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**Case report**

# Long-term Survival of a Patient with Typical Lung Carcinoid Tumor and Supraclavicular Lymph Node Metastasis Treated by Surgical Resection

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**Abstract**: Herein we report on the long-term survival of a surgical case of typical carcinoid tumor and supraclavicular lymph node metastasis at initial diagnosis. The present study is a follow-up to a previously published case report. Initially, a 73-year-old man was admitted to hospital for evaluation of an enlarged lymph node in his right supraclavicular fossa. Serum progastrin-releasing peptide (ProGRP) concentrations were markedly elevated, and carcinoid was diagnosed by histopathological examination of the excised supraclavicular lymph node. The patient underwent right upper lobectomy and mediastinal lymph node dissection via median sternotomy. The final diagnosis was Stage ⅢB (pT1aN3M0) typical carcinoid. Serum ProGRP concentrations decreased to within the normal range, and follow-up computed tomography, performed approximately 10 years after surgery, showed no recurrence. For this patient, radical resection of metastatic lymph nodes was an effective treatment for his typical lung carcinoid.

**Key words**: typical lung carcinoid, stage ⅢB, surgery, progastrin-releasing peptide (ProGRP), ossification

## Introduction

Carcinoid tumors are neuroendocrine tumors that arise from Kulchitsky cells. Pulmonary carcinoid tumors represent 1%−2% of all lung neoplasms[1]. Although it is well known that surgical cases of typical lung carcinoid have a good prognosis, the efficacy of surgical resection for Stage ⅢB carcinoid is unclear. Herein we report on the long-term survival of a surgical case of typical carcinoid accompanied by supraclavicular lymph node metastasis at initial diagnosis. The present report is a follow-up to a previously published case report[2].

## Case report

A 73-year-old man was admitted to Showa University Northern Yokohama Hospital for evaluation of enlarged lymph nodes in his right supraclavicular fossa and mediastinum in April 2006.

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He was asymptomatic and underwent computed tomography (CT) for postoperative surveillance of early gastric cancer.

Upon physical examination at the time of admission, the patient's temperature was 36.3°C, height 161 cm, and body weight 64 kg. His pulse rate was normal, heart rhythm regular, and heart sounds were clear. The patient's blood pressure was 130/80 mmHg. Blood chemistry revealed elevated serum pro-gastrin releasing peptide (ProGRP; 627.7 pg/ml) concentrations. Other tumor markers (neuron-specific enolase, carcinoembryonic antigen, squamous cell carcinoma antigen, cancer antigen 19-9, soluble interleukin-2 receptor) and renal functions tests were within normal limits.

Chest radiography revealed a 1 cm undefined pulmonary nodule in the right upper lung field. Chest CT revealed enlarged lymph nodes in the right supraclavicular fossa and superior mediastinum, and a small ossified nodule in the right upper pulmonary lobe (Fig. 1). There were no abnormal findings in the thymus. Positron emission tomography (PET) /CT revealed abnormal accumulation of 18-fluorodeoxyglucose ($^{18}$F-FDG) in the supraclavicular and mediastinal lymph nodes (maximum standardized uptake value [$SUV_{max}$] 17.0) and in the lung nodule in the right upper lung ($SUV_{max}$ 3.4). Brain magnetic resonance imaging (MRI), bronchoscopy, and abdominal/pelvic CT were normal.

Small cell lung cancer was suspected because of the elevated ProGRP concentrations, and the patient underwent excisional biopsy of a 3-cm supraclavicular lymph node. The histopathological findings were consistent with carcinoid tumor. After excision of the supraclavicular lymph node, serum ProGRP concentrations decreased to 363.0 pg/ml. Because of the decreased ProGRP concentration, insufficient therapeutic efficacy of chemotherapy and radiotherapy, and the rarity of distant metastases from typical carcinoid tumors, the patient underwent surgery 2 months after his initial evaluation. Dissection of the mediastinal lymph nodes and partial resection of the nodule in the right upper pulmonary lobe were performed via median sternotomy, followed by right upper lobectomy after pathological confirmation of lung carcinoid from a frozen section of the lung nodule.

Microscopically, the tumor consisted of uniformly round to polygonal cells with small oval nuclei containing finely granular chromatin. The cells were arranged in small nest shapes resembling rosettes or ribbons, and were separated by connective tissue with marked ossification. Necrosis was absent, and mitotic figures were infrequent, with less than two per 10 high-power fields (HPFs; Fig. 2). Immunohistochemistry of tumor cells revealed positive chromogranin A, synaptophysin, CD-56, and ProGRP expression. The mediastinal lymph nodes were positive for metastases, but the hilar lymph node was negative. The final diagnosis was Stage IIIB (pT1aN3M0) typical carcinoid.

The patient's serum ProGRP concentrations decreased to within the normal range after surgery and his postoperative course was uneventful. He did not receive any adjuvant therapy. Whole-body CT, brain MRI, and blood examination, including ProGRP, was performed every 6 months for postoperative surveillance. Nine years after surgery, whole-body CT and brain MRI reveal no evidence of recurrence.

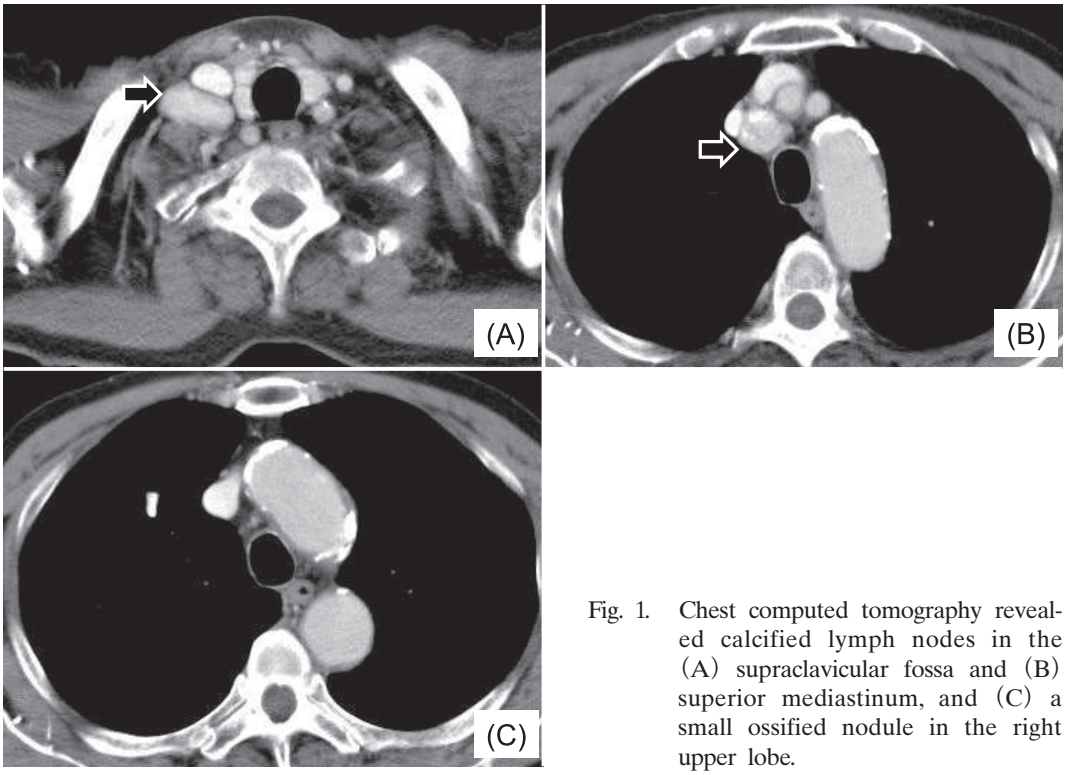


Fig. 1. Chest computed tomography revealed calcified lymph nodes in the (A) supraclavicular fossa and (B) superior mediastinum, and (C) a small ossified nodule in the right upper lobe.

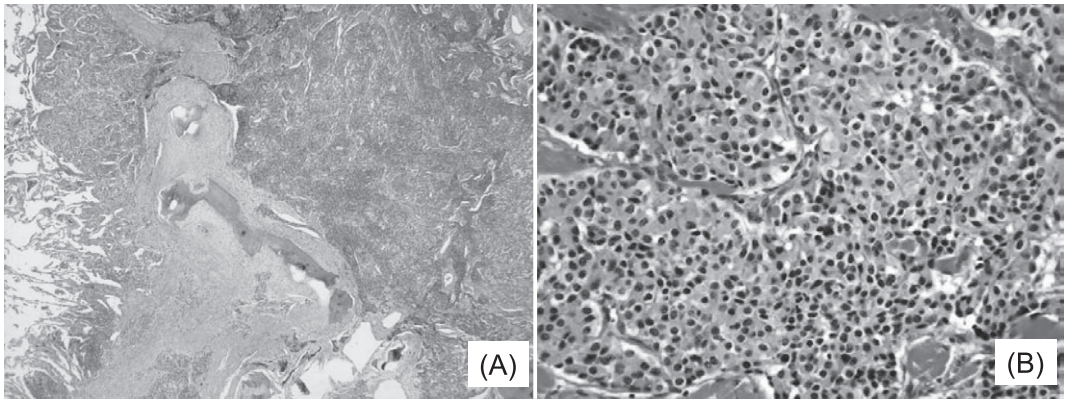


Fig. 2. Histopathological findings of the lung tumor. (A) Developing bone is seen adjacent to the tumor (hematoxylin and eosin staining; original manifestation ×40). (B) Tumor cells are uniform with round nuclei. Neuroendocrine morphology is obvious; cellular atypia and mitotic figures are rare (hematoxylin and eosin staining; original manifestation ×400).

## Discussion

Carcinoid tumors have been classified as typical or atypical according to the degree of malignant histological features[3, 4]. Microscopically, typical carcinoids manifest infrequent mitotic figures, with less than two per 10 HPFs, and there is no evidence of necrosis[3]. Current World Health Organization classification describes neuroendocrine tumors with fewer than two mitotic

figures per 10 HPFs and without necrosis as typical carcinoid tumors (low grade), tumors with between two and 10 mitotic features per 10 HPFs and/or with necrotic foci as atypical carcinoid tumors (intermediate grade), and tumors with more than 10 mitotic figures per 10 HPFs as large cell and small cell neuroendocrine carcinoma (high grade)[4]. The ossified lung tumor and mediastinal lymph nodes in the present case exhibited the pathological findings of typical carcinoid tumor.

Carcinoid tumors sometimes show histological findings of calcification or ossification, however the degree is insufficient to allow radiological visualization[5]. Although some cases of lung carcinoid with radiological findings of calcification have been reported[6–9], the radiological finding of prominent ossification, as found in this patient, is extremely rare. We thought that this lung nodule was benign until PET/CT revealed increased accumulation of $^{18}$F-FDG in the lesion.

The PET/CT findings of $SUV_{max}$ values of 17.0 and 3.4 in the supraclavicular and mediastinal lymph nodes and lung nodule, respectively, were very useful in the present case. However, $^{18}$F-FDG PET imaging is generally not useful for differentiating carcinoid tumors from benign nodules because carcinoid tumors do not show increased metabolic activity on the images[10, 11]. An initial report by Erasmus *et al*[10] on $^{18}$F-FDG PET imaging of seven carcinoid tumors showed that carcinoid tumors have low standardized uptake values, ranging from 1.6 to 2.4. Although the reason for the increased metabolic activity of the lung nodule in the present patient is unclear, the advanced tumor stage (IIIB) and elevated ProGRP expression may be involved factors.

ProGRP is a gut hormone that was originally isolated from porcine stomach and is widely expressed throughout the gastrointestinal and pulmonary tracts and mammalian nervous system[12]. Although ProGRP is a well-known biomarker of small cell lung cancer, increases in serum ProGRP concentrations in patients with carcinoid tumor are rare[13, 14]. In the present patient, the elevated serum ProGRP concentration decreased to within normal limits after surgery, and immunochemical analysis revealed that tumor cells were positive for ProGRP expression.

The most effective treatment for pulmonary carcinoid tumors is surgical resection for localized disease; chemotherapy and radiotherapy are thought not to be useful for patients with unresectable lung carcinoid tumors[1]. Although the present patient had a metastatic supraclavicular lymph node, which is not generally considered localized disease and for which surgical resection is not usually indicated, radical resection that included the supraclavicular node resulted in a good clinical outcome. Although lymph node metastases of typical lung carcinoids are rare, Martini *et al*[15] reported that the 5-year disease-free survival rate of 12 patients with typical carcinoids and metastatic with lymph nodes (N1 or N2) was 100%; recurrence was reported in only one patient after 8 years.

We could not find any other reports of patients with typical lung carcinoid and metastatic supraclavicular lymph node at the initial diagnosis, but we assumed that radical resection of metastatic lymph nodes may be an effective treatment for typical lung carcinoid.

In conclusion, herein we report on the long-term survival of a surgical case of typical carcinoid lung tumor and supraclavicular lymph node metastasis at initial diagnosis. For our patient, radical resection of metastatic lymph nodes was an effective treatment for his typical lung carcinoid.

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**Conflict of interest disclosure**

The authors declare they have no conflict of interest.

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