Three Cases of Resected Pleomorphic Carcinoma

Ryutaro Kikuchi, MD,1 Noritaka Isowa, MD,1 Hirokazu Tokuyasu, MD,2 Yuji Kawasaki, MD,2 Hideyuki Onuma, MD,3 and Hiroshi Miura, MD3

Pleomorphic carcinoma (PC) is a rare malignancy of the lung. We present 3 cases that were resected. Case 1: The patient was a 75-year-old asymptomatic man whose chest roentgenogram showed a cavity at the right apex. A right upper lobectomy was performed, and the pathological stage was IB (pT2N0M0). After 3 courses of adjuvant chemotherapy, he is alive without relapse 56 months after the operation. Case 2: The patient was a 60-year-old man with left high back pain whose chest roentgenogram showed a mass shadow in the left upper lung field. A left upper lobectomy with partial resection of S6 was performed after induction chemotherapy. The pathological stage was IIIA (pT2N2M0). He died of infection 4 months after the operation during adjuvant chemotherapy. Case 3: A 78-year-old man with hemoptysis underwent aortic arch replacement after a diagnosis of impending rupture of an aortic aneurysm. During the operation, a tumor in the left upper lung lobe was detected. A left upper division segmentectomy was performed one month later. The pathological stage was IIB (pT3N0M0). Despite adjuvant radiotherapy, the patient died of cancer 9 months after the segmentectomy. The final pathological diagnoses for all 3 cases were PC. More cases of PC should be reported to establish optimal management. (Ann Thorac Cardiovasc Surg 2010; 16: 264–269)

Introduction

Pleomorphic carcinoma (PC) was introduced into the third edition of the World Health Organization classifications.1 PC is grouped under the category of carcinomas with pleomorphic, sarcomatoid, or sarcomatous elements. It is defined as a poorly differentiated nonsmall cell lung cancer (NSCLC) with at least 10% giant and/or spindle cell components or a carcinoma comprised entirely of giant and spindle cells. PCs are rare and account for only 0.1–1.0% of all primary lung cancers,2–4 and the reporting of more cases is needed to establish optimal management. Herein we describe 3 cases of PC.

Case 1

A 75-year-old man presented to our hospital with clinical suspicion of sleep apnea syndrome in September 2003. Because his screening chest roentgenogram showed an abnormal shadow, he was admitted to our hospital for further examination. He had a 19 pack-year history of smoking, but had not smoked in 25 years. On a chest X-ray film, a nodular shadow was found in the apex of the right lung (Fig. 1 (a)). A computed tomography (CT) scan revealed that the lesion was a thin-walled cavity rather than a nodule (Fig. 1 (b)). Serum levels of carcinoembryonic antigen (CEA), cytokeratin 19 fragment (CYFRA 21-1), and progastrin-releasing peptide (ProGRP) were normal. A 24-hour creatinine clearance decreased to 45.8 ml/min, but other laboratory results were within normal limits. Neither a transbronchial biopsy with flexible bronchoscopy nor a CT-guided percutaneous needle biopsy provided a histological diagnosis.

A CT scan 2 months later revealed a reenlargement of the right cavitory lesion. Thus video-assisted thoracoscopic surgery was performed in November 2003. A frozen section of the cavitory lesion showed undifferentiated NSCLC
Three Cases of Resected Pleomorphic Carcinoma

containing adenocarcinomatous components. A right upper lobectomy and a radical lymph node dissection were performed.

Macroscopically, the tumor was gray-white, 3.5 × 3 × 2 cm in size, with a slight pleural indentation and cavitary formation resulting from central necrosis (Fig. 2 (a)). Microscopically, large, spindle-shaped atypical cells had proliferated sarcomatously into most portions of the tumor, and in some parts there were transitions to adenocarcinoma and squamous cell carcinoma (Fig. 2 (b)). Invasions to lymphatic and blood vessels and to visceral pleura were apparent.

The final pathological diagnosis was PC with a staging of IB (pT2N0M0). After 3 courses of adjuvant chemotherapy, he is alive without relapse 56 months after the operation.

Fig. 1. (a) A chest roentgenogram showed a nodular shadow in the apex of the right lung (arrows). (b) Computed tomography showed a thin-wall cavitary lesion at the apex of the right lung.

Fig. 2. (a) A gray-white tumor with slight pleural indentation and cavitary formation resulting from central necrosis was seen. (b) Large, spindle-shaped atypical cells proliferated sarcomatously into most portions of the tumor (hematoxylin and eosin stain, x1000).
Case 2

A 60-year-old man presented to our hospital in July 2004 with complaints of a gradually worsening left high back pain. A chest roentgenogram showed a mass shadow in the left upper lung field (Fig. 3 (a)). He had a 40 pack-year history of smoking, but had not smoked in 3 years. His physical examination was normal. A chest CT scan showed an irregularly enhanced mass straddling S1+2c and S6 of the left lung with bilateral mediastinal lymph node swelling (Fig. 3 (b)). Serum levels of carcinoembryonic antigen (CEA) and CYFRA 21-1 were slightly elevated (CEA = 6.1 ng/ml; CYFRA 21-1 = 9.3 ng/ml).

A CT-guided transthoracic needle biopsy revealed a poorly differentiated NSCLC. Clinical staging was IIIB (cT2N3M0), and systemic chemotherapy was initiated with carboplatin and paclitaxel. After 2 courses of chemotherapy, the tumor stage went down to IIIA (ycT2N2M0), diagnosed by 201Tl scintigraphy and CT scan (Fig. 4). A left upper lobectomy with partial resection of S6 was performed in October 2004. Unfortunately, complete resection was not achieved because of direct invasion of lymph node metastases to surrounding structures, and there were macroscopically residual diseases at sites #4L and #5.

Macroscopically, the tumor was located in S1+2c with pleural indentation, 5 × 4.5 × 3 cm in size. Microscopically, it comprised 50% spindle cells, 30% giant cells, and 20% squamous cells. The final diagnosis was PC (Fig. 5).

Although nearly half of the primary tumor was necrotic as a result of prior chemotherapy, a nest of residual viable tumor cells was observed in the #5 lymph node. Invasions to lymphatic and blood vessels and to visceral pleura were also apparent. The pathological stage was IIIA (pT2N2M0). After postoperative concurrent chemoradiotherapy with carboplatin and paclitaxel for the mediastinum, he underwent 1 course of systemic chemotherapy with gemcitabine and docetaxel.

Grade III pancytopenia occurred as an adverse effect, which resulted in left lobar MRSA pneumonia. Left MRSA empyema and right MRSA pneumonia followed, and the patient died 4 months after the operation.

Case 3

A 78-year-old man arrived at our hospital with complaints of hemoptysis in November 2004. Following a diagnosis of impending rupture of an aortic aneurysm, he underwent an aortic arch replacement. After the operation, a tumor in the left upper lobe was detected (Figs. 6 (a) and 6 (b)). He underwent a left thoracotomy for treatment and diagnosis of the tumor in December 2004. An intraoperative frozen section showed a malignant spindle cell tumor.

The lingular bronchus branched from the lower lobe bronchus, and the lingular segment and the left lower
Three Cases of Resected Pleomorphic Carcinoma

Fig. 4. Computed tomography after induction chemotherapy showed shrinkage of the tumor and mediastinal lymph nodes (arrows).

Fig. 5. (a) Nearly half of the tumor was necrotic because of prior chemotherapy. (b) The tumor comprised spindle, giant, and squamous cells (hematoxylin and eosin stain, x1000).

Fig. 6. (a) A chest roentgenogram showed an abnormal mass abutting the aortic arch. (b) A contrast-enhanced CT scan showed strong enhancement in the posterior aspect of the tumor.
lobe were unified completely. A segmentectomy of the upper division was more anatomically rational than an upper lobectomy in this case, and no metastases were found in the frozen section of #12u lymph nodes; therefore we performed a segmentectomy of the upper division. The tumor was macroscopically located in S1+2a, 4.5 × 3.7 × 2.5 cm in size. Microscopically, most of it consisted of keratin-positive spindle cells. Some were multinucleated, and some had nucleoli. Adenocarcinoma and squamous cell components were also present, which fulfilled the diagnostic criteria for PC (Fig. 7). The mediastinal margin was microscopically positive.

The final pathological stage was IIB (pT3N0M0). In spite of postoperative radiation to the mediastinal residual disease, he died of recurrence 9 months after the pulmonary resection.

**Discussion**

To date, only a few serial case reports for PC have been published.3-7) Hemostomum, cough, chest pain, and fever were common clinical symptoms.3,7) Polypoid endobronchial extension was sometimes present.3,5,6) Mean age at diagnosis was 60-65 years, and the male-to-female ratio was 2-10:1. Sixty to ninety percent of patients were smokers, suggesting a strong correlation with smoking.3,7) Radiologically, most lesions were peripheral large masses.3,4,7) Lesions with the longest diameter, >5 cm, often showed central low attenuation areas and myxoid degeneration, and also substantial enhancements at the tumor periphery on contrasted CT scans. The central low attenuation areas corresponded to regions of hemorrhage or necrosis.7) Cavitary lesions resulting from central necrosis were also frequently seen.6) PCs have a tendency to grow rapidly and to invade adjacent structures in the early stage.3,6,7)

The prognosis for PC is poor.3,7) The median survival time is 8 months according to Fishback et al.,3) and 19 months according to Rossi et al.6) Chang et al. reported that 7 patients who had undergone surgical resections succumbed to metastases within a few months. They occurred in bone and organs, including brain and adrenal gland, and in unusual sites, such as esophagus, jejunum, rectum, and kidney. There were also 9 inoperable cases that were treated by chemoradiotherapy with little effect; median survival time was only 3 months.6) Kim et al. also reported that 6 of 10 resected cases died within 5 months after surgery.7)

To date, no chemotherapeutic regimens for PC have been established, and conventional radiation therapy has had little effect on pleomorphic carcinoma. Therefore complete resection in the early stages is necessary to achieve a good prognosis. However, PC has a tendency to invade
adjacent structures early in the disease, so a complete resection is frequently impossible. Early recurrences are also seen, and it is important to develop an effective adjuvant treatment modality to improve the prognosis for PC.

In our cases, the patients were former or current male smokers. Chest pain was seen in case 2 and hemoptysis in case 3. Large mass lesions invading adjacent structures were observed in cases 2 and 3, and a cavitary lesion resulting from central necrosis was seen in case 1. Long-term survival was obtained for only case 1 after a complete resection. All these findings are concordant with previous reports.3-7)

In conclusion, pleomorphic carcinoma is a rare lung neoplasm that has a poorer prognosis than other nonsmall cell lung cancers. Further investigation with a larger number of cases is needed to establish effective treatment strategies.

References