Pulmonary carcinosarcomas: an evaluation of seven patients

Pulmoner karsinosarkom: Yedi olgunun değerlendirilmesi

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Background: Carcinosarcoma is a rare malignant mixed tumor of the lungs. We evaluated the diagnosis, treatment, and prognosis of this tumor along with the clinical and histological features.

Methods: The study included seven patients (all males; mean age 60 years; range 55 to 73 years) whose postoperative histopathologic diagnosis was pulmonary carcinosarcoma. The most common presenting symptom was cough (57%). Operations performed were upper lobectomy (n=2), pneumonectomy (n=2), lower lobectomy (n=1), sleeve upper lobectomy (n=1), and only exploration (n=1).

Results: Postoperative pathological examination showed positive margins in the patient treated with sleeve upper lobectomy. Histologically, epithelial characteristics of the tumors were consistent with squamous cell carcinoma (n=4), adenocarcinoma (n=2), and adenosquamous carcinoma (n=1). The sarcomatous component was of rhabdomyoblastic type in three, chondrosarcomatous type in two, and osteosarcomatous type in two tumors. Two patients had stage IB, two patients had IIB, two patients had IIIA, and one patient had IIIB tumors. Five patients had lymph node metastasis, involving the regional lymph nodes (N_1) in two patients, and mediastinal lymph nodes (N_2) in three patients. No mortality occurred in the early postoperative period. Two patients had prolonged air leak postoperatively. One patient died in the postoperative 14th month due to cranium metastasis and another patient died of myocardial infarction in the postoperative 21st month. The other patients were disease-free during a follow-up period of 6 to 103 months. The mean survival was estimated as 66 months, with one-year survival being 80% and five-year survival being 57%.

Conclusion: Complete surgical resection is the treatment of choice for early stage pulmonary carcinosarcoma. N_2 disease is an unfavorable prognostic factor in patients with carcinosarcoma.

Key words: Carcinosarcoma/pathology/surgery; lung neoplasms/pathology/surgery; prognosis; survival rate.

Amaç: Karsinosarkom, akciğerin nadir görülen malign mikst bir tümörüdür. Bu çalışmada bu tümörün tanı, tedavi ve prognozu klinik ve histolojik özellikleriyle birlikte değerlendirildi.

Çalışma planı: Çalışmada, ameliyat sonrası histopatolojik tanıları pulmoner karsinosarkom olarak konan yedi hasta (hepsi erkek; ort. yaş 60; dağılım 55-73) incelendi. Hastaların en sık başvuru nedeni öksürük (%57) idi. Uygulanan ameliyatlar iki olguda üst lobektomi, iki olguda pnömonektomi, bir olguda alt lobektomi, bir olguda sleeve üst lobektomi ve bir olguda sadece eksplorasyondu.

Bulgular: Ameliyat sonrası patolojik incelemede sleeve üst lobektomi uygulanan hastada pozitif cerrahi sınır bildirildi. Histolojik olarak, epitelyal özellikler bakımından dört tümör skuamöz hücreli karsinom, iki tümör adenokarsinom, bir tümör adenoskuamöz karsinom ile uyumlu bulundu. Sarkomatöz komponent açısından ise üç tümör rabdomiyoblastik, iki tümör kondrosarkomatöz, iki tümör de osteosarkomatöz tipteydi. Tümör evresi iki hastada IB, iki hastada IIB, iki hastada IIIA, bir hastada IIIB bulundu. Lenf nodu metastazı beş hastada saptandı; bunların ikisinde bölgesel (N_1), üçünde mediastinal (N_2) lenf nodu tutulumu vardı. Ameliyat sonrası erken dönemde ölüm gözlenmedi. Komplikasyon olarak iki olguda uzamış hava kaçağı görüldü. Uzun dönem takipte, bir hasta 14. ayda kranyum metastazı, bir hasta da 21. ayda miyokad infarktüsü nedeniyle kaybedildi. Diğer olgular 6 ay ile 103 ay arasında değişen takip süresi içinde hastalıksızdı. Hastaların ortalama sağkalım süresi 66 ay, bir yıllık ve beş yıllık sağkalım oranları sırasıyla %80 ve %57 olarak hesaplandı.

Sonuç: Erken evre pulmoner karsinosarkom tedavisinde komplet cerrahi rezeksiyon en seçkin yöntemdir. N_2 hastalık varlığı, cerrahi uygulanmış karsinosarkomlu hastalarda kötü prognostik faktörlerdendir.

Anahtar sözcükler: Karsinosarkom/patoloji/cerrahi; akciğer neoplazileri/patoloji/cerrahi; prognoz; sağkalım oranı.

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Pulmonary carcinosarcoma (PCS) is one of the rare tumors of the lungs containing both malignant epithelial and sarcomatoid components.[1,2] It accounts for 0.2 to 0.3% of all pulmonary cancers.[3] The tumor may be located in several organs such as the esophagus, salivary glands, thymus, thyroid glands, breast, stomach, urogenital system as well as in the lungs.[4,5] In this study, the results of seven patients operated on for PCS were evaluated.

PATIENTS AND METHODS

The study involved seven patients (0.36%) with PCS among 1,900 patients operated on in our clinic between January 1996 and July 2007 for pulmonary tumors. The patients were evaluated with respect to age, gender, primary disease, symptoms, surgical methods, and follow-up findings. All the patients were males, smokers and the mean age of the patients was 60 years (range 55 to 73 years).

All the patients underwent routine laboratory studies, respiratory function tests, and electrocardiography, and radiological investigations with chest-x ray, computer tomography of the thorax, cranial tomography, and abdominal ultrasound. Patients could not be evaluated by positron emission tomography. The most common presenting symptom was cough (57%).

All the patients were evaluated with bronchoscopy. Irregular mucosa was detected in the upper lobe entry in one patient, for which a biopsy specimen was obtained. No endobronchial lesions were observed in the remaining patients. Cytologic examination of bronchial lavages showed no malignancy. In two patients with tumors adjacent to the thoracic wall, fine-needle aspiration biopsy was performed, which revealed malignant epithelial tumor. We performed mediastinoscopy in Two patients having mediastinal lymphadenopathies underwent mediastinoscopy, but frozen section analysis of the specimens did not show any malignancy. Thus, all patients underwent thoracotomy without the diagnosis of PCS.

Six patients (84%) had solid-like tumors with peripheral localization. Only one tumor was located centrally without any endobronchial lesion.

RESULTS

The surgical approaches used are presented in Table 1. All tumoral masses were evaluated intraoperatively by frozen section analysis. One patient underwent explorative surgery alone with biopsy collection due to the tumoral invasion to the intrapericardial superior pulmonary vein. After lymph node sampling and obtaining a biopsy specimen, the operation was discontinued. Two patients underwent upper lobectomy, and two patients underwent pneumonectomy due to involvement of the other lobe. Lower lobectomy was performed in one patient and sleeve upper lobectomy was performed in one patient due to irregular mucosa at the entry of the upper lobe.

All the patients who underwent curative surgical resection were subjected to systematic mediastinal lymph node sampling. Negative tumor margins were confirmed by intraoperative frozen section analysis. However, postoperative pathological evaluation showed positive bronchus surgery margins in the patient who had undergone sleeve upper lobectomy. The patient did not accept reoperation and thus was scheduled for chemotherapy.

Based on postoperative pathological examination, epithelial characteristics of the tumors were consistent with squamous cell carcinoma (n=4), adenocarcinoma (n=2), and adenosquamous carcinoma (n=1). The sarcomatous component was of rhabdomyoblastic type in three, chondrosarcomatous type in two,

Table 1. Characteristics of the patients and postoperative follow-up data

Age	Location/ surgery performed	Diameter (cm)	Stage/local invasion/ metastasis	Histological component	Follow-up/ prognosis
57 / M	Left upper lobe Exploration	10	$T_4N_2M_0$ Mediastinal invasion	Squamous Rhabdomyoblastic	14th month Dead
60 / M	Left upper lobe Upper lobectomy	4	$T_2N_0M_0$	Squamous Chondrosarcoma	103 months Disease-free
73 / M	Left upper lobe Pneumonectomy	11	$T_2N_2M_0$ (No: 7+, No: 10+)	Adenocarcinoma Osteosarcoma	21st month Dead
60 / M	Left lower lobe Pneumonectomy	5	$T_2N_1M_0$ (No: 10+)	Squamous Osteosarcoma	48 months Disease-free
57 / M	Left lower lobe Lower lobectomy	5	$T_2N_1M_0$ (No: 10+)	Squamous Rhabdomyoblastic	29 months Disease-free
57 / M	Left upper lobe Sleeve upper lobectomy	4.5	$T_2N_2M_0$ (No: 4+, No: 7+)	Adenosquamous Rhabdomyoblastic	10 months Disease-free
55 / M	Right upper lobe Upper lobectomy	4.5	$T_2N_0M_0$ Visceral pleura	Adenocarcinoma Chondrosarcoma	6 months Disease-free

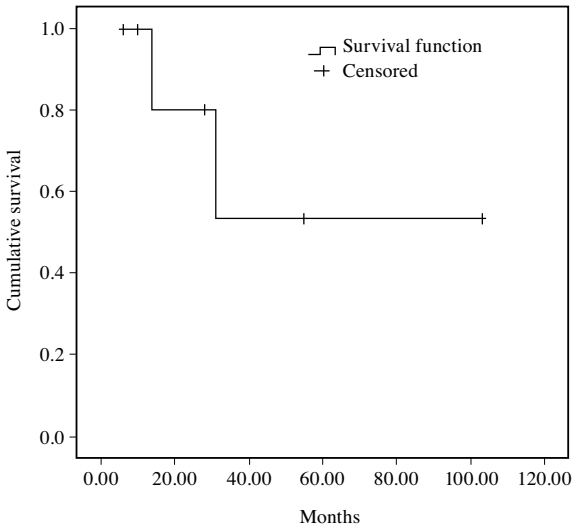

Fig. 1. The cumulative survival graph.

and osteosarcomatous type in two tumors (Table 1). Histopathologically, two patients had stage IB, two patients had stage IIB, two patients had stage IIIA, and one patient had stage IIIB tumors. Five patients had lymph node metastasis, with regional lymph node involvement in two patients, and mediastinal lymph node involvement in three patients. Patients with mediastinal lymph node involvement (N_2) were scheduled for chemotherapy. The patients with N_1 lymph node involvement did not receive chemotherapy. None of the patients received radiotherapy.

Two patients had prolonged air leak in the postoperative period. The other patients were discharged without any complaints within a normal range of time. One patient died in the postoperative 14th month due to cranium metastasis and another patient died of myocardial infarction in the postoperative 21st month. The other patients were disease-free during a follow-up period of 6 to 103 months.

The mean survival of the patients was estimated as 66 months, with expected one-year survival being 80% and five-year survival being 57%. The cumulative survival graph is presented in Fig. 1.

DISCUSSION

Carcinosarcomas are highly rare, biphasic tumors with malignant epithelial and mesenchymal components. They are also termed as metaplastic carcinoma, pseudosarcoma, and/or polypoid carcinoma.[6]

Pulmonary carcinosarcoma is more common among males than in females; it particularly affects males over 50 years of age and with a smoking history. Takeda et al.[7] reported the male-to-female ratio as 4:1, while Cohen-Salmon et al.[8] reported a rate of 5.25 to 1. All of our patients were male, above 50 years of age, and smokers.

Preoperative diagnostic tests are limited in definitions of the tumor. Therefore, the definitive diagnosis is established in the light of pathological findings and immunohistochemical studies.[3,6,8] Similarly, the diagnoses of our patients could not be made by preoperative diagnostic tests.

Depending on the tumor location, common findings are bronchial irritation or bronchial obstruction. Central endobronchial or solid parenchymal type was first described by Moore[9] based on the clinicopathological findings. According to Moore, in addition to airway obstruction, central or endobronchial tumors often lead to cough, fever, dyspnea, and hemoptysis due to obstruction. In tumors containing endobronchial components, atelectasis, obstructive pneumonia, and pleural effusion may be observed. Koss et al.[6] reported the incidence of the endobronchial type as 34%.

Peripheral solid parenchymal type PCSs often present an appearance of a large mass. These tumors are asymptomatic in the early stage, while they may involve the adjacent organs or structures such as the mediastinum, pleura, and thoracic wall.[10,11] Moore[9] reported that one-third of these tumors were located peripherally. Koss et al.[6] reported peripheral localization in 38% of the tumors. In our small series, the rate of peripheral location was 85.7%.

In PCS, the most common epithelial component is squamous cell carcinoma. Takeda et al.,[7] in their series of 78 patients, reported a rate of 69% for squamous cell carcinoma, 24% for adenocarcinoma, and 6% for combination of carcinomas. Kim et al.[12] reported squamous cell carcinoma as the most common type. Likewise, squamous cell carcinoma was the most common type in our series. This tumor is composed of a mixture of carcinoma and sarcoma containing differentiated sarcomatous elements such as malignant cartilage, bone, or skeletal muscle. The carcinomatous component is non-small cell lung carcinoma including squamous cell carcinoma, adenocarcinoma, and large cell carcinoma. Sometimes epithelial component is similar to fetal adenocarcinoma. Sarcomatous component involves poorly differentiated osteosarcoma, chondrosarcoma or rhabdomyosarcoma. Epithelial component may be stained by keratin, EMA, and CEA. Chondrosarcoma is positive for S100 protein. Rhabdomyosarcoma shows positivity for muscle markers.

Radiation may lead to sarcomatous changes in carcinosarcomas. Nakajima et al.[5] reported sarcomatous changes in a patient with adenocarcinoma following radiotherapy.

Pulmonary carcinosarcomas are aggressive with a poorer prognosis compared to other pulmonary cancers.

Fishback et al.[13] showed that tumor diameter of larger than 5 cm, disease stage of higher than I, and presence of lymph node involvement had negative effects on prognosis. Rainosek et al.[14] and Koss et al.[6] reported a better prognosis for tumors of smaller diameter and earlier stage. In our series, five patients (71.4%) had lymph node involvement, being N_2 in three patients and N_1 in two patients. The diameter of the tumor was 5 cm or smaller in five patients (71.4%).

Huwer et al.,[2] on the other hand, claimed that the prognosis of PCSs depended on the sarcomatous component rather than the tumor stage. In their patients, they found no significant differences between the survival rates with regard to the stage of the tumor.

Metastasis is frequent in PCSs. Koss et al.[6] reported 25 patients with metastasis. The most common metastasis was to the lymph nodes, followed by the involvement of the kidneys, bones, liver, and brain. In our series, none of the patients required reoperation due to local recurrence or pulmonary metastasis. Distant metastasis was observed in only one patient.

Complete surgical removal of the tumor with negative tumor margins constitutes the desired treatment approach. Although chemotherapy and/or radiotherapy are the other treatment options for these tumors, there is limited information on systemic treatment options. A case report recommended cisplatin and doxorubicin in the treatment of PCS.[15] Nevertheless, the aggressive nature and histological heterogeneity of this tumor renders the treatment difficult. The five-year cumulative survival rate was reported as 49.3% by Petrov et al.[16] and as 43% by Xu et al.[17] However, this rate was reported as low as 21.3% by Koss et al.[6] In our series, the mean survival was 66 months and expected one-year and five-year survival rates were 80% and 57%, respectively.

In conclusion, the optimal approach to PCSs is surgical resection of the tumor. Although the sarcomatous component of the tumor seems to be a highly prognostic factor, the diameter, stage, and lymph node involvement of the tumor are among factors that determine the prognosis. Chemotherapy after radical surgical treatment improves survival.[15]

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