Pulmonary carcinosarcoma with heterologous component: report of two cases with literature review

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Abstract: Carcinosarcoma is an uncommon malignant biphasic tumor that accounts for less than 1% of all lung cancers. It is defined by coexisting histologic elements of carcinomatous and sarcomatous components. We report two cases of carcinosarcoma in a 68-year-old patient and a 78-year-old patient explored for lung masses. Macroscopically, the resected tumors were 7 and 10 cm in diameter. Histologically, they consisted in adenosquamous carcinoma with osteosarcoma in one case and adenocarcinoma with chondrosarcoma in the other case.

Keywords: Carcinosarcoma; lung; histology

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Introduction

Pulmonary carcinosarcoma is a rare and highly malignant lung neoplasm characterized by a biphasic histopathological pattern consisting of both epithelial and sarcomatous components (1-6). It usually affects men, generally heavy smokers, between the fifth and eighth decades of life (2,3). Medical treatment, chemotherapy and radiotherapy are not active in this kind of tumour, so surgery is the treatment of choice. Prognosis is poor with a median survival time of 9 to 12 months after potentially curative surgical resection.

Case report 1

A 78-year-old male, smoker, was explored for chest pain and haemoptysis since one month. The chest X-ray and computed tomography showed a bilobar huge mass involving the upper and lower left lobes with left atrium contact (*Figure 1*). Bronchoscopy demonstrated a large bleeding endobronchial tumor. The biopsy revealed a non small cell carcinoma. A left pneumonectomy with lymph node dissection was performed. Macroscopically, the tumor was large, 7 cm in diameter. Microscopically, it was biphasic composed of carcinomatous and sarcomatous component (*Figure 2*). The carcinomatous component consists in well differentiated adenocarcinoma (*Figure 3A*) and the sarcomatous component of chondrosarcoma (*Figure 3B*) expressing Ps100 (*Figure 3C*). These findings were consistent with carcinosarcoma. There was no lymph nodes metastasis. No extrapulmonary tumor was detected on tumor staging.

The patient received adjuvant chemotherapy. He was still alive 6 months after surgery with no reccurence or metastasis.

Case report 2

A 68-year-old male, smoker, was explored for cough, chest pain and haemoptysis since 1 month. The chest X-ray showed a spiculated tumor shadow in the right upper pulmonary lobe. Chest CT scan found a 6 cm excavated pulmonary mass with in the right upper lobe. Bronchoscopy demonstrated a large endobronchial tumor. The biopsy revealed a non small cell carcinoma.

A right upper lobectomy with lymph node dissection was performed. Gross examination of the resected specimen demonstrated an ill defined, yellowish-white tumor, 10 cm in diameter, containing a necrotic cavity. Histopathological examination showed a biphasic proliferation made of carcinomatous and sarcomatous components. The carcinomatous component consisted in a well-differentiated squamous cell carcinoma with definite keratinization

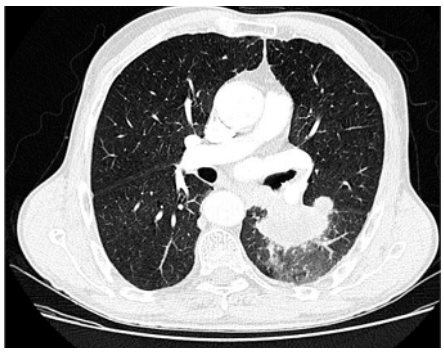

Figure 1 CT scan shows a bilobar huge mass involving the upper and lower left pulmonary lobes with left atrium contact.

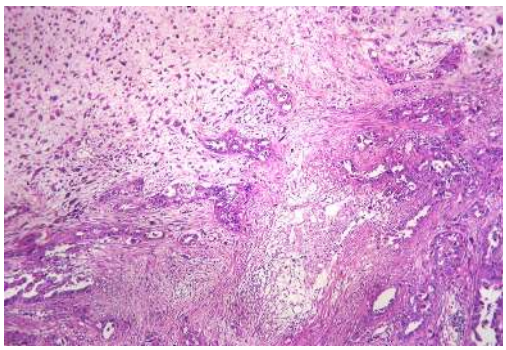

Figure 2 Histology of the tumor demonstrating a mixture of well differentiated adenocarcinoma and heterologous elements of cartilage.

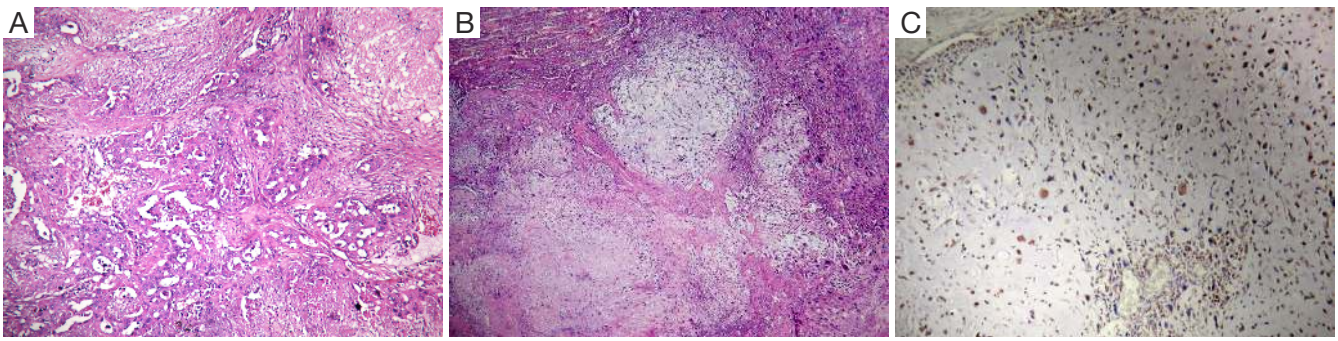

Figure 3 Carcinosarcoma consisting in adenocarcinoma and chondrosarcoma. (A) The carcinomatous component consists of well differentiated adenocarcinoma; (B) the sarcomatous component consist in heterologous elements of cartilage; (C) the chondromatous component express Ps100.

intermingled with areas of fetal adenocarcinoma (*Figure 4A*). The sarcomatous component consisted in sheets of spindle and sometimes giant cells with scanty eosinophilic cytoplasm and highly atypical and frequently mitotic nuclei with osteoid matrix, corresponding to osteosarcoma (*Figure 4B*). These findings were consistent with carcinosarcoma composed of adenosquamous carcinoma and osteosarcoma. There was no lymph node metastasis. No extrapulmonary malignant lesion was detected on tumor staging.

The patient received adjuvant chemotherapy. He is still alive nine months after with no reccurence or metastasis.

Discussion

Pulmonary carcinosarcomas account for less than 1% (0.2-0.3%) of all primary pulmonary neoplasms (1-4,6). The first reported case of carcinosarcoma in the lung is attributed to Kika in 1908 (6). In a retrospective analysis of 2,400 lung cancer patients between 1975 and 1995 conducted by Huwer H *et al.* (2), only seven patients (0.3%) had pulmonary carcinosarcoma. Diaconita reported eight cases among 3,000 patients with malignant pulmonary tumors (3).

The average age of diagnosis is 60 years with men to women ratio of 4/1. More than 90% of the patients have a history of heavy smoking (3). They have also been described with asbestosis (2,6).

The histogenesis of carcinosarcomas remains unclear. The prevailing theories suggest that a single stem-cell lineage exhibits multipotency and differentiates across germ layers into both epithelial and mesenchymal lineages, or that metaplasia of carcinoma into sarcoma cells occurs (3-5).

Clinically, two subtypes have been described: a central endobronchial type and a peripheral invasive type also called parenchymal carcinosarcoma. The endobronchial lesions are usually slowly growing and locally invasive, while the

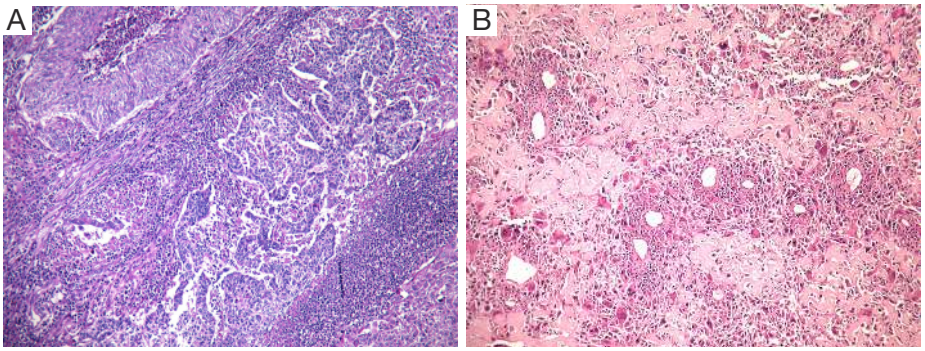

Figure 4 Carcinosarcoma consisting in foetal adenocarcinoma, squamous cell carcinoma and osteosaroma. (A) The carcinomatous component consists of squamous cell carcinoma and foetal adenocarcinoma; (B) component of osteosarcoma. Note the abundant malignant osteoid and cellular pleomorphism.

parenchymal tumors tend to metastasize early and widely.

The radiographic findings consist generally of a solitary huge mass or extensive opacity due to associated obstructive pneumonitis and atelectasis or of the large masses from the associated pleuroparenchymal changes and showed extensive tumor necrosis as well as local invasion. Intratumorous calcifications on CT scans may correspond to ossification in the osteosarcomatous component (2).

According to the 2004 WHO classification of lung tumors, carcinosarcomas are defined as tumors consisting of an admixture of malignant epithelial and mesenchymal elements. It is included in a group of poorly differentiated non-small cell lung carcinomas that contain a component of sarcomatoid differentiation, so called sarcomatoid carcinoma (2,3,5,6).

The carcinomatous component is more often squamous cell carcinoma (69%), followed by adenocarcinoma (20%) and large cell carcinoma (11%). A small cell carcinoma component has been only described in two cases, Tsubota *et al*. and by Huwer H *et al*. (2), whereas the most common mesenchymal component is poorly differentiated spindle cell sarcoma. Foci of rhabdomyosarcoma, osteosarcoma, and chondrosarcoma are often found (3,7).

When heterologous sarcoma elements such as cartilage or skeletal muscle are present, it is easier to confirm the biphasic nature of the tumor, although immunostains can be of further help such as Myogenin and Myo D1 for rhabdomyosarcoma, smooth muscle actin and desmin for leiomyosarcoma, and S100 for chondrosarcoma (3).

Because of this heterogeneity, carcinosarcomas are difficult to diagnose preoperatively. Biopsy of the tumor, especially when centrally located, often shows only one component, and peripheral tumors are difficult to reach endoscopically (3,6,7). The diagnosis was made preoperatively in our second case.

Surgical resection treatment is the most important part of therapy. In addition, radiation is well established and effective. Even if the sarcoma is resected incompletely and the resection margins show residual tumor on microscopy, the rate of local recurrence can be reduced to about 15% by local radiation therapy.

Chemotherapeutic agents; doxorubicin, adriamycin, ifosfamide and dacarbazine, are known to be effective. If distant metastases occur, a combination with chemotherapy is indicated. The overall response rate after systemic treatment of advanced tumors is estimated to be 40% in soft tissue sarcomas (7).

Several investigators maintain that central endobronchial tumors have a better prognosis than do peripheral invasive tumors because of the earlier development of symptoms that leads to earlier medical attention. However, as more cases accumulate, this opinion appears to be true only when the tumor is small (<3 cm) and when no metastases are present (2,8,9).

The prognosis of patients with pulmonary carcinosarcoma is generally assessed as unfavourable, due to the marked tendency of the tumor to metastasize at distant sites and the high rate of local recurrence especially for the sarcomatous component (7).

The metastatic lesions have been described as only carcinomatous in 50%, only sarcomatous in 40% and as both components in 10% lesions (10).

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