# Solitary Fibrous Tumors of the Pleura: Report of Eight Cases and Literature Review

A Huaringa, N Zetola, M Naro

**Citation**

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**Abstract**

Primary pleural tumors have been classified as diffuse or localized types. The diffuse type or malignant mesothelioma (MM) is the most frequently encountered lesion. Localized variety is less frequent and defined.

Although its hystogenesis is not well established, new histological and immunohistochemical techniques are giving us a better understanding of it. Now, the common consensus is that this tumor origins from a primitive submesothelial mesenchymal cell (16,17,18,19).

Concerning the advances done during the last decade in the understanding, imaging, diagnostic and therapeutic approaches to this rare tumor, we decided to conduct a retrospective study of the cases seen at our institution and a review of the available English literature.

## INTRODUCTION

Primary pleural tumors have been classified as diffuse or localized types. The diffuse type or malignant mesothelioma (MM) is the most frequently encountered lesion. Localized variety is less frequent and defined. First classified at 1931 by Klemperer and Rabin as a localized primary pleural neoplasm ([1]), this neoplasm has been reported under different names, including benign mesothelioma, fibrous mesothelioma, submesothelioma, solitary or localized mesothelioma, or subserosal fibroma. The term “solitary benign fibrous tumor of the pleura” is now preferred because histologically these tumors do not have epithelial cells, but is thought that derives from a primitive submesothelial mesenchymal cell with fibroblastic differentiation. We also prefer to avoid using the term benign because of the malignant behavior of some of them.

The solitary fibrous tumor of the pleura (SFTP) arises from the visceral pleura in around 70% of the cases ([2]). However have been reported cases in the peritoneum and pericardium ([2,3,4,5]), lung parenchyma, paranasal sinuses, mediastinum, nose and tunica vaginalis among other sites ([2,5,6,7,8,9,10,11,12,13,14,15]).

Although its hystogenesis is not well established, new histological and immunohistochemical techniques are giving us a better understanding of it. Now, the common consensus is that this tumor origins from a primitive submesothelial mesenchymal cell ([16,17,18,19]).

Concerning the advances done during the last decade in the understanding, imaging, diagnostic and therapeutic approaches to this rare tumor, we decided to conduct a retrospective study of the cases seen at our institution and a review of the available English literature.

## MATERIALS AND METHODS

Eight cases of Solitary Fibrous Tumor of the Pleura (SFTP) were identified from the computer database of our institute from 1990 to 1999. The medical records were reviewed and follow-ups were obtained when it was possible. The clinical relevant information was taken directly from the charts. The chest x-rays, CT scans and pathological lectures were taken from charts and newly reviewed by a pulmonologist and pathologist respectively. All tissues were routinely processed and stained. One of them was examined by electron microscopy. Although there are not well-established criteria for malignancy still available, we considered a SFTP to be malignant if it has high cellularity with crowding and overlapping of nuclei, more than 4 mitotic figures (mf) per 10 high powered fields (hpf), or pleomorphism based of nuclear size, irregularity, and nucleolar prominence ([2]). All

cases were strongly positive for vimentin and CD34 and remained negative for keratins. Other immunohistochemestry is described when it was available.

## RESULTS

### CLINICAL FINDINGS

From our 8 patients, 4 were male and 4 were female, ranging between 31 and 76 years old (mean 52.25) at the time of diagnosis. Most of them were Caucasians (7 patients) and only one Latin. Although is described that most of the patients are usually asymptomatic ([2,20,21]) only 3 of our patients were diagnosed with a routine chest x-ray. The symptoms referred by the others were shortness of breath (2 pts), mild chest pain (2 pts), cough (1 pt), severe weakness (not related to hypoglycemia) in 1 patient, and arthritis (1 pt). There were not referred weight loss, hemoptysis, hypoglycemia, fever or night sweats by any patient. The physical exam was unremarkable in most of them (7 pt); finding rales, diminished breath sounds, and tubular sound only in one. Five patients had history of hard tobacco exposure and one of these had also history of asbestos exposure. It is important to mention that this patient was the only one who had recurrence and one of the most aggressive behaviors although all its immunochemical markers were coincident with SFTP. Other epidemiological information and laboratory data were noncontributory.

### RADIOGRAPHIC FINDINGS

The radiographic appearance of each patient varied depending on the size and particular characteristics of each tumor. The lesions tend to be more frequent at the bases, finding 5 in the left side and 3 in the right (2 metastases were also found in right hemithorax). The size of the tumors ranged from 1 to 20 cm at the CXr and from 2 to 22 cm at the CT scan, having a good correlate with the size observed at the pathology (2 to 22 cm). The tumors were homogeneous, usually lobulated, sharply delineated and solitaries (in 7 cases), showing intermediate and high attenuation at the CT. There was not possible to detect calcifications at the CXr of any patient, although the CT detected them in 2 patients and the pathology showed them in 3 cases. The CT was also more sensitive detecting the pedicles, encapsulation and attachment to soft tissues. Only the patient 1 had pleural effusion. All this 7 tumors had an obtuse angle within the chest wall suggesting its chest wall origin. The patient number 1 (who had the malignant aggressive tumor) had a radiographic pattern that differed from all others. It seemed to be more diffuse and heterogeneous at the CT, with apparent soft tissue invasion. It also was the only one that showed metastases to the diaphragm and pericardium.

### PREOPERATIVE DIAGNOSIS

Five of our patients underwent a fluoroscopically guided trans-thoracic fine needle biopsy (FNAB). Based on the cytologic study, the correct diagnosis could be established only in one patient. One case was incorrectly diagnosed as a high-grade osteogenic sarcoma by a pathologist from other institution. There was not possible to establish any diagnosis in the rest. Bronchoscopy was done in 2 patients and was non-contributory in both.

### PATHOLOGY

### GROSS FINDINGS

The lesions were widely distributed, tending to be at the bases of the thorax. The tumors were solitary in 7 patients, showing metastases in one. The smallest tumor was 2 cm in greatest diameter and the largest one was 22 cm. The mean diameter was 9 cm. All tumors were encapsulated and almost all pedunculated (6 cases). The capsule was sharp circumscribed as it was described at the CTs. Neither of the malignant cases (2 pt) had pedicle. The pedicles were very vascular. Attachment to soft tissues was observed in 2 cases and one of infiltrated them. Cut section often revealed a firm white, gray, or brown surface. Hemorrhage necrosis and myxoid degeneration was observed in the case #1. Only one other case had necrosis, and none other one had either hemorrhage or myxoid degeneration. Some cases had also little cystic formations.

### LIGHT MICROSCOPIC FINDINGS

### IMMUNOHISTOCHEMICAL FINDINGS

All our cases were strongly positive for CD34 and vimentin and remained negative for keratins. From those, 6 were diffusely positive and the other one presented a focally positively reaction. Other markers were only available for patients 1,2 and 5. The case 1 was also positive for VIM, p53 and Ki-67 (30%). None of these 3 patients were positive for keratins, CAE, SMA, C31, S-100, actin or desmin.

## DISCUSSION

### EPIDEMIOLOGY

Giving the rarity and usually asymptomatic presentation of this neoplasm, its incidence is not well known. An incidence of 2.8 cases per 100,000 registrations was reported by Okike et al. ([21]); however, only among 650 cases have been

reported so far. The SFTP could presents in a wide age range. Pediatric cases have been reported ([2,22,23]), but over half of the cases are seen during the 6th and 7th decades of life, with a median age between 51 to 57 ([2,20,21]). Coincidentally with our results, there is no significant sex predominance,. Most series show it to be more prevalent among Caucasians, but none good study proves it. Its geographic distribution is still not studied. This tumor is not related to asbestos and there is no history of exposure to other industrial pollutants. Few cytogenetic studies have associated the SFTP with trisomy 8 ([24]) and some specific translocations ([25]) but its relationship is still unclear.

## HISTOGENESIS

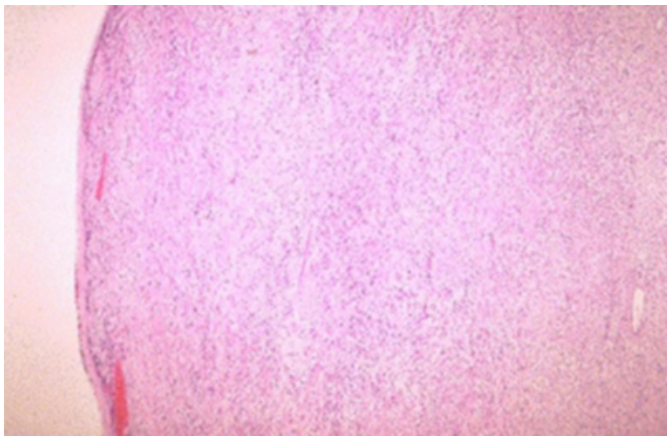
Stout and Sano (1942 and 1950 respectively) suggested in different studies the mesothelial origin of this neoplasm ([26,27]). They reported that cultures of fragments this fibrous tumors produce cells similar to the mesothelial ones. Latter, studies based on ultrastucturaly analysis resulted in the same conclusion ([20,28,29,30]). However, also based on previous ultrastuctural analyses, in 1979 Dalton et al proposed a submesothelial origin of this neoplasm, based on its ability to differentiate into superfitial mesothelium, non-mesothelial cells, or fibroblast-like cells ([16,17]). After that, Burrig et al observed the presence of mesenchymal undifferentiated, immature fibroblasts and mature fibroblasts on biopsies of this tumor ([18]). As is discussed above, actual immunohistochemical studies are also against the mesothelial origin. However, although these immunohistochemical studies define a population of cells able to be the precursor of this neoplasm, they still do not point the exact cell origin ([19]).

## CYTOLOGY

The cytology of these tumors shows different degrees of cellularity and include 2 cell populations (Picture 1): sheet and clusters of mesothelial cells, and singly dispersed or loosely cohesive spindle cells ([31,32]).

**Figure 1**

Picture 1: Fibrous tumor of the pleura: Histology



The benign cases tend to show greater degree of cohesion, with many bland-appearing, ovoid spindle cells with mostly naked nuclei or scant cytoplasm arranged in clusters. The nucleoli are usually inconspicuous and there is appreciable low grade of mitotic activity. Cell blocks show collagen with spindle cells juxtaposed ([31]). There has also been proposed the presence of transitional forms between epithelioid and spindles cell ([33]) as a characteristic feature. The immunoreactivity to specific markers can also help in the diagnostic process. The malignant cases tend to show greater degree of cellularity, fewer cohesive clusters, and larger number of single cells. The nucleoli are usually prominent and moderate degree of nuclear pleomorphism is present. Mitotic figures are not as notorious at cytology as at histology ([31]). All cases (benignant and malignant) are involved in a bloody and collageous background ([31]).

Although some authors suggest cytology as a good diagnostic method ([32,34,35,36,37,38,39]), neither the cytologic characteristics nor the malignancy diagnostic criteria are well established. The value of cytology is still under debate.

## HISTOPATHOLOGY

The distinctive histologic features of this tumor are usually not enough to exclude other processes in the differential diagnosis ([40]). Microscopically, this neoplasm is diagnosed and classified based on its pattern, degree of pleomorfism, mitoses and angiogenesis ([41]). Its microscopic patterns have been grouped as solid-spindle (the “patternless pattern”, or the hemangiopericytoma-like appearance), and the diffuse-sclerosing pattern ([31,32]); both presenting most of the times with a very low mitotic rate (less than 1 mf per 10 hpf). However, because of its nonspecific morphologic patterns and the absence of distinctive electron microscopic features,

the SFTP could be very difficult to differentiate from other spindle cell neoplasms. It could mimic features of many mesenchymal processes such as fibromatosis, synovial sarcoma, fibrous histiocytoma, fibrosarcoma, or smooth muscle, neural neoplasms, and hemangiopericytomas ([40,42]). Classically the diagnosis was made based on the histologic appearance and the lack of reactivity to the markers for other tumors (S-100, EMA, keratin, LeuM1, and others). However, this lack of reactivity was usually difficult to interpret because antigen loss could also be responsible for the negative reaction. Until few years ago, many immunohistochemical studies failed to identify a positive marker for the SFTP ([40]), making the diagnosis of the SFTP uncertain. One of the first positive markers recognized was vimentin (VIM). However this finds lacks of diagnostic value, since most mesenchymal and some epithelial neoplasms are also positive. Latter, Westra et al. ([43]) and van de Rijn et al. ([40]) proved in two different studies that CD-34 (a marker first described in hematopoietic stem cells, vascular and smooth muscle tumors) is a good positive marker for the SFTP ([40,44]).

The criteria of malignancy are still not well established and the prognosis correlate of the histologic features is not clear. At the first big case review, Briselli et al. ([20]) found that that the best indicator of malignancy was the infiltration of the tumor to the surrounding tissues. In the other side, England et al. found that a high mitotic rate (more than 4 mf per 10 hpf), a high cellularity and pleomorphism correlate with the patient survival, although the best prognostic indicator was the complete resectability of the tumor ([2]). Encapsulation and pedunculation of the tumor have also been proposed as prognostic factors. Aggressive behavior and metastases has been reported in many tumors that didn't have microscopic features of malignancy. Based on the available data most experts believe, as Briselli et al, that lack of cellular atypia, mitosis and pleomorphism does not exclude malignancy.

## CLINICAL FEATURES

The most usual presentation is as an asymptomatic mass, discovered incidentally in a routine CXr (36 to 53% of the cases) ([20,21]). When present, mild chest pain, shortness of breath and cough are the most frequent symptoms. Hypoglycemia, weight loss, weakness, arthralgias, pulmonary osteoarthropaty, hemoptysis, fever and night sweats have also been described ([2,20,45,46]). Symptoms usually resolve when the tumor is resected. The hypoglycemia has been attributed mostly to the intrinsic production of Insulin Grow Factor I (IGF-I) ([47,48,49]). The physical exam is usually unremarkable and findings are mostly related to the mass effect. The clinical behavior of SFTP is still not well known ([50]). Most of these tumors are histologically benign (88%). However, rapid enlargement, local recurrences and local and distant metastases have been described among them ([37,38,45,51]). Malignant tumors are rarely pedunculated, often presenting in atypical locations (lung fissures, mediastinal pleura or intraparechymals), and are frequently greater than 8 cm ([20,21,52,53]). Rapid enlargement, local recurrences and local and distant metastases are more frequent in this group.

## DIAGNOSIS

## PLEURAL FLUID

Clinically significant pleural effusion is rare in the SFTP. Fluid production is seen in less than 10% of the patients ([2,20]) and usually associated with malignant lesions. However cases with huge pleural effusions has been reported ([2,20,54]). Usually these effusions are exudates, but may also be a transudate. Some authors have proposed that the pH could be of diagnostic and prognostic value separating SFTP from MM ([55]). Pleural fluid analysis and cytology have not proven diagnostic ([21]) and more reports are necessary before establishing the value of them as a useful diagnostic and prognostic tool.

## IMAGING

a) Chest X-rays and CT Scan

Usually CXR and CT are the imaging studies of choice. CXR usually shows a sharply well circumscribed nodule or mass lesion (Picture 2 and 3) forming an obtuse angle with the chest wall, suggesting its pleural origin.

**Figure 2**

Picture 2: Fibrous tumor of the pleura: Posterior-anterior view of a chest radiograph showing a mass in the right cardiophrenic angle.

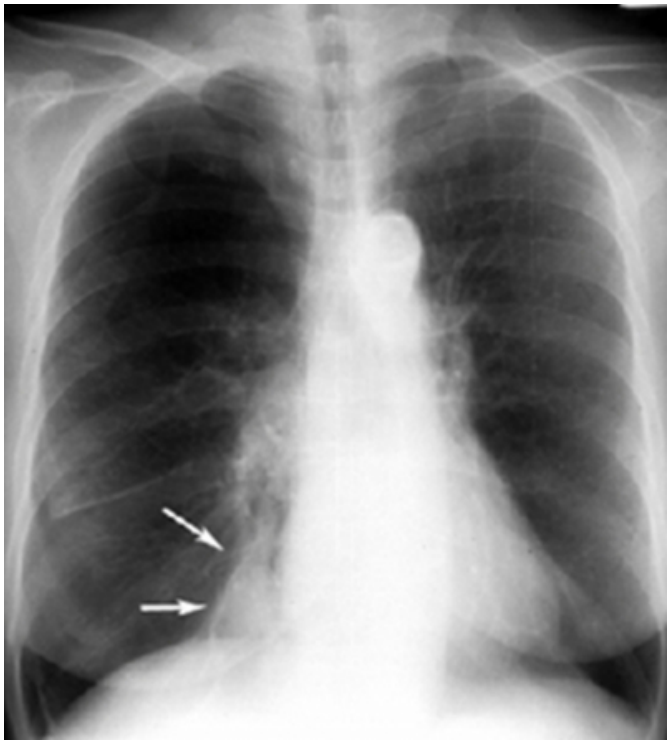
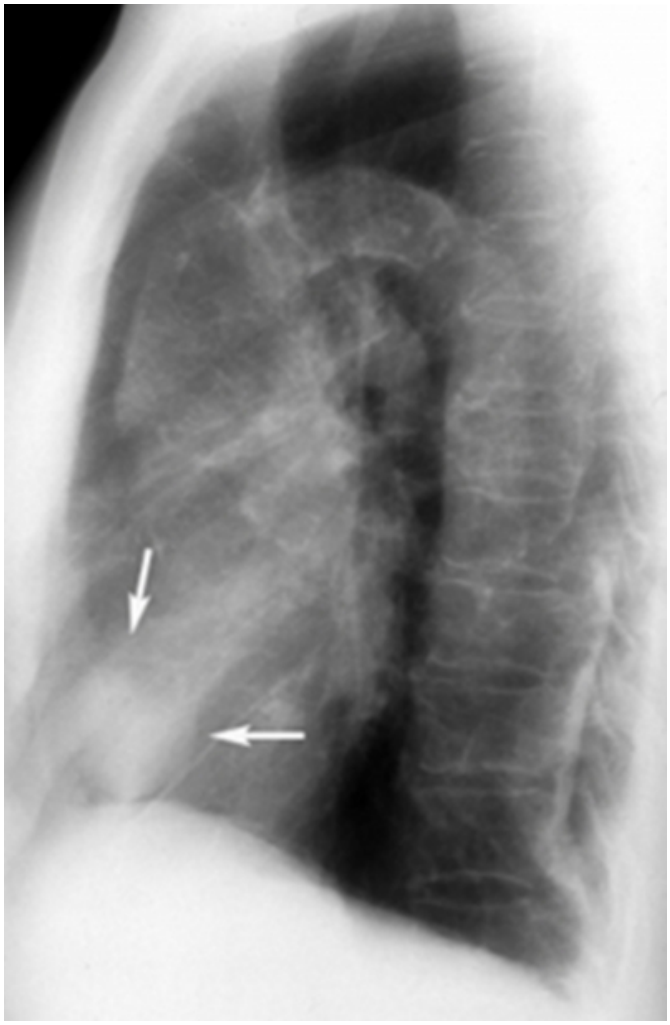


**Figure 3**

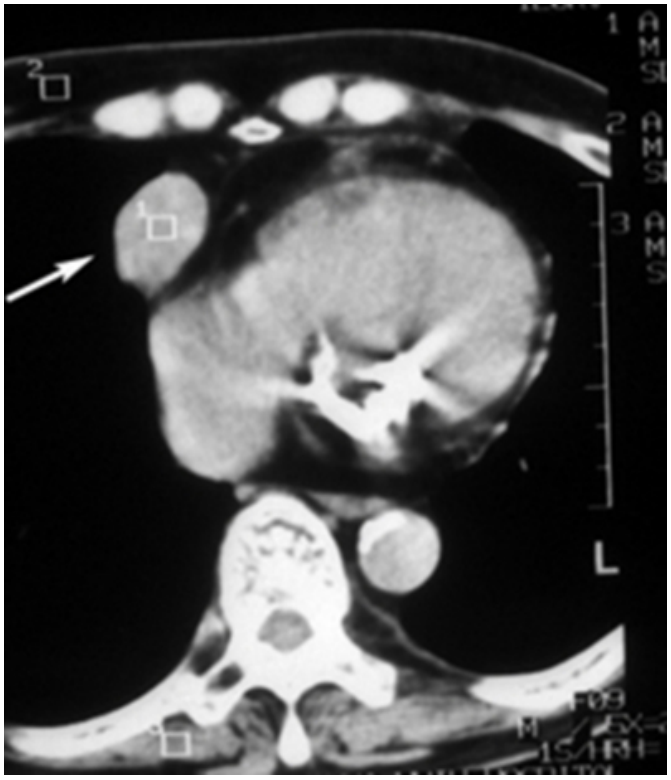
Picture 3: Fibrous tumor of the pleura: Lateral chest radiograph in the same patient as in Picture 2.



At the CT scan, the tumors appear as circumscribed lobulated lesions (Picture 4). Usually an intermediate attenuation on unenhanced CT and high intensity on enhanced scans is observed ([56]). Low attenuation is seen in relation to myxoid degenerated or hemorrhages areas ([56]). Cystic degeneration appears as cystic fluid attenuated areas on the scans ([56]). The pedicle could be observed and provide a clue in the diagnosis ([57]). Calcification areas are not frequent.

**Figure 4**

Picture 4: Fibrous tumor of the pleura: Chest CT scan of the same patient as in pictures 2 and 3. The arrow points at a pedunculated pleural noncalcified soft tissue mass.



b) RM and Angiography

RM the tumors are usually of intermediate to low signal intensity on T1 and of low signal intensity on T2 or proton density-weighted images ([58,59]). After the gadolinium administration intense enhancement has been reported ([60]). RM is also helpful for assessing possible vascular invasion, although angiograms are more definitive. Angiograms are the imaging studies of choice for finding the mayor feeding vessels, which could be used for embolization before surgery. However, unlikely the findings on the CT scan, the RM and angiography are nonspecific.

c) Others

The utility of other imaging and invasive procedures as gallium scan or bronchoscopy is very limited in this entity and is only limited to exclude the presence of other lesions and to rule out another diagnosis. Gallium uptake has been reported ([61]).

## FINE NEEDLE ASPIRATION BIOPSY (FNAB)

The value of this diagnostic procedure is still under debate. Accordingly to some authors, FNAB can yield characteristic morphologic that permit the diagnosis([31,39,62,63,64,65]). However, other authors think this technique is neither sensitive nor specific for this purpose ([2,37,38,39,53,64,66]). The difficulty at the diagnosis with FNAB is mainly because of the impossibility to distinguish between reactive mesothelium and the well-differentiated malignant cells and because of lack of well defined cytologic criteria for the diagnosis ([41]). Based on the available data, FNAB is not routinely recommended since usually do not permit a definitive diagnosis and do not modify the therapeutic approach.

## TREATMENT

When possible, surgery is always the treatment of choice for primary tumor and recurrences. The entire tumor should be removed. Although most of them could be encapsulated and well circumscribed, some authors recommend large resections of lung parenchyma and surrounding pleura, especially for those presenting a broad base of attachment to the pleural surface ([67]).

Adjuvant chemotherapy and radiotherapy have been tried, especially for malignant cases. However there is not enough evidence and its benefits remain unproved.

## PROGNOSIS

On a review of 52 patient Okike et al. reported 8 patients with malignant SFTP. All of these patients had recurrence or metastases between 6 month and 8 years of follow up. Besides, local recurrence (even after complete resection) has been reported as late as 17 years after the surgery ([21]). Based on this information, although the prognosis of this entity is usually good, close follow-up should be done for years after resection, especially for the cases with malignant behavior.

## CORRESPONDENCE TO

Armando Huaringa, MD, MHA, FACP, FCCP, FCCM
Associate Professor of Medicine
Loma Linda University School of Medicine
White Memorial Medical Center
1720 Cesar Chavez Ave. Los Angeles, CA 90033, USA
Telephone: (323) 260-5802

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## Author Information

**Armando J. Huaringa, M.D.**
The University of Texas M. D. Anderson Cancer Center

**Nicola Zetola, M.D.**
The University of Texas M. D. Anderson Cancer Center

**Manuel H. Naro, M.D.**
Department of Medicine, White Memorial Medical Center