Clinicopathological Characteristics and Treatment Outcomes of Pulmonary Carcinosarcoma in Eight Patients

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ABSTRACT

Background: *Pulmonary carcinosarcoma (PC) is a rare malignant tumour of the lung. Due to its rarity, few studies have been reported and its clinicopathological characteristics and treatment outcomes remain unclear. The aim of the present study was to evaluate clinical, radiological and pathological findings and treatment outcomes of patients with PC.*

Methods: *We retrospectively reviewed the records of the Pathology Department from the beginning of 2005 to the end of 2013.*

Results: *The present study included eight cases with PC. All patients were male and their ages ranged from 56 to 77 years, with a mean age of 63.1 years. The most common radiological finding was a solitary mass, followed by atelectasis and mass. All patients underwent surgical resection, in the form of lobectomy (n = 6), bilobectomy inferior (n = 1) and pneumonectomy (n = 1). Pathological diagnosis of PC was made by surgical resection, in all patients. Pathologically, the epithelial component of the tumour was squamous cell carcinoma in four patients and adenocarcinoma in four patients. The most common sarcomatous component was spindle cell, followed by chondrosarcoma. Four patients received adjuvant chemotherapy. Survival time for four of the patients was shorter than one year. The median survival time was 21.5 months (range: 1–75 months).*

Conclusions: *Pulmonary carcinosarcoma of the lung is a rare biphasic tumour. Complete surgical resection is the treatment of choice. The prognosis of patients with PC is poor despite complete surgical resection and adjuvant chemotherapy.*

Keywords: Carcinosarcoma, diagnosis, lung tumour, prognosis, treatment

Características Clínico-patológicas y Resultados del Tratamiento del Carcinosarcoma Pulmonar en Ocho Pacientes

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RESUMEN

Antecedentes: *El carcinosarcoma pulmonar (CP) es un tumour maligno del pulmón poco frecuente. Debido a su rara ocurrencia, se han reportado pocos estudios sobre esta enfermedad, y no hay aún claridad en relación con sus características clínico-patológicas, ni sobre los resultados del tratamiento. El objetivo del presente estudio fue evaluar los hallazgos clínicos, radiológicos y patológicos y los resultados del tratamiento de los pacientes con CP.*

Métodos: *Se revisaron retrospectivamente las historias clínicas del Departamento de Patología desde el inicio de 2005 hasta finales de 2013.*

Resultados: *El presente estudio incluyó ocho casos con CP. Todos los pacientes eran hombres y sus edades oscilaron entre 56 y 77 años, con una edad promedio de 63.1 años. El hallazgo radiológico más común fue una masa solitaria, seguida de atelectasia y masa. Todos los pacientes experimentaron la resección quirúrgica, en forma de lobectomía (n = 6), bilobectomía inferior (n = 1) y la neumonectomía (n = 1). El diagnóstico patológico del CP fue realizado mediante resección quirúrgica en todos los pacientes. Patológicamente, el componente epitelial del tumour fue un carcinoma de células escamosas en cuatro pacientes, y adenocarcinoma en cuatro pacientes. El componente sarcomatoso más común fue la*

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célula fusiforme, seguido del condrosarcoma. Cuatro pacientes recibieron quimioterapia adyuvante. La supervivencia de cuatro de los pacientes fue menor de un año. El tiempo promedio de supervivencia fue de 21.5 meses (rango: 1–75 meses).

Conclusiones: *El carcinosarcoma del pulmón es un tumour bifásico de rara ocurrencia. Resección quirúrgica completa es el tratamiento de elección. El pronóstico de los pacientes con CP es pobre a pesar de la resección quirúrgica completa y quimioterapia adyuvante.*

Palabras claves: *Carcinosarcoma, diagnóstico, tumour pulmonar, prognosis, tratamiento*

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INTRODUCTION

Pulmonary carcinosarcoma (PC) is a biphasic tumour containing an admixture of malignant epithelial and mesenchymal elements (1). It is a rare tumour of the lung, accounting for only 0.1 to 1% of all pulmonary neoplasms (2, 3). Pulmonary carcinosarcoma is more common in elderly male patients and there is a strong association of this tumour with smoking history (3, 4). Pre-operative diagnosis of PC is difficult and a definitive diagnosis is made by surgical resection in most cases (4, 5). Complete surgical resection is the treatment of choice for early-stage PC (2, 3). The prognosis of PC is poorer than that of non-small cell lung carcinoma (3, 6). We evaluated clinical, radiological, and pathological findings and treatment outcomes of eight patients with PC.

SUBJECTS AND METHODS

This retrospective study was conducted at Süreyyapaşa Center for Chest Diseases and Thoracic Surgery Training and Research Hospital, Istanbul, Turkey. We reviewed the records of the Pathology Department from the beginning of 2005 to the end of 2013. We identified nine patients with PC during this period. All the pathological material was re-examined by an expert pathologist. Haematoxylin and eosin stained slides were present in all cases. Immunohistochemical staining including: epithelial membrane antigen, keratins and vimentin was performed in seven cases. The diagnosis of PC was based on the criteria set by World Health Organization [WHO] (7). One patient was excluded from this study because the tumour did not meet the criteria set by the WHO. Thus, the present study included eight cases with PC. This retrospective study was approved by the local scientific committee of the institute.

The patients' clinical files were evaluated for the following: age, gender, history of smoking, symptoms, radiological features, diagnostic investigations, pathological findings, stage of the tumour, treatment and outcomes.

All of the patients underwent routine laboratory studies, electrocardiography, respiratory function tests, chest X-ray, computed tomography (CT) of the thorax and fibreoptic bronchoscopy. Computed tomography-guided transthoracic fine needle aspiration was performed in two patients. Metastatic disease was investigated by positron emission tomography (PET-CT) in all patients and by magnetic resonance of brain in four patients. The mediastinal lymph nodes were evaluated by mediastinoscopy in four patients. All patients underwent surgical resection and mediastinal lymph node dissection for lung cancer. The clinical and pathologic staging of the tumour was made according to the seventh edition of international TNM staging system. For statistical analysis; the postoperative survival rate was calculated by the Kaplan-Meier method.

RESULTS

All patients were male. Their ages ranged from 56 to 77 years, with a mean age of 63.1 years. While one patient was a non-smoker, seven patients were smokers, with a mean smoking history of 47.1 pack-years. The most frequent symptom was cough. Clinical data of each patient are given in Table 1.

Table 1: Clinical data in eight patients with pulmonary carcinosarcoma

Case	Age (years)	Gender	Smoking status	Smoking pack-years	Co-morbidity	Symptoms
1	61	M	S	40	No	Fatigue, weight loss
2	62	M	S	80	Chronic bronchitis	Cough, sputum production, fever, weight loss
3	60	M	S	20	No	Pain
4	77	M	S	60	HT	Cough, haemoptysis
5	52	M	S	60	No	Chest pain, cough, sputum production, weight loss
6	67	M	S	40	HT, DM	Cough, haemoptysis, dyspnoea
7	70	M	NS	–	No	Dyspnoea
8	56	M	S	30	No	Cough

M: male, S: smoker, NS: non-smoker, HT: hypertension, DM: diabetes mellitus

Chest X-ray demonstrated a solitary mass lesion in four patients, atelectasis in three patients, and a solitary nodule in one patient. Computed tomography, bronchoscopic, PET-CT and pre-operative pathologic data are summarized in Table 2. Computed tomography scan showed a solitary mass in four patients, atelectasis and mass in two patients, atelectasis in one patient and a solitary nodule in one patient. Fibreoptic bronchoscopy revealed endobronchial tumour in six (75%) cases and normal endobronchial appearance in two (25%) patients. According to CT and/or bronchoscopy findings, the tumours were located in the right upper lobe (n = 3), left upper lobe (n = 3), left lower lobe (n = 1) and right bronchus intermedius (n =1). Pathologic diagnosis of bronchoscopic biopsies was non-small cell carcinoma in five patients and squamous cell carcinoma in one case. Computed tomography-guided transthoracic fine needle aspiration (TFNA) was performed in two patients which revealed non-small cell carcinoma in one patient and a negative result in the remaining patient. The minimum standardized uptake value (SUVmax) on PET-CT ranged from 7.9 to 26.3, with the mean SUVmax value of 14.7.

All patients underwent surgical resection. Operations included three right upper lobectomies, two left upper lobectomies, one left lower lobectomy, one right bilobectomy inferior and one left pneumonectomy. Systematic lymph node dissection was performed in all patients. Nevertheless, all the patients were N0 after the pathological examination. Tumour size ranged from 1 cm to 8 cm, with mean size of 4.1 cm. None of the patients had lymph node metastasis. Pathologically, the epithelial component of the tumour was squamous cell carcinoma in four patients and adenocarcinoma in four patients. The most common sarcomatous component was spindle cell, followed by chondrosarcoma. No mortality occurred in the postoperative period. Two patients had prolonged air leak and were treated with chest tube placement. Three patients received adjuvant chemotherapy, but chemotherapy was deemed necessary for the others. Survival time for four patients was shorter than one year. Three patients were alive at the time of evaluation (Table 3). The Figure presents the cumulative survival graph. The median survival time was 21.5 months (range: 1–75 months).

Table 2: Computed tomography, bronchoscopic, position emission tomography and pre-operative pathologic data

Case	CT findings	Bronchoscopic findings	Involved lobe	Location	SUVmax on PET-CT	Pre-operative diagnosis Bronchoscopy/TFNA
1	Atelectasis	Endobronchial mass	RUL	Central	13.7	Squamous/No
2	Mass	Normal	Apical segment of RUL	Peripheral	12.6	Negative/Negative
3	Nodule	Normal	Anterior segment of RUL	Peripheral	26.3	Negative/NSCLC
4	Mass	Endobronchial mass	Superior segment of LLL	Peripheral	17.5	NSCLC/No
5	Atelectasis and mass	Endobronchial mass	Right bronchus intermedius	Central	12	NSCLC/No
6	Atelectasis and mass	Endobronchial mass	LUL	Central	7.9	NSCLC/No
7	Mass	Endobronchial mass	LUL	Central	17.3	NSCLC/No
8	Mass	Endobronchial mass	Anterior segment of LUL	Central	11	NSCLC/No

CT: computed tomography; PET-CT: positron emission tomography; SUV max: maximum standardized uptake value; TFNA: thoracic fine needle aspiration; RUL: right upper lobe, LLL: left lower lobe, LUL: left upper lobe; NSCLC: non-small cell carcinoma

Table 3: The data of treatment, stage, pathology, follow-up, and survival on eight patients with pulmonary carcinosarcoma

Case	Resection	Size (cm)	Clinical stage	Pathologic stage	Local invasion/ metastasis	Cellular components	Adjuvant therapy	Follow-up/ Survival	Follow-up findings
1	RU lobectomy	1	T2aN0M0	T2aN0M0	No	Squamous Spindle cell	No	37 months/alive	—
2	RU lobectomy	6	T2aN0M0	T2bN0M0	No	Adenocarcinoma Spindle cell	No	1 month/died	Respiratory failure
3	RU lobectomy	2.5	T1aN0M0	T1bN0M0	No	Adenocarcinoma Chondrosarcoma	No	12 months/ died	—
4	LL lobectomy	3.2	T2aN0M0	T2aN0M0	No	Adenocarcinoma Chondrosarcoma	No	31 months/ died	—
5	Right bilobectomy inferior	2	T2aN0M0	T2aN0M0	No	Squamous Leiomyosarcoma	Yes	75 months/ alive	—
6	LU lobectomy	5	T2aN0M0	T2aN0M0	No	Adenocarcinoma Spindle cell	Yes	7 months /died	Malignant pleural effusion
7	Left pneumonectomy	5	T2aN2M0	T3N0M0	Chest wall	Squamous Spindle cell	Yes	9 months/ died	Brain metastasis
8	LU lobectomy	8	T2bN0M0	T3N0M0	No	Squamous Chondrosarcoma	Yes	48 months/ alive	—

RU: right upper, LL: left lower, LU: left upper

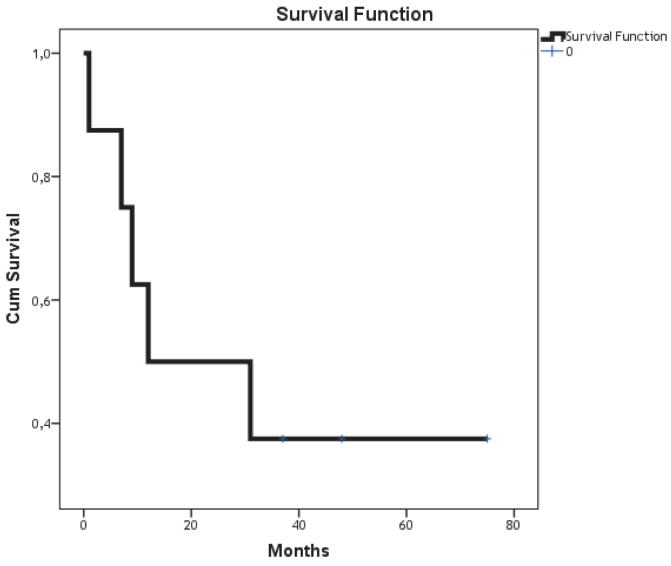

Figure: The cumulative survival graph of patients diagnosed with pulmonary carcinosarcoma.

DISCUSSION

Pulmonary carcinosarcoma is a rare tumour of the lung, accounting for only 0.1 to 1% of all pulmonary neoplasms (2, 3). This tumour was classified in the subgroup of pulmonary sarcomatoid carcinomas by the 2004 WHO classification of lung and pleural tumours. It was defined as a malignant tumour with a mixture of carcinoma and sarcoma containing differentiated sarcomatous elements, such as malignant cartilage, bone or skeletal muscle (7). According to this definition, we identified only eight cases of pulmonary carcinosarcoma during nine years. More than 1000 cases of primary pulmonary cancer have been diagnosed annually in our centre. These results point out that PC is a rare tumour.

Pulmonary carcinosarcoma more commonly occurs in elderly male patients, with an average age of 60 years and there is a strong association of this tumour with cigarette smoking, as was seen in our series (3, 8). Most patients present with non-specific symptoms such as cough, haemoptysis and dyspnoea. However, they can be asymptomatic for a long-time. Clinical symptoms depend on the size and localization of the tumour. Pulmonary carcinosarcomas are classified either as central endobronchial type or peripheral parenchymal type on the basis of the location of the tumour.

Central type involves main, lobar or segmental bronchi and frequently produces several symptoms as a result of bronchial irritation or obstruction. Peripheral type can be asymptomatic for a long-time (2, 3, 8, 9). While Koss *et al* (10), reported that 62% of the tumours were located centrally, many authors reported that peripheral type was more frequent than central type (3, 11). In our series, 75% of the tumours had a central location and there was no asymptomatic patient. The most frequent presenting symptom was cough. The present series had upper-lobe predilection of the tumour, as was reported in many previous reports (10, 11).

The radiological findings of PCs are non-specific and similar to other primary lung cancers. Most patients present with a solitary pulmonary mass on radiographs and CT (1, 2, 8, 9). Other radiological findings include, a solitary pulmonary nodule, atelectasis, consolidation due to pneumonia and pleural effusion (1, 3, 12). The most common radiological finding was a solitary mass, followed by atelectasis and mass in our series. The number of reports about using (FDG PET) scans in PCs is limited. These reports pointed out that patients with PC had high SUV of 18F-FDG in the lesions, as was seen in our patients (3, 12, 13).

The value of pre-operative diagnostic tests such as bronchoscopy and TFNA in diagnosing pulmonary carcinoma is limited. Bronchoscopy and TFNA can yield a small amount of tissue for pathological examination. Also, they often demonstrate only one component of the tumour. Pre-operative diagnosis, when available, was significant in detecting malignancy; a correct differential diagnosis of PC has always been established on the basis of definitive postoperative specimen examination (4, 5, 8, 9). Although pre-operative diagnostic methods revealed a diagnosis of lung cancer in 87.5% of our patients, they were insufficient to diagnose a tumour of the lung as PC.

Pulmonary carcinosarcoma is a biphasic tumour consisting of a mixture of carcinomatous and sarcomatous elements. The most common epithelial components are squamous cell carcinoma and adenocarcinoma. Sarcomatous components usually include; spindle cell carcinoma, osteosarcoma, chondrosarcoma and rhabdomyosarcoma (4, 5, 9). It is difficult to discriminate PC from other sarcomas at the light microscopic level. Thus, immunohistochemical studies and/or electron microscopic examinations play an important role in the differential diagnosis of PC (3, 5, 8, 9). Several antibodies are used to differentiate components of PC. While epithelial component shows positive staining for keratins, carcinoembriyonic antigen and epithelial membrane antigen, sarcomatous component shows positive staining for vimentin, actin and desmin (6, 8, 9).

Pulmonary carcinosarcomas present an aggressive clinical behaviour (11). At presentation, local invasion of mediastinal structures, chest-wall and pleura, and metastasis to mediastinal lymph nodes are frequent (3, 6, 11). These tumours also have a marked tendency for distant metastasis (6, 11). Complete surgical resection of the tumour with clear tumour margins is the treatment of choice and potentially curative in early-stage patients with PC (3, 5, 6, 9, 11). Adjuvant or neoadjuvant chemotherapy and radiotherapy can be considered in selected cases (3, 5). The rate of local recurrence after surgery is high (5, 6). It was reported that PCs had a worse prognosis than classical non-small cell carcinomas (6). The survival rate can be associated with several factors. The localization, diameter, stage, sarcomatous component and

lymph node involvement are among factors that determine the prognosis (4, 6, 8, 11, 14).

Central tumours have a better prognosis than peripheral tumours (4, 14). The one-year survival rate was reported as 35.7% in central type and 6.9% in peripheral type by Takeda *et al* (14). The high stage, a tumour size larger than 3 cm and the presence of rhabdomyosarcoma component are important predictors of poor prognosis (4, 8). The median survival time is nine months (3). In our series, there was no distant or lymph node metastasis. All patients underwent surgical resection. None of the patients had lymph node metastasis. While there was no local invasion in seven patients, the tumour invaded the chest-wall in one patient. Four patients received adjuvant chemotherapy. Survival time for four patients was shorter than one year. The median survival time was 21.5 months.

CONCLUSION

Pulmonary carcinosarcomas of the lung is a rare biphasic tumour. Diagnosis of PC is frequently established by surgical resection. Complete surgical resection with clear margins is the treatment of choice for this tumour. The prognosis of patients with PC is poor despite complete surgical resection and adjuvant chemotherapy.

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