Clinicopathological investigation of pulmonary pleomorphic carcinoma

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Abstract

**Background:** Pleomorphic carcinoma is an uncommon malignant tumor of the lung. As there are few large-scale studies of patients with pleomorphic carcinoma, the clinical characteristics and behavior of the disease have been unclear until now. In this study, we investigated the clinicopathological findings and prognosis of 21 patients with pleomorphic carcinoma.

**Patients and methods:** We identified 930 cases of pulmonary carcinoma in which the patient underwent a lung resection in our institute between January 1999 and June 2007. Of those patients, 21 (2.6%) were diagnosed with pleomorphic carcinoma as determined by the three pathologists in our institute.

**Results:** The 21 study subjects consisted of 18 male and 3 female patients. The locations of the lesions were as follows: 13 cases, right upper lobe; 5 cases, left upper lobe; 2 cases, right lower lobe; and 1 case, left lower lobe. The mean diameter of the tumor in this series was 55.2 mm (17—100 mm). As for the pathological stage, four cases were stage IA, seven cases were stage IB, five cases were stage IIB, two cases were stage IIIA, and three cases were stage IIIB. The overall 5-year survival rate was 80.0%. There were no significant differences between the symptomatic group and the asymptomatic group, or between the p-factor positive group and the p-factor negative group. On the other hand, there was a significant difference in the disease-free survival rate between the node negative group and the node positive group, and there was also a significant difference in the overall survival rate between the curative operation group and the non-curative operation group.

**Conclusions:** In this clinical study, the presence of lymph node metastasis and the treatment by a curative resection of the tumor were the most important prognostic factors for pulmonary pleomorphic carcinoma. However, further investigation of a large number of cases is needed in order to gain a clearer understanding of the clinical characteristics and behavior of pleomorphic carcinoma.

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1. Introduction

A pleomorphic carcinoma is a rare pulmonary epithelial malignant tumor. The clinical characteristics and the behavior of this tumor have been unclear until recently as there are few studies which involve more than a small series of patients with pulmonary pleomorphic carcinoma [1]. The purpose of this study is to better understand the clinical behavior and the pathological characteristics of this histotype of pulmonary carcinoma.

2. Patients and methods

We identified 930 cases of pulmonary carcinoma involving patients who had undergone a lung resection at our institute from January 1999 to June 2007. Of those patients, 21 cases (2.6%) were diagnosed to have a pleomorphic carcinoma by the three expert pathologists in our institute.

In this study, the patients were operated upon (at least lobectomy) with systemic lymph node dissection except for one case (No. 19) who had right upper wedge resection with systemic nodal sampling (Table 1). We detected mediastinal lymph node swelling by CT scan; there were no patients who had preoperative mediastinoscopy.

A diagnosis was obtained based on the light microscopic findings and it was confirmed based on immunohistochemical examinations. Each case met the WHO criteria [2]. Cases were classified as spindle cell carcinoma if at least 10% of the tumor was composed of fusiform malignant cells.
Immunohistochemical procedures were performed by using antibodies against cytokeratin and vimentin.

We used the Kaplan—Meier method to generate the survival curves, and the proportional hazards model, Cox regression for inspection of significance.

3. Results

The 21 study subjects included 18 male and 3 female patients (Table 1). The mean age was 65 years (range 44–81 years). Fourteen of the patients were asymptomatic. Of the seven symptomatic patients, four had hemoptysis, two had coughs, and one had fatigue. Nineteen of the patients were smokers. The locations of the lesions were as follows: 18 cases were in the upper lobe, with 13 on the right side and 5 on the left side; 2 cases were in the right lower lobe; and 1 case was in the left lower lobe. The mean diameter of the tumor was 55.2 mm (17–100 mm). Regarding the pathological staging of the tumors, four cases were stage IA, seven cases were stage IB, five cases were stage IIB, two cases were stage IIIA, and three cases were stage IIIB. The overall 5-year survival rate was 80.0% (Fig. 1) and the disease-free survival rate was 63.3% (Fig. 2). Patient No. 1 and 3 with malignant cell invasion to the multiple mediastinal lymph node stations died of recurrent cancer. Patient No. 4 died of pyothorax after an operation (Table 1). In the surviving group, patient No. 7 and 11 had lung metastasis. Patient No. 11 had a segmental lymph node invasion. There were no significant differences between the symptomatic group and the asymptomatic group (Fig. 3). Regarding the pathological pleural invasion factor (p-factor), there was a tendency for a poor rate of survival in the p-factor positive group as compared with the p-factor negative group. Otherwise, there was no significant difference between the p-factor positive group and the p-factor negative group (Fig. 4). On the other hand, there was a significant difference in the disease-free survival rate between the node positive group and the node negative group.
negative group (Fig. 5). We considered the lung resection with systemic lymph node dissection for T4 lung tumor as a non-curative operation. There was a significant difference in the overall survival rate between the curative operation group and the non-curative operation group (Fig. 6).

4. Discussion

Pleomorphic carcinoma has been recognized to be a neoplasm in the category of ‘carcinoma with a pleomorphic, sarcomatoid, or sarcomatous element’, together with carcinosarcoma and pulmonary blastoma by the WHO classification in 1999 [2]. In the diagnosis of this tumor, the spindle cell or giant cell component should comprise at least 10% of the neoplasm. Before 1999, the diagnosis of this histotype was confusing because of the lack of any uniform diagnostic criteria. This has been a flexible category, because of the difficulty in obtaining a sufficiently large number of cases to acquire clinical experiences with pleomorphic carcinoma. Therefore, the characteristics and the clinical behavior of pleomorphic carcinoma are still unclear. The absence of a universally accepted disease criteria and the rarity of this pulmonary carcinoma have made the appropriate treatment difficult to determine.

Generally, the preoperative diagnosis of a pleomorphic carcinoma is very difficult. In this study, none of the patients had a preoperative diagnosis of this tumor. Therefore, for the pleomorphic carcinoma patients, it is difficult for us to choose the preoperative strategy, which may include the use of an induction chemotherapy or radiation therapy.

There have been few reports so far regarding the use of chemotherapy for pleomorphic lung cancer, and evidence of the benefit of chemotherapy for pleomorphic carcinoma is also lacking and therefore this treatment regimen still remains controversial [3,4]. We have no fixed criteria and regimen of chemotherapy for pleomorphic carcinoma. In this series, we administered CBDCA + paclitaxel to five patients, CDDP (CBDCA) + CPT-11 to one patient, and UFT to one patient. Although none of these patients experienced a recurrence of the carcinoma, the use of chemotherapy for a pleomorphic carcinoma has not yet reached a level with a sufficiently proven success rate.

The use of radiation therapy for pleomorphic carcinoma of the lung also remains controversial. In this series we attempted to perform adjuvant radiation therapy on four patients. One of those patients, who had a non-curative operation, died of a recurrence of the carcinoma only 9.1 months after surgery. The remaining three patients are all doing well now without any recurrence of the disease. In this study, the effect of radiation therapy for pleomorphic carcinoma of the lung thus remains unclear.

In a previously reported study, it was found that nodal status did not have any significant effect on the disease prognosis [5], while another report stated that nodal involvement shortened the survival duration of pleomorphic
carcinoma patients [3,4,6]. Despite having very few lymph node metastasis-positive patients (three cases) in this study, the nodal status was considered to be a very important parameter of disease-free survival. A curative operation is also an important factor in the overall survival rate. Of course this factor should be emphasized not only for pleomorphic carcinoma but also for other malignancies. Because of the difficulties concerning the pathological categorization and in the establishment of the preoperative diagnosis, a curative resection of the tumor is now one of the most effective surgical options for pulmonary pleomorphic carcinoma.

5. Conclusions

In this clinical study, the presence of lymph node metastasis and the performance of a curative resection of the tumor are the most important prognostic factors regarding the pulmonary pleomorphic carcinoma. However, further investigation with a large number of cases is needed for an improved understanding of the clinical characteristics and the behavior of pulmonary pleomorphic carcinoma.

References