

# Spindle Cell Carcinoma of the Lung: Benefits of Immunohistochemical Studies

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## Abstract

Sarcomatoid carcinoma is a rare histologic type of non-small cell lung cancers (NSCLC) which represents only 0.3 to 3% of primitive lung cancers.

In 2004, the World Health Organization (WHO) defined in its classification a new entity, sarcomatoid carcinoma, as “any proliferation that can offer permanently epithelial-mesenchymal morphological transition.”

The term sarcomatoid carcinoma is generic; it includes various entities such as spindle cell carcinomas which are without well-known clinical and immunohistochemical features.

We report the case of a 53-year-old smoker patient, with a history of bullous emphysema discovered 8 years ago and who was hospitalized for exploration of a large pleuro parenchymal mass. The functional signs were dyspnea and alteration of the condition. Percutaneous Computed Tomography (CT) guided biopsy of the mass concluded to a pulmonary spindle cell carcinoma. Staging revealed adrenal nodule with mesenteric and peritoneal invasions. The patient died two months after diagnosis despite an attempt of chemotherapy based on carboplatin/docetaxel.

**Keywords:** Lung cancer; Sarcomatoid carcinoma; Spindle cell; Immunohistochemistry

## Introduction

Sarcomatoid carcinomas are extremely rare tumors which are characterized by biphasic combination of malignant epithelial and mesenchymal cells [1]. The lung is one of several primary sites of these tumors, which may affect the bladder, the colon, the uterus, ovaries and breasts. In 2004, the WHO histologic classification divided sarcomatoid carcinoma of the lung into five subtypes [2]. Their radio-clinical presentations have some characteristics but do not enable doctors to make a positive or differential diagnose. The histopathological study plays an important role in the characterization and classification of these tumors requiring a specific diagnosis and an adequate treatment. To the best of our knowledge, very few cases of sarcomatoid spindle cell carcinomas has been published.

## Case Report

A 53-year-old man, a heavy ex-smoker (smoking 60 packs/year, quitting 3 months ago), with a history of bullous emphysema discovered 8 years ago, presented to the hospital because of a two months history of symptoms of worsening shortness of breath and alteration of the condition (asthenia, anorexia and unexplained weight loss). Physical examination revealed clubbing and thoracic decreased breath sounds at the left pulmonary base and the two apexes. Abdominal examination showed abdominal distending with sloping side dullness.

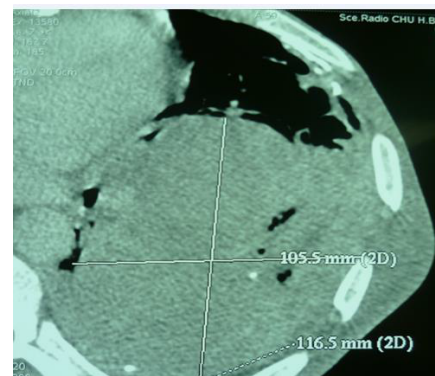
The chest radiograph showed an heterogeneous left hilar axillaire opacity, measuring 11 cm, associated with lucency at both lung apexes more marked on the left and at the left lung base.

Biology showed leukocytosis to 33.770 elements/mm<sup>3</sup> and microcytic hypochromic anemia to 10.3 g/dl.

Bronchoscopy disclosed an extrinsic compression at the left lower lobe bronchus. A chest CT showed a large lingular and left lower lobe mass, with heterogeneous enhancement landscaping central areas of necrosis, measuring 11 × 10 × 14 cm anteroposterior, transverse and cranio caudal diameters (Figure 1). This mass included a collapsed

lingular bronchus and a still permeable lower lobe bronchus. It had invaded the mediastinal pleura, parietal left pericardium and the left lower lobe artery (Figure 2). The analysis of the mediastinum showed right hilar lymph node invasion measuring 20 and 21 mm. All these abnormalities were associated with a significant paraseptal emphysema predominant in the upper lobes (Figure 3).

To determine the histological nature of this mass, a percutaneous CT guided biopsy was performed. Pathological examination revealed



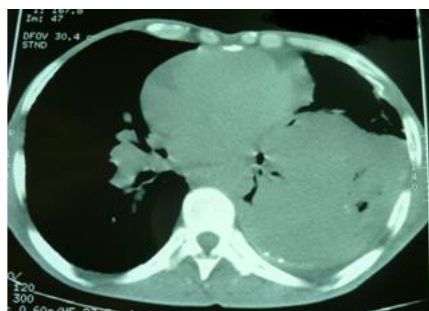
**Figure 1:** Large lingular and left lower lobe mass, with heterogeneous enhancement landscaping central areas of necrosis, measuring 11 × 10 × 14 cm anteroposterior, transverse and cranio caudal diameters.

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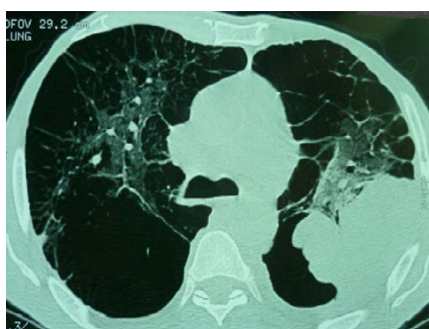
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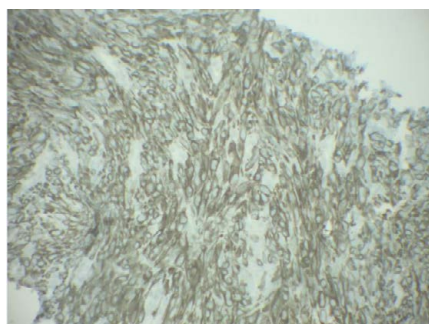
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**Figure 2:** Invasion of the mediastinal pleura and parietal left pericardium and the left lower lobe artery.



**Figure 3:** Significant paraseptal emphysema in the upper lobes.



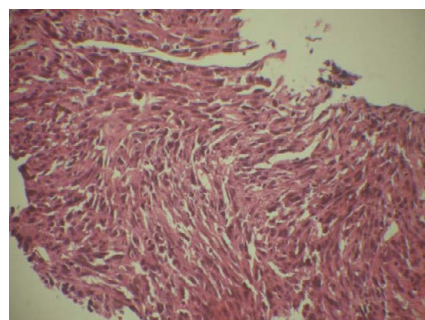
**Figure 4:** Proliferation of atypical spindle cells arranged in fascicles.

a malignant proliferation made of spindle or epithelioid cells (Figure 4). The cytoplasm was scant and the nucleus was hyper chromatic. Mitoses were numerous and atypical. These cells were arranged in short fascicles.

The immunohistochemical study showed positive immunostaining for keratin 7 (Figure 5) and vimentin. Immunostaining for TTF1, calretinen, HBME1 and Keratin 20 were negative. The diagnosis of pulmonary sarcomatoid carcinoma was considered. To stage the disease, a brain scan and an abdominal CT scan were performed and confirmed a right adrenal nodule measuring 25 × 14 mm with mesenteric and peritoneal invasion. Chemotherapy based on carboplatin/docetaxel was started. However, the subsequent evolution was marked by the rapid deterioration of the general condition and our patient died two months after the diagnosis.

## Discussion

Lung sarcomatoid carcinomas are rare tumors representing 0.3 to



**Figure 5:** Tumor cells were positive for Keratin 7.

3% of all primitive lung cancers [3]. They represent an heterogeneous group including NSCLC containing a sarcoma or sarcoma-like component [4]. According to the WHO classification in 2004, five different subtypes have been recognized: pleomorphic carcinoma, spindle cell carcinoma, giant cell carcinoma, carcinosarcoma and pulmonary blastoma [2].

Clinically, these tumors have a similar presentation to other NSCLC. Although difficult to use for positive or differential diagnosis, several common features of sarcomatoid carcinomas may be mentioned [5]. Patients are predominantly male (sex ratio of 4/1). The mean age at diagnosis is higher (65-70 years) with an age bracket of 30 years to 85 years. All patients are heavy smokers or ex-heavy smokers. A significant proportion of patients is symptomatic at diagnosis and depend on the location of the tumor. In cases of proximal tumors, symptoms are especially cough, hemoptysis (50% of cases), progressive dyspnea or recurrent pneumonia due to bronchial obstruction [3]. Whereas, in peripheral tumors, chest pain was often described, especially in pleomorphic carcinomas (25% of cases) [6].

Radiologically, sarcomatoid carcinomas are often presented as a single large lesion, measuring 2 cm to 18 cm in diameter (mean of 7 cm), with peripheral location and often in the upper lobes. A pleural, parietal and / or vascular invasion is frequent (40-70% of cases) [6] as our case.

At gross exam, sarcomatoid carcinomas are morphologically very variable reflecting the heterogeneity of the different subtypes. Thus, peripheral tumors are often greater than 5 cm, well demarcated and unencapsulated. The cut sections show that these tumors are grey-yellow with mucoid or hemorrhagic necrosis. Whereas proximal tumors are often endobronchial, sessile or pedunculated and smaller, with infiltration of the adjacent lung parenchyma.

The histopathological diagnosis of sarcomatoid carcinoma is difficult. The preoperative diagnosis of sarcomatoid carcinoma is unknown in nearly 60% of cases [6]. Different morphological components must be mentioned in the final histopathological report.

The immunohistochemical expression of epithelial markers in spindle and giant cells is not required for the diagnosis of sarcomatoid carcinoma if there is an epithelial and differentiated component type [7].

In other cases, the expression of cytokeratin and epithelial membrane antigen (EMA) are needed to highlight the epithelial cells in the sarcomatous component. The expression of cytokeratin-20 and surfactant protein-A is consistently negative [8] in contrast to the expression of TTF-1 and keratin-7, which can be found in the spindle and giant cells in respectively 55% and 70% of patients. In our case,

immunohistochemical study showed positivity for vimentin and keratin 7 whereas immunostaining for TTF1 was negative.

Besides its importance for positive diagnosis, the immunohistochemical study may play an essential role in the differential diagnosis especially in cases of mesotheliomas or sarcomas [9].

Sarcomatoid carcinomas are known to be aggressive tumors [10]. In fact, systemic metastases occur early, not only in the usual NSCLC metastatic sites (brain, bone, liver), but also in unusual sites such as the esophagus, the small intestine, the peritoneum, the subcutaneous tissue and the kidney [11].

Therapeutic alternatives are similar to those of other NSCLC. In the early stages, most series reported in the literature are surgical. Surgery may provide sufficient local control [12]. The role of adjuvant therapy is difficult to assess due to the lack of controlled prospective series. However, the frequency of parietal, mediastinal and vascular involvement and early local relapse make eligible the indication of chemotherapy and radiotherapy, as recommended for other NSCLC [13]. Accurate modalities of adjuvant radiotherapy or chemotherapy are not detailed in the available publications, and their effectiveness is difficult to assess, especially in terms of local or systemic control. Overall survival remains worse than other NSCLC, even after adjuvant therapy.

In metastatic stages, cytotoxic agents reported to have been used are identical to those used for NSCLC. No response, even partial has been reported. In some published cases, the association Adriamycin/cyclophosphamide/vincristine is indicated with a rationale based on obtaining cytotoxicity in both epithelial and pseudosarcomatoid components. Tumor control rates remain low [14]. A recent Japanese observation reported a response to carboplatin, paclitaxel, and bevacizumab [15].

The indication of inhibitors of the tyrosine kinase of the EGFR in sarcomatoid carcinoma is limited. No activating mutation of EGFR has been demonstrated in limited series.

The prognosis of these tumors remains a subject of controversy. In fact, some reports suggest a poor prognosis [16] and others show no difference with other NSCLC. This controversy is due, on the one hand, to the small number of studies focusing on the prognostic aspect, and on the other hand, to the small-sized studies with limited information about evolution. Among these studies, Fishback et al. [16] identified some prognostic factors such as tumor size >5 cm, mediastinal, lymph node involvement and advanced tumor remains as in the majority of NSCLC main prognostic factor. Other factors such as pleural invasion and sarcomatoid portion (> 50% tumor volume) were discussed in the study of Nakajima et al. [7]. However, the histologic subtype epithelial-predominant adenocarcinoma, squamous cell carcinoma, or large cell carcinoma has not been retained as significant prognostic factor.

As in all NSCLC early detection, accurate diagnosis and complete surgical resection are predictors of better survival.

The median disease-free survival is shorter compared to other types of NSCLC. It is between 6 and 8 months, with rare local recurrences (15% of all recurrences [17], and often systemic, occurring in more than 60% of the patients. The median overall survival is between 6 and 20 months, with a 5-year survival less than 10-20% [6].

## Conclusion

Sarcomatoid carcinomas are aggressive tumors occurring mainly in male smokers. Given the lack of specific tests for the early detection, diagnosis of these tumors is often made when therapy resources are no longer effective. These advanced stages are due to systemic extension with frequent unusual metastases.

The prognosis of these tumors is more reserved than in other NSCLC because of their greater aggressiveness, high metastatic potential and chemoresistance.

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