Pleomorphic Carcinoma of the Lung: Clinicopathological Characteristics and Treatment Outcomes of 20 Cases

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ABSTRACT

Background and Aims: *Pleomorphic carcinoma is a rare tumour of the lung. The aim of the present study was to evaluate the clinicopathological characteristics and treatment outcomes of patients with pleomorphic pulmonary carcinoma.*

Methods: *The records of the Pathology Department at Süreyyapasa Chest Disease and Thoracic Surgery Training and Research Hospital, Istanbul, Turkey, from January 2005 to December 2013, were reviewed. Twenty cases of pleomorphic pulmonary carcinoma were identified and studied.*

Results: *There were 18 male and two female patients. Their ages ranged from 38 to 81 years, with the mean age of 63.4 years. Eighteen (90%) of the patients had smoking history. All the patients were symptomatic. The most common radiological finding was a solitary mass, followed by a solitary pulmonary nodule. Fiberoptic bronchoscopy revealed an endobronchial lesion in six (30%) of the patients. A pathological diagnosis of pleomorphic carcinoma was made using bronchoscopic biopsy in two (10%) of the patients and surgical biopsy in 18 (90%) of the patients. Four (20%) of the patients had metastatic disease at the time of the diagnosis. Fifteen of the patients underwent surgical resection. Lobectomy was the most common surgical procedure used. Pathologically, the epithelial component of the tumour was squamous cell carcinoma in 13 (65%) patients and adenocarcinoma in seven (35%) of the patients. Survival time for 11 of the patients was six months or shorter than six months. Survival time ranged from one-month to 97 months, with a median survival time of six months.*

Conclusions: *Pleomorphic carcinoma is a rare tumour of the lung. The pathological diagnosis of this tumour is usually established by surgical biopsy. The prognosis of patients with pleomorphic pulmonary carcinoma is poor despite complete surgical resection.*

Keywords: Lung, pleomorphic carcinoma, prognosis, treatment

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INTRODUCTION

Pleomorphic carcinoma (PC) is a rare tumour of the lung. It accounts for 0.1 – 1% of all pulmonary malignant tumours (1, 2). According to the 2004 World Health Organization (WHO) classification of the lung, pleomorphic carcinoma is one of five subgroups of pulmonary sarcomatoid carcinoma (3). An accurate pre-operative diagnosis of this tumour using bronchoscopic or transthoracic needle biopsy is difficult due to the heterogeneity of the tumour (4). Many case reports, but very few studies, have been published in the literature regarding the clinical and pathological characteristics of pulmonary pleomorphic carcinoma. As a result, its clinical and pathological characteristics are not well known (2, 5). The purpose of the present study was to evaluate the clinicopathological characteristics and treatment outcomes of selected patients with pleomorphic pulmonary carcinoma.

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METHODS

This retrospective study was conducted at Süreyyapaşa Chest Diseases and Thoracic Surgery Training and Research Hospital, Istanbul, Turkey. The study was approved by the local scientific committee of the institute. The records of the Pathology Department from January 2005 to December 2013 were reviewed. Twenty-one cases of pleomorphic pulmonary carcinoma were identified during this period. All the pathological materials were re-examined by an expert in pathology. Haematoxylin and eosin stained slides were present in all the cases. Immunohistochemical staining was performed in 18 cases. The diagnosis of pulmonary pleomorphic carcinoma was based on the criteria set by the WHO (3). One patient was excluded from this study because the patient's tumour did not meet the criteria set by the WHO. Thus, the present study included 20 cases of pleomorphic carcinoma.

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 the patients underwent routine laboratory studies, electrocardiography, chest X-ray, computed tomography

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(CT) of the thorax, and fiberoptic bronchoscopy. Computed tomography-guided transthoracic fine needle aspiration (TFNA) was performed in nine of the patients. Pulmonary function tests were done in the patients who underwent a surgical procedure. Metastatic disease was investigated by positron emission tomography (PET-CT) in 18 of the patients, by magnetic resonance of the brain in 10 of the patients, by CT of the brain in one of the patients, CT of the abdomen in two of the patients and bone scintigraphy in two patients. Fifteen of the patients underwent surgical resection. The standard surgical technique was used accompanied by routine systemic dissection or sampling of the hilar and mediastinal lymph nodes in these patients. A surgical biopsy of lesions was performed in three of the patients. The clinical and pathologic staging of the tumour was made according to the seventh edition of international TNM staging system. Follow-up information was completed in December 2014. The duration of overall survival was defined as the interval between the day of the operation or diagnosis and the date of death or the last follow-up date. The overall survival rate was calculated by using the Kaplan-Meier method.

RESULTS

There were 18 (90%) male and 2 (10%) female patients (male to female ratio, 9 to1). The mean age was 63.4 (range 38–81) years. Eighteen (90%) of the patients had positive smoking history. All the patients were symptomatic. The most common symptom was chest-pain, followed by dyspnoea. The clinical data are shown in Table 1.

Table 1: The clinical data of the patients

	n	%
Male	18	90
Female	2	10
Mean age (range) years	63.4 (38–81)	
Age groups		
< 40 years	1	5
40–60 years	8	40
≥ 60 years	11	55
Smoking history		
Yes	18	90
No 2 10		
Mean smoking duration (range), years	59.5 (25–150)	
Symptoms		
Chest-pain	9	45
Dyspnoea	8	40
Cough	7	35
Haemoptysis	5	25
Sputum production	3	15
Constitutional	4	20

Chest X-ray showed a solitary mass in 13 of the patients, a solitary pulmonary nodule in four, atelectasis in one, cavitation in one and cavitation and infiltration in one. Computed tomography scan of the thorax demonstrated a solitary mass in 14 of the patients, a solitary pulmonary nodule in three, multiple pulmonary nodules in one, atelectasis and mass in one, and cavitation and infiltration in one. Tumour size on CT scan ranged from 10 mm to 96 mm, with the mean size of 51.7 mm. While the size was smaller than 5 cm in five (25%) of the cases, it was 5 cm or larger than 5 cm in 15 (75%) of the cases. All the patients underwent flexible bronchoscopy. It revealed endobronchial lesions in six (30%) of the patients and normal endobronchial appearance in 14 (70%) of the patients. According to CT and/or bronchoscopy findings, the tumours were located in the right upper lobe (n = 6), left upper lobe (n = 5), left lower lobe (n = 3), right lower lobe (n = 2), right upper and lower lobes (n = 1), left lower and right lower lobes (n = 1), right middle lobe (n = 1), and right bronchus intermedius (n = 1). Positron emission tomography-computed tomography was performed in 18 of the patients. The maximum standardized uptake value on PET-CT ranged from 5.7 to 36, with the mean SUVmax value of 14.1.

Pleomorphic carcinoma was diagnosed in only two (10%) of the patients by pre-operative diagnostic procedures. Pathological diagnosis was established by surgical biopsy in three of the patients and by surgical resection in 15 of the patients. Pathologically, the epithelial component of the tumour was squamous cell carcinoma in 13 (65%) of the patients and adenocarcinoma in seven (35%) of the patients. The pathological results of flexible bronchoscopy and CT-guided TFNA are shown in Table 2.

Table 2: The results of flexible bronchoscopy and computed tomography-guided transthoracic fine needle aspiration

Bronchoscopy (n = 20)	n	%
Negative	15	75
Pleomorphic carcinoma	2	10
Squamous cell carcinoma	2	10
Non-small cell lung carcinoma	1	5
CT-guided TFNA (n = 9)		
Negative	4	44.5
Squamous cell carcinoma	2	22.2
Non-small cell lung carcinoma	2	22.2
Adenocarcinoma	1	11.1

The data of stage, treatment, follow-up and survival on 20 patients with pleomorphic carcinoma are summarized in Table 3. Four (20%) patients had metastatic disease at the time of the diagnosis. Metastatic sites included lung (n = 1), bone (n = 1), adrenal gland (n = 1) and brain (n = 1). While three of the patients were treated with chemotherapy, the others refused treatment. One patient was medically inoperable because of poor cardiopulmonary status. He was treated with chemotherapy. The remaining 15 patients underwent surgical resection. The operations included: 11 lobectomies, two inferior bilobectomies and two pneumonectomies. The surgical resection was accompanied by routine systemic dissection in 14 patients and sampling of the hilar lymph nodes in one patient. No mortality occurred in the postoperative period. Four patients had prolonged air

Table 3: The data of stage, treatment follow-up and survival on 20 patients of pleomorphic carcinoma

Cases	Clinical stage	Pathological stage	Metastasis	Resection	Adjuvant therapy	Follow-up (months)	Survival
1	T3N2M0	T3N0M0	—	LU Lobectomy	Chemotherapy	28	Died
2	T3N0M0	T3N0M0	—	LU Lobectomy and chest-wall resection	Chemotherapy	6	Died
3	T2aN1M0	T3N1M0	—	LU Lobectomy	Radiotherapy	48	Died
4	T2bN0M0	T2bN0M0	—	RU Lobectomy	No	2	Died
5	T1bN2M0	T2bN0M0	—	Bilobectomy inferior	No	1	Died
6	T1aN1M0	T1aN2M0	—	Left pneumonectomy	Chemotherapy	4	Died
7	T3N2M0	T3N0M0	—	Bilobectomy inferior and chest-wall resection	No	2	Died
8	T2bN0M0	T2bN0M0	—	RU Lobectomy	Chemotherapy	15	Alive
9	T1aN2M0	T1aN2M0	—	RU Lobectomy	Chemotherapy	24	Died
10	T2bN0M0	T3N1M0	—	RL Lobectomy and chest-wall resection	Chemotherapy	6	Died
11	T4N0M0	T4NXMX	—	—	Chemotherapy	31	Died
12	T2aN0M0	T2aN0M0	—	RU Lobectomy	Chemoradiotherapy	97	Alive
13	T2bN0M1	—	Lung	—	Refused	2	Died
14	T3N2M1	—	Adrenal	—	Chemotherapy	2	Died
15	T2bN0M0	T2bN0M0	—	Right pneumonectomy	No	14	Died
16	T1aN0M1	—	Bone	—	Chemotherapy	35	Died
17	T3N0M0	T3N0M0	—	LL Lobectomy	No	3	Died
18	T3N0M0	T3N0M0	—	LU Lobectomy and chest-wall resection	Chemoradiotherapy	40	Alive
19	T2bN0M0	T3N0M0	—	LL Lobectomy	No	2	Died
20	T2bN0M1	—	Brain	—	Chemotherapy	3	Died

LU: Left upper, RU: Right upper, LL: Left lower

leak and they were treated with chest tube placement. While six patients received adjuvant chemotherapy, two patients received adjuvant chemoradiotherapy. Survival time ranged from one-month to 97 months, with the median survival time of six months. The time for the 11 patients was six months or shorter than six months. Three patients were alive at the time of evaluation. Figure 1 presents the cumulative survival graph.

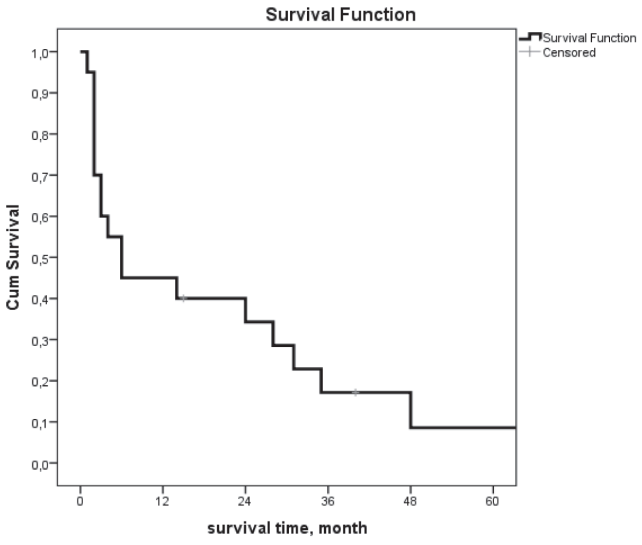

Figure: The cumulative survival graph.

DISCUSSION

According to the 2004 World Health Organization classification of lung tumours, pleomorphic carcinoma is one of five subgroups of sarcomatoid carcinoma (3). Histologically, pleomorphic carcinoma is defined as either a non-small cell lung carcinoma combined with neoplastic spindle and/or giant cells or a carcinoma that consists of only spindle and giant cells. At least 10% of the carcinoma should comprise spindle and/or giant cells for it to be classified as a pleomorphic carcinoma (3, 6). It accounts for 0.1–1% of all malignant lung tumours (1, 2). Nearly 1100 cases with primary pulmonary malignancy have been diagnosed annually in our centre. According to these results, its incidence is 0.2% in our centre.

Pleomorphic carcinoma predominantly occurs in elderly men who smoke heavily, with similar findings to ours (7–9). The male: female ratio ranged from 2.3:1 to 10.3:1 (5, 7). The mean age at diagnosis was 57–66 years (9, 10). There is a strong association of this tumour with cigarette smoking. The rate of the smoking in patients was between 80–95% (4, 5). Most patients showed non-specific pulmonary symptoms including chest-pain, cough, haemoptysis, and dyspnoea, whereas they can be asymptomatic for a long time (4–6, 11, 12). Chang *et al* (13), reported that all patients had one or more symptoms. Two previous reports noted that symptoms were seen in 72.7% and 90% of the patients (5, 6). In our study, all the patients were symptomatic. The symptoms are associated with the location and size of the tumour.

Pulmonary pleomorphic carcinomas are classified either as central endobronchial type or peripheral parenchymal type on the basis of the location of the tumour. Central type produces several symptoms as a result of bronchial irritation, obstruction or obstructive pneumonia. Peripheral type produces symptoms due to the early pleural and chest-wall invasion (7, 11, 13). Pleomorphic carcinomas tend to be large peripheral tumours, as in our study. They are often found as a large mass, more than 4-5 cm in diameter. Large tumours are usually symptomatic (6, 11).

The radiological findings of pulmonary pleomorphic carcinoma are non-specific and similar to those of other primary lung cancers. Most of the patients displayed a solitary pulmonary mass or nodule on radiographs and CT. The images frequently demonstrate intratumoral cavities (6, 10, 13). While the lesions are generally unilateral and solitary, bilateral or multiple lesions can be identified on radiographic images (11). There is a predilection for peripheral location and upper lobes (7, 10). Those findings are consistent with those in our study.

The pre-operative diagnosis of pleomorphic carcinoma is very difficult because the diagnostic value of pre-operative diagnostic methods including bronchoscopy and transthoracic needle aspiration is limited (4–7, 14). Yamamato *et al* (4), reported that none of the patients had a pre-operative diagnosis of pleomorphic carcinoma. Ito *et al* (6), noted that transbronchial biopsy was diagnostic in three of 22 cases and there were no cases diagnosed with cytological examination. This is due to the heterogeneity and rare incidence of this tumour (7, 14). Bronchoscopy and transthoracic fine needle aspiration can yield small amounts of tissue for pathological examination. Also, they often demonstrate only one component of the tumour. As a result, a definitive diagnosis is established based on the examination of surgical specimens in the majority of the cases (5, 7). In this study, only two patients had pre-operative diagnosis of pleomorphic carcinoma. The definitive diagnosis was established with the examination of surgical specimens in the remaining 18 patients.

Pleomorphic carcinoma displays an aggressive behaviour. At the time of presentation, local invasion of adjacent structures, metastasis to hilar and mediastinal lymph nodes, and distant metastases are frequent (5–7, 13). Chang *et al* (13), reported that among seven of the patients who underwent surgical resection, four of them had mediastinum, pleura and chest-wall invasions and three of them had regional lymph node metastases. Mochizuki *et al* (9) noted that vascular invasion and lymph node metastases were observed in 86% and 41% of the patients, respectively. They reported that 7% of the patients had pathological stage IV disease.

According to Fishback's report (11), 12% of the patients had stage IV lesions at the time of diagnosis. In our study, four patients had chest-wall invasion. There were N1 lymph node metastases in two patients and N2 lymph node metastases in two patients. Four patients had distant metastases at the time of presentation. Pleural effusion was diagnosed in one patient with distant metastases.

Complete surgical resection of the tumour with clear tumour margins is the treatment of choice in especially early stage patients with pulmonary pleomorphic carcinoma (4–7, 9, 11, 13). Raveglia *et al* (5), suggested that surgery for preoperatively proven pulmonary pleomorphic carcinoma should be restricted to N0 patients. Adjuvant and neoadjuvant chemotherapy and radiotherapy are controversial and they can be considered in selected cases (4–7, 13). The rates of local recurrence and distant metastases after surgery are high (6, 7, 9, 15). Mochizuki *et al* (9), reported that 24 patients had died as a result of distant metastases or recurrence 27 days to 36 months after surgery. Raveglia *et al* (5), noted that 16 of the 20 patients died from early distant metastases after surgery.

Pleomorphic carcinoma has a worse prognosis than the other non-small cell carcinoma cases (7, 9). The overall five-year survival rate, median survival time, disease-free survival rate and median disease-free survival time were 36.7%, 22.8 months, 40.8% and 14.7 months, respectively (9). Five-year overall survival was found as 39.2% in another study (7). Prognosis can be associated with several factors. These factors include: location, size, and stage of the tumour, the presence of distant metastases and lymph node metastases (5, 9, 11, 13). The central type has a better prognosis than the peripheral type because of its limited extension to the surrounding parenchyma and there are early symptoms. Early dissemination is more frequent in the peripheral type (13). The size of tumour greater than 5 cm, stage greater than one at presentation, the presence of any lymph node metastases and distant metastases indicate a poor prognosis for survival (5, 11). In our study, most of the patients had one or more poor prognostic factors. The median survival time was six months. Survival time for 11 of the patients was six months or shorter than six months.

In conclusion, pleomorphic carcinoma is a rare tumour of the lung. Pathological diagnosis of this tumour is usually established by surgical biopsy. The prognosis of the patients with pleomorphic pulmonary carcinoma is poor despite complete surgical resection.

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