

Double Primary Lung Carcinoma Consisting of Large Cell Neuroendocrine Carcinoma and Squamous Cell Carcinoma: Report of a Case

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We report a rare case of double primary lung carcinoma including large cell neuroendocrine carcinoma (LCNEC). A 67-year-old man underwent an annual medical checkup in 2000, pulmonary carcinoma was strongly suspected by sputum cytology and radiological images. Preoperative diagnosis was double primary lung carcinoma with a squamous cell carcinoma in the right lower lobe and non-small cell carcinoma in the right upper lobe. The histological carcinoma type in the right upper lobe could not be determined preoperatively. The patient underwent a right lower lobectomy and wedge resection of the right upper lobe. Histologically, the tumor in the right upper lobe was LCNEC and the tumor in the right lower lobe was a moderately differentiated squamous cell carcinoma. The patient had right supraclavicular lymph node metastases of LCNEC and died of multiple pulmonary metastases 10 months after the operation. (Ann Thorac Cardiovasc Surg 2005; 11: 397–400)

Key words: pulmonary, large cell neuroendocrine carcinoma, squamous cell carcinoma, double primary, synchronous, operation

Introduction

Pulmonary large cell neuroendocrine carcinoma (LCNEC) was proposed as a new category of pulmonary neuroendocrine tumors by Travis et al. in 1991.¹⁾ In 1999 the World Health Organization²⁾ classified LCNEC as a variant of large cell carcinoma. Iyoda et al.³⁾ analyzed that 50 of 119 large cell carcinoma cases were LCNEC, and he reported that LCNEC appear to be more clinically aggressive than classic large cell carcinomas. This tumor has been categorized as lying between atypical carcinoid and small cell lung carcinoma in terms of clinical aggressiveness. Although the clinical behavior of LCNEC has been studied, it has not been elucidated.

As we experienced a rare case of double primary lung

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carcinoma including LCNEC and squamous cell carcinoma, but not combined LCNEC, we reported this case with new evidence.

Case Report

A 67-year-old man underwent an annual medical checkup in 2000. Pulmonary carcinoma was strongly suspected by sputum cytology. He had smoked 15 cigarettes daily over 42 years. Serum laboratory data were within normal limits except for elevated SYFRA (8.1 ng/ml), and SCC (16 ng/ml). A respiratory function test revealed a slightly restrictive breathing disorder (FVC 2.18L, %FVC 66%, FEV1.0 1.93L, FEV1.0%, 88.5%). A roentgenogram of the chest and computed tomography (CT) (Fig. 1) revealed a tumor shadow, 40×22 mm in diameter, in the right upper lobe and another shadow, 63×22 mm in diameter in the right lower lobe with no enlargement of the mediastinal or hilar lymph nodes.

A transbronchial aspiration biopsy suggested a keratinizing squamous cell carcinoma in the segment 6 mass

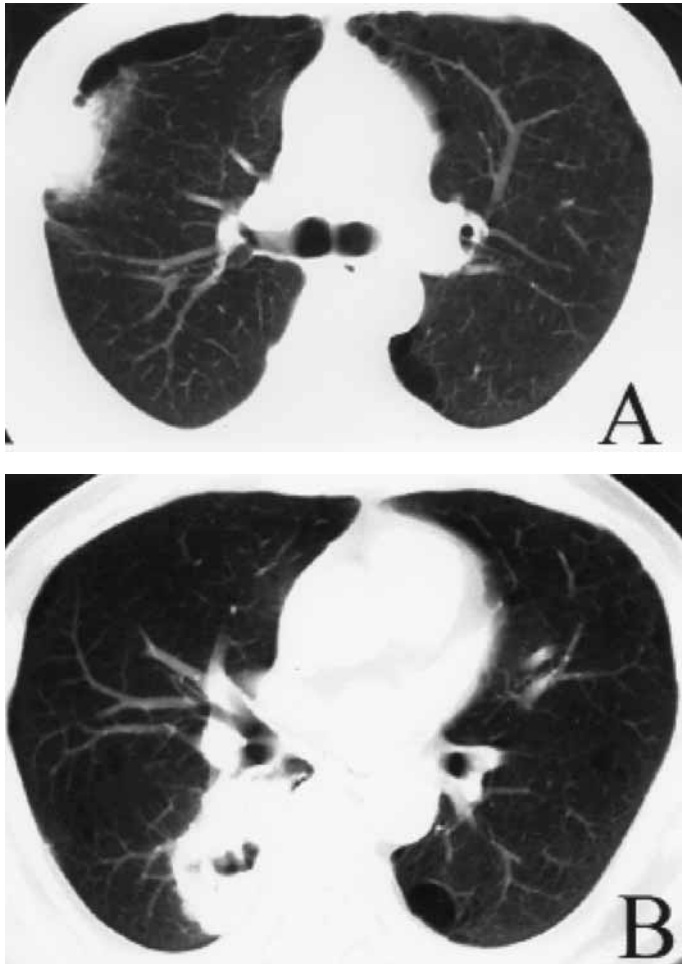


Fig. 1.

A: The chest CT showed a tumor shadow, 40×22 mm in diameter, in the peripheral segment 3 of the right lung, with irregular shape and unclear margin.

B: The chest CT showed a tumor shadow with cavity, 63×22 mm in diameter, in the peripheral segment 6 of the right lung, with irregular shape and unclear margin.

and non-small cell lung carcinoma in the segment 3 mass, whose histological type could not be determined cytologically. Abdominal ultrasonography, bone scintigraphy and magnetic resonance imaging of the brain revealed no evidence of distant metastasis. The patient was preoperatively diagnosed as having double primary lung carcinoma with clinical-T2N0M0 stage IB for segment 3 tumor and clinical-T2N0M0 stage IB for segment 6 tumor. A right lower lobectomy and a wedge resection of the right upper lobe were performed, because the patient's respiratory function was inefficient, a pneumonectomy was contraindicated, double lobectomies of the right upper lobe and the right lower lobe might lead to an instability of the middle lobe, and the segment 6 tumor was too close to the mediastinum to perform a wedge resection.

Seven months after the operation, the chest CT showed multiple pulmonary metastases in the rest of the right upper lobe, and metastases of right supraclavicular lymph nodes were detected. The aspiration cytology for the supraclavicular lymph node revealed the metastasis of

LCNEC. He died of recurrence of carcinoma 10 months after the operation.

Histopathological findings

There was no metastatic lymph node in dissected mediastinal and hilar lymph nodes. In segment 3 of the right upper lobe, a well defined tumor measuring 44×27×24 mm was compressing surrounding normal lung parenchyma and a giant bulla. Microscopically (Fig. 2), this tumor was diagnosed as LCNEC with pathological t2n0m0p1 stage IB. This tumor did not include the component of squamous cell carcinoma.

In segment 6 of the right lower lobe a well defined tumor measuring 47×45×26 mm was observed. Microscopically, this tumor was diagnosed as moderately differentiated squamous cell carcinoma (Fig. 2), with pathological-t4n0m0p1pm1-stage IIIB. This tumor did not include the tumor tissue of LCNEC. Therefore, we evaluated this patient as a rare case with double primary lung carcinomas with LCNEC and squamous

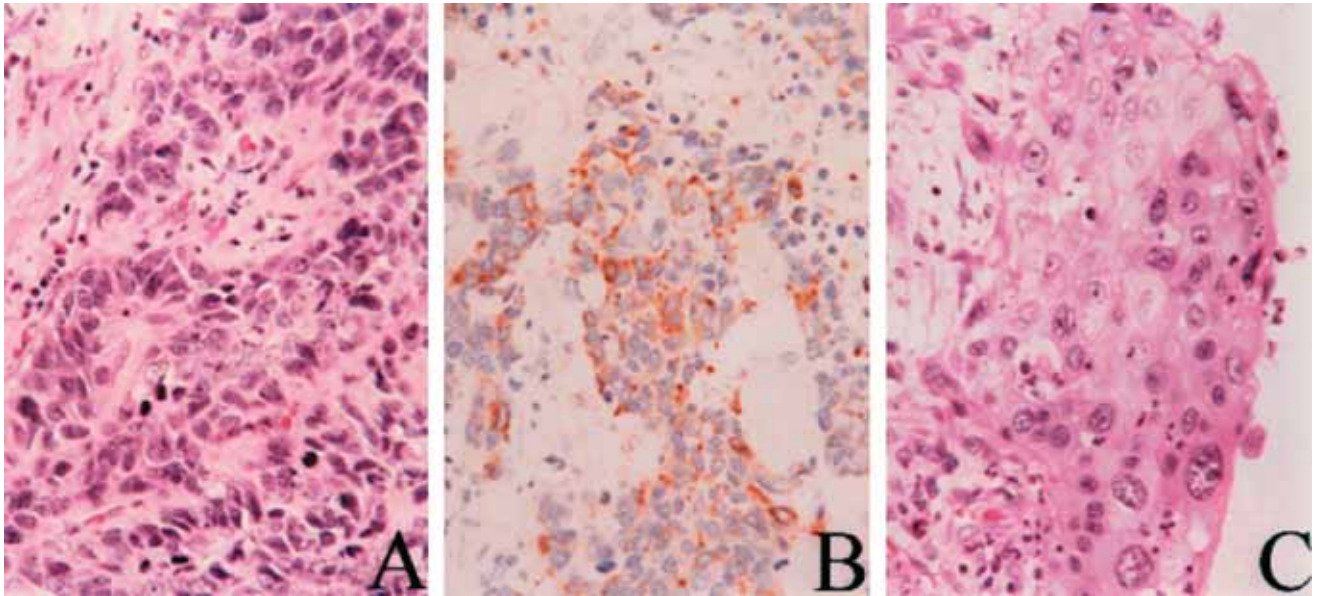


Fig. 2.

A: Large cell neuroendocrine carcinoma.

Microscopically, the individual tumor cells were polygonal to round and had a high N/C ratio and scant eosinophilic cytoplasm. The nuclei were vesicular and contained coarse granular chromatin with nucleoli. The tumor had a prominent organoid pattern and was composed of cell nests with peripheral palisading separated by fibrovascular septa. Rosette formation was seen. (HE stain, $\times 40$)

B: Large cell neuroendocrine carcinoma.

These tumor cells were strongly positive for chromogranin A. (Immunohistochemical stain, $\times 40$)

C: Squamous cell carcinoma.

The tumor cells were polygonal to round, exhibited hyperchromatic nuclei. Stratification, parakeratosis and intercellular bridges were seen in tumor tissue. The tumor tissue had vast necrosis. (HE stain, $\times 40$)

cell carcinoma.

Discussion

Deschamps et al.⁴⁾ reported 117 of 9,611 patients (1.2%) were diagnosed as multiple primary lung cancers including synchronous and metachronous. Most cases were related to squamous cell carcinoma or adenocarcinoma, and 6 cases (0.062%) to large cell carcinoma. Jiang et al.⁵⁾ described combined LCNEC with squamous cell carcinoma or adenocarcinoma in four of their 22 cases of LCNEC. However, this report was not of double primary lung carcinoma, but combined LCNEC. Niho et al.⁶⁾ described synchronous double primary lung cancer with neuroendocrine features, but this case was not based upon the criteria for LCNEC proposed by Travis et al.¹⁾ Therefore, reports on double primary pulmonary carcinomas with LCNEC and other histological types are very rare, and its clinical behavior or prognosis is not elucidated.

Iyoda et al.⁷⁾ reported that LCNEC has significantly

high proliferative activity than classic large cell carcinoma. Dresler et al.⁸⁾ revealed that the 5-year survival of the patients with LCNEC stage I was 18%, that the 5-year survival for all stages was 13%, and that LCNEC had a remarkably poor prognosis even in very early stage disease. Jiang et al.⁵⁾ showed that 5-year survival for patients with LCNEC was 44.8%. Iyoda et al.³⁾ reported that pulmonary large cell carcinoma with neuroendocrine features, including LCNEC, has a poorer prognosis than classic large cell carcinoma. In this case, he had recurrent LCNEC tumor 7 months after the operation, and died due to recurrent tumor 10 months. This case shows that LCNEC is aggressive and patients with LCNEC need to undergo complete resection of the tumor. There are few reports on the benefit of adjuvant chemotherapy for LCNEC, however, Iyoda et al.⁹⁾ reported that adjuvant chemotherapy prolongs survival of patients with LCNEC. Although we planned to perform adjuvant chemotherapy for this patient, we could not do because the condition of the patient got worse due to recurrent tumors. We expect further discussion on this topic to proliferate.

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