected Case of Pulmonary Large Cell Neuroendocrine Carcinoma Showing Aggressive Progression

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ABSTRACT —— ***Background.*** In 1991, Travis et al. proposed a new category of large cell neuroendocrine carcinoma (LCNEC). Some investigators reported poor prognosis of LCNEC patients, with 5-year survival rates similar to small cell carcinoma. We report a case of LCNEC with aggressive progression after complete resection. ***Case.*** A 71-year-old man underwent left pneumonectomy and lymph node dissection for lung cancer on June 13, 2002. No finding suggested distant metastasis. The pathological diagnosis was large cell neuroendocrine carcinoma, T2N1M0, stage IIB. Two months after surgery, he presented with lumbago. Bone scintigram and magnetic resonance imaging revealed bone metastasis to the right sacroiliac joint. A brain metastasis was also detected by computed tomography. He received 30-Gy brain irradiation and 30-Gy bone radiotherapy to relieve the pain. Although the radiotherapy alleviated the pain, the brain and sacroiliac joint metastases did not shrink. The patient died of recurrent lung cancer 99 days after the surgical resection. ***Conclusion.*** We reported an aggressive progression case of pulmonary LCNEC. Prognosis and treatment efficacy in LCNEC patients remain controversial, and further investigation is needed.(*JJLC.* 2005;45:751-754)

KEY WORDS —— Large cell neuroendocrine carcinoma (LCNEC), Lung cancer, Surgery

INTRODUCTION

In 1991, Travis et al. proposed a new category of large cell neuroendocrine carcinoma (LCNEC).[1] Some investigators reported poor prognosis of LCNEC patients, with 5-year survival rates similar to small cell carcinoma.[2-7] We report a case of LCNEC with aggressive progression after complete resection.

CASE REPORT

A 71-year-old man had bloody sputum on April 25, 2002. A chest radiograph revealed a mass shadow in the left middle lung field. Bronchoscopic washing cytology at a local hospital yielded findings suspicious of squamous cell carcinoma. He was then referred to our institution.

The patient had received medication for hypertension and atrial fibrillation for 7 years. The family history was unremarkable. He had smoked 90 pack-years from 16 to 60 years old. The serologic test revealed elevated CEA (22.8 ng/ml), NSE (13.1 ng/ml), and CYFRA (25.1 ng/

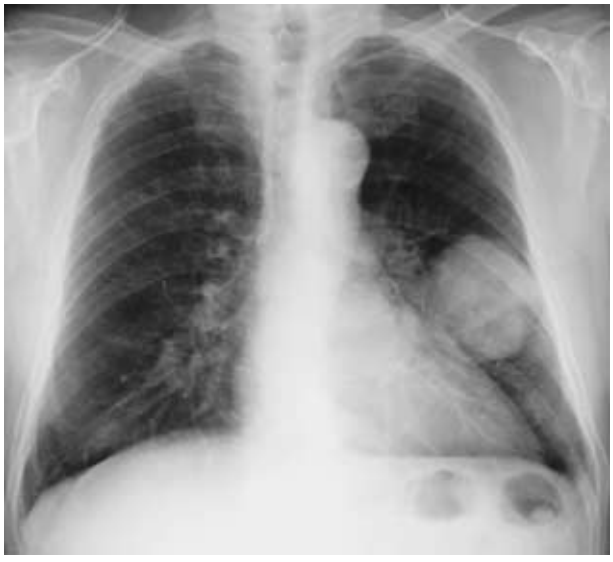

Figure 1. Chest radiograph showing a 7 cm mass shadow in the left middle lung field.

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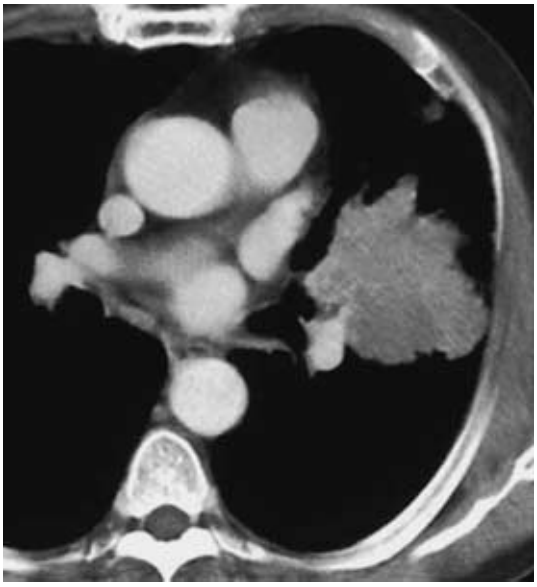

Figure 2. Chest CT scan showing a mass in the left lingula. Invasion to the lower lobe and pulmonary artery was suspected.

ml). Other laboratory data were normal.

A chest radiograph revealed a well-defined 7 cm mass (Figure 1). Computed tomography (CT) revealed an 8× 7 cm solid tumor with an irregular surface in the left lingular segment. Invasion to the lower lobe and the origin of the left lingular segmental pulmonary artery was suspected (Figure 2). There was no hilar or mediastinal lymphadenopathy. Distant metastases were not detected by abdominal CT, brain magnetic resonance imaging (MRI), and bone scintigram. We performed transbronchial brushing cytology after admission, and findings suspicious of LCNEC were obtained. The disease was clinically T2N0M0, stage IB.

Surgery was performed on June 13, 2002. The tumor invaded the left lower lobe and the origin of the left lingular segmental pulmonary artery. We performed left pneumonectomy and systematic lymph node dissection. The postoperative course was uneventful.

Macroscopically, the cut surface was creamy-white, with necrosis and hemorrhage. Histopathologic examination showed an organoid pattern and central necrosis (Figure 3A). High-power magnification of the tumor showed large tumor cells, with palisading and rosette-like structures (Figure 3B). The mitotic count was 28 per 10 high power fields. Lymphatic permeation and venous invasion were observed. Tumor cells stained positive for Lu243. Synaptophysin and Chromogranin stainings were negative. A hilar lymph node was positive for tumor cells. Based on the histopathological and immunohistochemical features, a diagnosis of LCNEC, T2N1M0, stage IIB was made.

The patient was discharged on the 14th postoperative day. However, he complained of right-sided lumbago two months after lung resection. Although his serum CEA level decreased to 6.5 ng/ml after surgery, it elevated again. NSE and CYFRA levels were not re-examined. Bone scintigram and spinal MRI revealed metastasis in the right sacroiliac joint. CT scan showed a brain metastasis, but he had no neurological symptoms. He received 30-Gy whole brain irradiation and 30-Gy radiotherapy for bone metastasis to relieve the pain. Although his pain was alleviated, the sacroiliac joint and brain metastases did not shrink. We planned chemotherapy, but his general condition rapidly worsened and he became cachectic. He died on September 20, 2002, on the 99th postoperative day.

DISCUSSION

Dresler and co-workers reported an 18% 5-year survival in stage I LCNEC patients.[4] García-Yuste and associates reported 33% for the same population, and stage II and IIIA patients lived no longer than 18 months.[8] Takei and his co-workers reported the 5-year survival rate for stage I LCNEC patients was 67%. The prognosis of stage I patients with LCNEC was similar to that of stage I small cell carcinoma.[2] Zacharias et al. reviewed 15 LCNEC cases, and 3 patients with stage IIB and IIIA died of their disease within 3 months.[3] Although their 5-year survival rate for stage I patients was 88%, they reported that patients with more advanced disease had a dismal outcome. However, as their cases included large cell carcinoma with neuroendocrine morphology, their report differs from other LCNEC-only reports. LCNEC patient prognosis remains controversial. In the present case, a hilar lymph node was involved, and postoperative tumor recurrence was very aggressive, killing the patient in about 3 months.

There is no evidence that supports different effect of postoperative adjuvant therapy for LCNEC patients. Cooper and co-workers recommended lobectomy and lymph node dissection followed by adjuvant therapy.[7] Iyoda and associates studied 50 patients with LCNEC, 9 with large cell carcinoma with neuroendocrine differentiation, and 14 with large cell carcinoma with neuroendocrine mor-

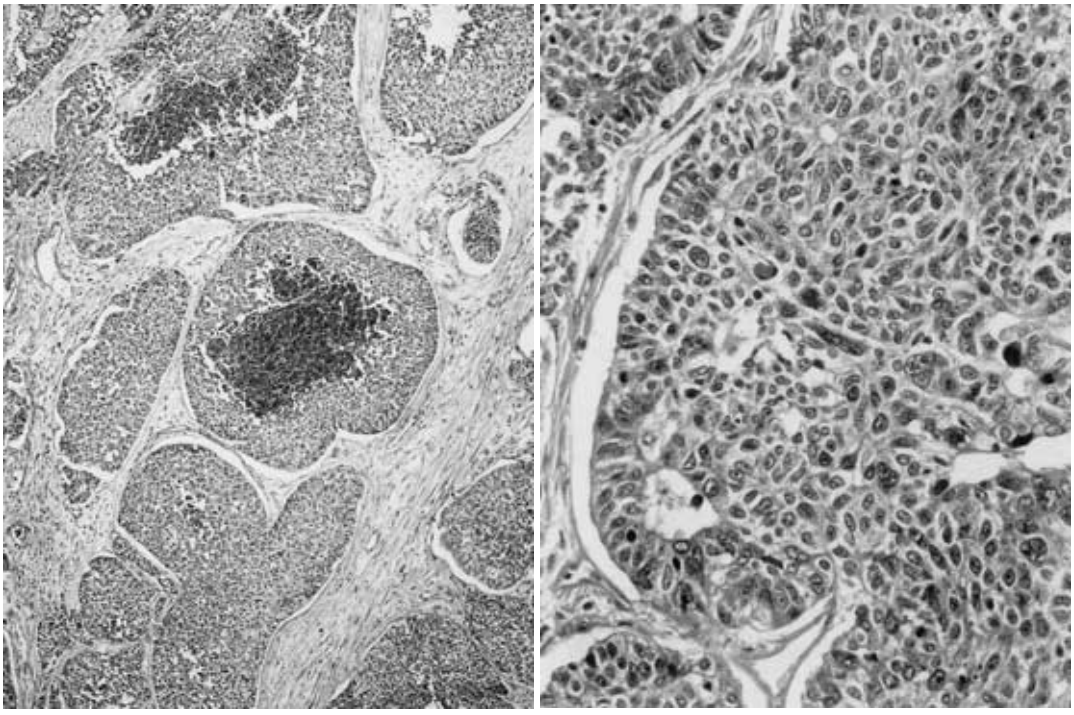

Figure 3. **A.** Low magnification view showing organoid pattern and central necrosis (Hematoxylin and eosin). **B.** High magnification view showing large tumor cells, palisading and rosette-like structures (Hematoxylin and eosin).

phology.[9] Eleven patients with LCNEC and 5 patients with large cell carcinoma with neuroendocrine morphology underwent adjuvant chemotherapy. They resulted in significantly higher overall survival than the remaining 57 patients who did not receive adjuvant chemotherapy.[9] However, as their study design was retrospective and the number of patients was small, adjuvant chemotherapy efficacy is still not proved. Mazières reported that in 10 LCNEC patients with metastasis receiving palliative platinum-etoposide chemotherapy the partial response rate was 20%.[10] Additional studies are necessary to determine the role of adjuvant treatment in LCNEC management.

Radiation is an effective modality in pulmonary small cell carcinoma management. However, there have been no reports describing radiotherapy efficacy in LCNEC patients. We used radiotherapy for the brain and sacroiliac joint metastases in the present case. Although sarcoiliac pain was alleviated, the metastatic lesions did not shrink.

In summary, we reported an aggressive progression case of pulmonary LCNEC. Prognosis and treatment efficacy in LCNEC patients remain controversial, and further investigation is needed.

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