Combined Atypical Carcinoid Tumour and Squamous Cell Carcinoma of the Lung

Mikio Okazaki¹, Yoshifumi Sano¹, Yoshiko Soga², Hitoshi Katayama³, Nobuhiko Sakao¹, Yoshinobu Shikatani¹, Syungo Yukumi³, Hisayuki Shigematsu¹, Atsuro Sugita² and Hironori Izutani¹

Abstract

A 71-year-old man diagnosed with lung cancer in the right lower lobe with invasion to the middle lobe underwent right lower and middle lobectomy with mediastinal lymph node dissection. The cancer was pathologically diagnosed as stage IIB (pT3N0M0) with combined squamous cell carcinoma and an atypical carcinoid tumour. To the best of our knowledge, this is the first report of a combined atypical carcinoid tumour and non-small cell lung cancer. This case further expands the histological spectrum of combined neuroendocrine tumours.

Key words: lung cancer, neuroendocrine tumour, atypical carcinoid tumour, combined tumour

(DOI: 10.2169/internalmedicine.54.3846)

Introduction

Neuroendocrine tumours of the lung are classified into typical and atypical carcinoid tumours, large cell neuroendocrine carcinoma and small cell carcinoma (1). Cases of large cell neuroendocrine carcinoma and small cell carcinoma have been described in combination with non-small cell carcinoma (NSCLC) (2-4). Nicholson et al. reported that a high percentage of resected small cell carcinomas (28%) are found in combination with NSCLC (5). In addition, there have been reports of large cell neuroendocrine carcinoma in combination with adenocarcinoma, squamous cell carcinoma and spindle cell carcinoma (4, 6, 7). In contrast, to date, only two cases of combined lung tumours containing NSCLC and carcinoid tumours have been documented (8, 9). We herein report the clinical and pathological findings of a case of a combined atypical carcinoid tumour and squamous cell carcinoma of the lung. To the best of our knowledge, this is first report of a combined lung tumour containing NSCLC and an atypical carcinoid tumour. This case further expands the histological spectrum of combined lung tumours.

Case Report

A 71-year-old man presented for an examination after an abnormal lung shadow was detected during a population-based radiological screening assessment. The patient was a former smoker with a 75 pack-year history. The serum levels of carcinoembryonic antigen and cytokeratin 19 fragment were 10.0 ng/mL and 4.4 ng/mL, respectively; other tumour markers were within the normal limits. Chest computed tomography (CT) revealed a mass with tumour necrosis and obstructive pneumonia, measuring 70×45 mm, in the right lower lobe (Fig. 1). Cerebral magnetic resonance imaging (MRI) showed no brain metastasis. In addition, positron emission tomography (PET) revealed a mass with tumour necrosis and obstructive pneumonia, measuring 70×45 mm, in the right lower lobe (Fig. 1). Cerebral magnetic resonance imaging (MRI) showed no brain metastasis. In addition, positron emission tomography demonstrated negative uptake in the tumour [standardized uptake value (SUV) max =13.9], lymph nodes and other remote sites, and bronchoscopy disclosed stenosis of the right B7 and B8 bronchus. Biopsy specimens of the lesion exhibited squamous cell carcinoma

¹Center of Chest Medicine and Surgery, Ehime University, Japan, ²Pathology Division, Ehime University, Japan, ³Department of Cardiology, Pulmonology, Hypertension & Nephrology, Ehime University, Japan and ¹Department of Surgery, National Hospital Organization Ehime Medical Center, Japan

Received for publication August 8, 2014; Accepted for publication October 8, 2014

Correspondence to Dr. Mikio Okazaki, mikio.ok@io.ocn.ne.jp
of pathological stage pT3N0M0, stage IIB, and the patient underwent right lower and middle lobectomy with mediastinal lymph node resection.

A pathological examination of the resected specimen showed a biphasic tumour morphology (Fig. 2A). One component was squamous cell carcinoma of predominantly non-keratinizing cells (Fig. 2B), while the other comprised trabecular and organoid nests containing a small amount of fibrovascular stroma with regular compact cells exhibiting round nuclei that were smaller than those observed in the squamous cell carcinoma component (Fig. 2C). These cellular and structural characteristics were suggestive of neuroendocrine features, which was immunohistochemically confirmed with anti-chromogranin A and anti-synaptophysin antibodies (Fig. 3). The neuroendocrine tumour cells contained necrosis and <10 mitoses/10 high power fields. Overall, the non-squamous area was interpreted to be an atypical carcinoid tumour. The histological results confirmed the diagnosis of a combined atypical carcinoid tumour and squamous cell carcinoma of the lung. Both components were observed in the same field (Fig. 2A).

The patient was subsequently treated with postoperative adjuvant chemotherapy comprising four cycles of oral fluoropyrimidine S-1 plus carboplatin followed by S-1 maintenance. One month after the S-1 maintenance therapy (nine months after the surgery), the patient developed a headache, and brain MRI showed a metastatic lesion. Although he received treatment with gamma knife radiosurgery and four cycles of docetaxel chemotherapy, CT and MRI revealed disease progression in the brain and left adrenal gland. He subsequently underwent whole brain radiation therapy for brain metastasis and radiation therapy for adrenal metastasis; however, both areas of metastasis increased in size. The patient ultimately died of pneumonia 21 months after surgery.

Discussion

Carcinoid tumours rarely present in combination with NSCLC; however, typical carcinoid tumours have been reported to occur in combination with NSCLC. Owens et al. described a case of a combined lung tumour containing squamous cell carcinoma and a typical carcinoid tumour (8), while Sen et al. documented a combined lung tumour comprised of adenocarcinoma and a typical carcinoid tumour (9). Moreover, a case of a laryngeal composite tumour consisting of squamous cell carcinoma combined with an atypical carcinoid tumour has also been reported (10). However, to the best of our knowledge, this is the first report of a combined lung tumour containing NSCLC and an atypical carcinoid tumour.

Pulmonary carcinoid tumours are neuroendocrine malignant lesions that account for 1-2% of all lung tumours (11, 12). According to histopathological criteria, carcinoid tumours can be divided into low-grade malignant typical carcinoid and intermediate malignant atypical carcinoid tumours. The distinction between typical and atypical carcinoid tumours is clinically important, being based on the number of mitoses, the best predictor of the prognosis (13). The presence of necrosis also distinguishes atypical from typical carcinoid tumours. Patients with atypical carcinoid tumours have a significantly reduced 5-year survival (61-88%) rate compared to those with typical carcinoid tumours (92-100%) (11, 13, 14), and lymph node metastasis is present in 35-64% and only 4-14% of patients with atypical and typical carcinoid tumours, respectively.

Combined lung tumours containing NSCLC and carcinoid tumours are very rare, and their prognosis is unclear. The present case was relatively aggressive and resistant to both chemotherapy and radiotherapy. Other problems associated with combined tumours are how to administer adjuvant chemotherapy after surgery and which treatments should be selected for recurrence and metastasis. Intermediate-grade atypical carcinoid tumours are less aggressive than squamous cell carcinoma. However, carcinoid tumours are relatively resistant to chemotherapy and radiation therapy (14), and there is no proven optimal therapy for metastatic unresectable carcinoid tumours. The present patient was treated with postoperative adjuvant chemotherapy using S-1 plus carboplatin, as the squamous cell carcinoma component was considered to be the target of the adjuvant therapy. Although the more aggressive components may be susceptible to recurrence and metastasis and the target of treatment is usually determined based on this criterion, it is challenging to specifically identify which component is actually responsible for inducing recurrence, metastasis or both. Sen et al. reported a case of a combined typical carcinoid tumour and adenocarcinoma with hilar lymph node metastasis comprised of only an adenocarcinoma component (9). In the current case, it is unclear which component caused the brain and adrenal metastases, because a biopsy of the metastatic lesions was not performed and the patient’s family did not give permission for an autopsy. However, the rapid disease progression suggests that the squamous cell carcinoma component contributed to the metastasis.
In summary, we herein reported a case of a combined atypical carcinoid tumour and squamous cell carcinoma of the lung. This case does not fit the International Multidisciplinary Classification of Lung Adenocarcinoma; therefore, we must clinically consider various mixed histological patterns and attempt to place the lesion within a spectrum of combined neuroendocrine tumours of the lung.

The authors state that they have no Conflict of Interest (COI).
References


