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The incidence, clinical features, differential diagnosis, and treatment of solitary fibrous tumors of the pleura are reviewed.

Solitary Fibrous Tumor of the Pleura

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Background: *The solitary fibrous tumor of the pleura (SFTP) is a rare primary tumor arising from mesenchymal cells in the areolar tissue subjacent to the mesothelial-lined pleura. Only about 800 cases have been reported in the medical literature. The tumor appears to be unrelated to malignant pleural mesothelioma, the most common primary tumor of the pleura.*

Methods: *In just over half of these cases, the neoplasm presents as an asymptomatic mass, is often quite large, and is benign in 78% to 88% of patients. The initial evaluation and diagnosis, tumor classification, surgical treatment, results of therapy, and long-term prognosis are reviewed, based on a selective review of the literature from MEDLINE beginning 1980.*

Results: *Complete en bloc surgical resection is the preferred treatment of benign and malignant varieties of the tumor. The pedunculated tumors attached to the visceral pleura can be effectively treated with a wedge resection of lung. Sessile tumors arising on the lung require a larger lung resection. Sessile tumors on the chest wall require wide local excision, often with chest wall resection because of their propensity for local recurrence. Adjuvant therapy remains controversial in SFTP.*

Conclusions: *Benign SFTP has a high cure rate and an 8% local recurrence rate that is usually amenable to curative re-excision. Malignant SFTP, especially the more common sessile type, has a 63% recurrence rate even with complete resection. The majority of patients with recurrent disease die of the tumor within 2 years. Nevertheless, the overall long-term cure rate for all patients is 88% to 92%.*

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Submitted March 28, 2006; accepted June 14, 2006.

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Abbreviations used in this paper: SFTP = solitary fibrous tumor of the pleura.

Introduction

Primary tumors of the pleura present grossly as either diffuse or localized neoplasms. The tumors with a diffuse pattern, known as diffuse pleural mesotheliomas arising from the mesothelial cells lining the pleura, are usually highly malignant and are commonly associated with asbestos exposure. The less common localized tumor, now known as a solitary fibrous tumor of the pleura (SFTP), appears to arise from the submesothelial

mesenchymal layer.¹ In earlier years, controversy about the origin of this uncommon tumor led to a variety of terms applied to the neoplasm including localized pleural mesothelioma, pleural fibroma, localized fibrous mesothelioma, submesothelial fibroma, and localized fibrous tumor.² However, advances in immunohistochemistry and electron microscopy have led to the localized tumor being specifically named a SFTP and have clarified its status as a separate tumor from the more lethal pleural mesothelioma.¹

SFTP was probably first mentioned by Wagner³ in 1870, but the first pathologic description did not appear until 1931 by Klemperer and Rabin.² The first large collected review series of SFTP describing the clinicopathologic features of the neoplasm subsequently appeared in 1981 by Briselli et al⁴ (368 cases) and in 1989 by England et al⁵ (223 cases). Subsequent series have refined our understanding of the clinical behavior of this somewhat unpredictable tumor.

Incidence

SFTP is a rare neoplasm, with fewer than 800 cases reported in the literature.² This contrasts with the most common primary pleural tumor, diffuse mesothelioma, with an incidence of 3,000 new cases yearly in the United States.⁶

The SFTP appears to arise from the noncommitted mesenchymal cells in the areolar tissue subjacent to the mesothelial-lined pleura. With the strong immunohistochemical evidence for a mesenchymal cell origin for SFTP, it should be no surprise that similar solitary fibrous tumors have been reported to arise primarily in extrathoracic locations, including the meninges, nose, oral cavity, pharynx, epiglottis, salivary gland, thyroid, breast, kidney, bladder, and spinal cord.²

Although SFTP occurs in a wide age range (5 to 87 years), it predominantly occurs in the sixth and seventh decades of life with a fairly equal frequency in both sexes.⁷ Only one report of the familial occurrence of SFTP in family members has been published, involving a mother and her daughter.⁸ Generally, there is no apparent genetic predisposition for the tumor and no relationship to exposure to asbestos, tobacco, or any other environmental agent. Cytogenetic data on SFTP are sparse and show scattered various abnormal karyotypes, although a supernumerary chromosome 8 suggests a more malignant behavior of the tumor.⁹

Clinical Features

Symptoms

The majority of patients present with some symptom, commonly cough, chest pain or dyspnea (Table 1).^{5,10,11}

Table 1. — Incidence of Symptoms in Patients With Solitary Fibrous Tumor of the Pleura

	Okike et al ¹⁰ 1978 (n = 52)	England et al ⁵ 1989 (n = 138)	Sung et al ¹¹ 2005 (n = 63)
Asymptomatic	54%	67%	43%
Cough	33%	12%	8%
Chest pain	23%	19%	17%
Dyspnea	19%	11%	25%
Fever	17%	1%	2%
HPO	19%	—	2%
Weight loss	6%	2%	3%
Hemoptysis	2%	—	—
Pneumonitis	2%	—	—

HPO = hypertrophic pulmonary osteoarthropathy

Patients with benign SFTP have symptoms 54% to 67% of the time, while over 75% of malignant tumors cause symptoms.⁷ The larger the tumor, the more likely that symptoms will be present.

Chest pain occurs more commonly in the patient whose tumor arises from the parietal pleura. Occasionally, the larger tumor causes compression of a bronchus and leads to atelectasis with symptoms or, rarely, hemoptysis. Paraneoplastic syndromes may occur but are more likely seen in patients with larger tumors.

Hypertrophic pulmonary osteoarthropathy (HPO) is the most common paraneoplastic syndrome in SFTP. HPO is reported in up to 22% of patients (especially in tumors over 7 cm in diameter)⁴ compared to a 5% incidence in lung carcinoma.⁷ Patients with HPO commonly report bilateral arthritic-like symptoms, including stiffness or swelling of the joints, edema of the ankles, arthralgias, and pain along the long bones, especially in the tibiae from periosteal elevation. They also may report clubbing of the fingers and toes and, rarely, gynecomastia or galactorrhea.

The causes of HPO and clubbing are unknown.⁷ The HPO symptoms generally resolve dramatically after removal of the tumor, often within hours to a few days, suggesting it is caused by a short-lived ectopic hormone commonly believed to be a growth hormone-like substance. Osseous radiographic changes and the clubbing may take months to resolve after tumor resection. Recurrence of symptoms may herald recurrence of the tumor.

The incidence of severe symptomatic hypoglycemia in SFTP patients is low at 3% to 4%.^{4,7} A number of other diverse mesenchymal tumors, such as neurofibroma, rhabdomyosarcoma, leiomyosarcoma, liposarcoma and others, may infrequently manifest symptomatic hypoglycemia. The mechanism causing this symptom is likely the tumor-producing nonsuppressible insulin-like active substances and insulin-like growth factors. Relief of the hypoglycemia occurs rapidly after complete tumor removal.

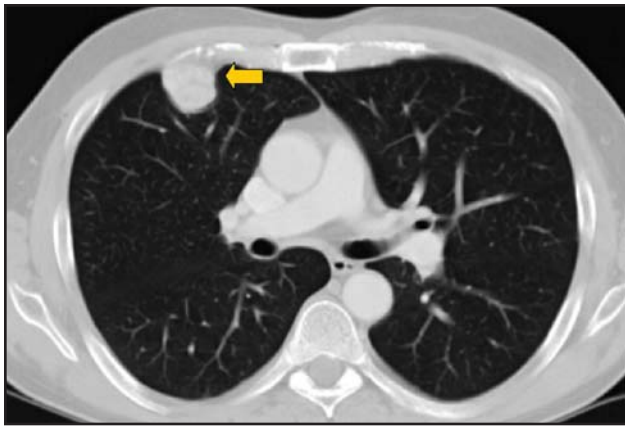


Fig 1. — Computed tomographic scan image, just inferior to the level of the carina, of a 3.3-cm diameter benign sessile SFTP attached to the parietal pleura on the right third rib. The arrow shows the typical obtuse angle that a pleural-based mass makes with the pleural surface. The tumor was resected along with the underlying rib and cartilage with chest wall reconstruction carried out with a rigid methylmethacrylate/Marlex prosthesis.

Physical Signs

In patients with SFTP, few (if any) physical signs are commonly present. A large tumor may cause enough lung compression to result in wheezing, dullness to percussion, or decreased breath sounds in the affected hemithorax. Clubbing is the most frequent physical finding in SFTP in the few patients (2% to 19%) who present with HPO. Clinically, the distal phalanx is enlarged and widened, with the characteristic spongy sensation on depression of the proximal nail bed. The etiology of clubbing is unknown, but the finding is associated with arteriovenous anastomoses in the distal fingers along with periosteal new growth and lymphocytic and plasma cell infiltration of connective tissue in the nail beds. Although patients with a variety of nonneoplastic pulmonary disorders, such as emphysema and idiopathic pulmonary fibrosis, may show clubbing, these benign conditions rarely show signs of the arthropathy of HPO.⁷

Radiographic Features

The usual initial diagnostic test for SFTP is a chest radiograph, which is not specific but serves to document the presence of a mass in the chest. The lesion can vary in size, and it commonly has well-circumscribed margins. It is usually located near the lung periphery or in the projection of an interlobar fissure. Tumors arising as a parietal chest wall mass typically produce at least one obtuse angle with the pleural surface, shown by the arrow in Fig 1. Unfortunately, only one third of the parietal pleural-based masses demonstrated an obtuse angle.¹²

The chest computed tomography (CT) scan is the key examination, which more clearly shows the size and location of the tumor and aids in surgical planning. Both the benign and malignant varieties of SFTP usually appear as well-delineated, often lobulated masses that are usually heterogenous in attenuation.¹² Most SFTPs arise from the visceral pleura and half are pedunculated. Some tumors are located in the interlobar fissures, and the occasional tumor appears to grow into the lung parenchyma, the so-called “inverted” tumor, which usually requires major lung resection for removal. An occasional pedunculated tumor will show movement with change in patient position on fluoroscopy or on chest CT scan.¹³ Figs 2A and 2B show a large, moveable pedunculated tumor attached to the visceral pleura of the interlobar fissure.

Low attenuation is usually seen in the tumor in areas of myxoid or cystic degeneration, hemorrhage, or central necrosis. Two thirds of the tumors enhance with contrast administration, suggesting a more vascular nature to the tumor. Areas of calcification are present in up to 26% of tumors. A small pleural effusion is present in 6% to 37%. Large lesions can compress adjacent vascular structures or bronchi (Fig 2A). Rarely, chest wall invasion or rib notching can be seen.

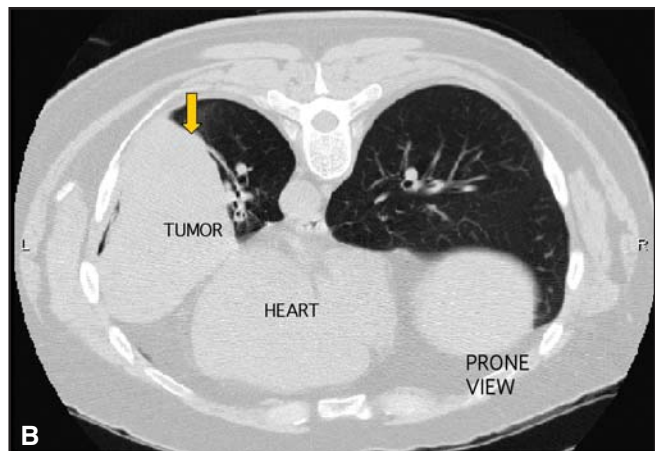
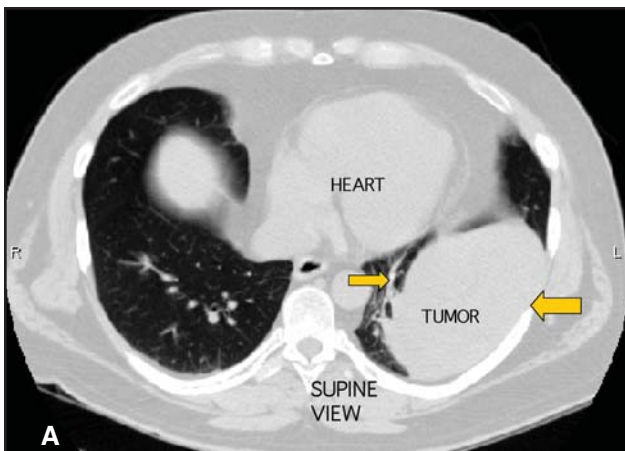


Fig 2. — (A) Computed tomographic scan, just superior to the diaphragm, of a 12.5-cm diameter pedunculated benign SFTP (large arrow) with a 3-cm diameter stalk arising from the visceral pleura of the left upper lobe in the major fissure compressing the left lower lobe. The small arrow shows adjacent vessels and bronchi along the medial border of the tumor being displaced by the mass and not incorporated into it. (B) Computed tomographic scan of the same patient performed in the prone face-down position at the same anatomic level as Fig 2A. The arrow shows the pedunculated mobile tumor that moved anterior with the change in patient position from supine (Fig 2A) to prone.

Magnetic resonance imaging (MRI) is occasionally useful in evaluating potential invasion of the chest wall by a sessile tumor. Since 79% of tumors extended into the lower thorax and 28% abutted the diaphragm in one series,¹² MRI with its sagittal and coronal views can help to clarify the tumor's relationship to the diaphragm. The tumor typically shows heterogeneous signal intensity on T1-weighted images, and contrast enhancement following gadolinium administration.

Positron-emission tomography (PET) likely adds little to the evaluation of this tumor. Few cases utilizing PET are reported in the literature; in one report of three SFTPs, two had no FDG uptake and one had only minimal uptake (SUV 2.1).¹⁴ The tumors in Fig 1 and Fig 2A showed no FDG uptake on PET.

Differential Diagnosis

The preoperative differential diagnosis that arises in a patient with an SFTP is essentially that of any mass lesion in the chest, ranging from carcinoma of the lung to various intrapleural sarcomas. A posterior paraspinal location might suggest a neurogenic tumor or round atelectasis. A more anterior and medial location might raise the possibility of a thymic neoplasm, germ cell tumor, or teratoma. The usual well-circumscribed appearance of the SFTP generally rules out malignant pleural mesothelioma since the latter invariably consists of multiple scattered pleural masses or is a more diffuse mass encasing the lung.

Aside from radiographic studies, bronchoscopy is of no benefit other than to rule out other lesions. Sputum cytology and pleural fluid analysis likewise do not aid in the diagnosis of SFTP. Percutaneous transthoracic needle biopsy of the mass rarely provides enough tissue to give a definite diagnosis. Most authors^{2,7,15,16} recommend against needle biopsy in this neoplasm since it does not influence the need for surgical treatment of this obviously resectable mass. Still, Sung et al¹¹ report a fair success rate of 43% with fine-needle aspiration in obtaining a definite preoperative diagnosis of SFTP, although it did not appear to affect their choice of surgery as treatment for all of their patients.

The usual radiographic appearance and clinical presentation of this neoplasm gives the surgeon the preoperative clinical suspicion that an SFTP is present. In experienced hands, prompt surgical treatment can be carried out safely without a preoperative diagnosis.

Treatment

Surgery

In virtually all cases, the mainstay of treatment of SFTP is surgical resection. Since this tumor is not a primary lung neoplasm, the surgeon should strive to save as much lung as possible in both the benign and malig-

nant varieties while obtaining histologic negative margins, if the tumor arises from the visceral pleura.

The tumor most commonly arises as a pedunculated discrete mass arising on a stalk usually attached to the visceral pleura of the lung. Resection of these lesions, which are almost always benign, requires only a margin of normal lung tissue, occasionally amenable to video-assisted thoracic surgical (VATS) techniques, if the lesion is small.¹¹ However, great care must be exercised to avoid any contact of the tumor with the VATS port sites to prevent tumor cell contact metastases, which have been described at port sites.¹⁷

An open thoracotomy is needed to remove larger masses, such as that seen in Figs 1 and 2A or even the giant tumors such as described previously (14.5-cm diameter, 1.2 kg).¹⁶ Sessile masses of the visceral pleura or inverted tumors within the lung parenchyma might require a major lung resection such as a lobectomy or rarely a pneumonectomy.¹¹ Intraoperative frozen sections should be done to ensure that the resection margins are free of tumor.

Less commonly, the SFTP arises as a sessile tumor developing from the parietal pleura of the chest wall, diaphragm, or mediastinum. These tumors are more prone to recur and require a wide local extrapleural excision. En bloc resection of a portion of the chest wall may be necessary when there is clear evidence that the tumor is malignant. Malignant SFTPs tend to be larger in size and more invasive, and they are almost never pedunculated. Adhesions may be seen in the larger tumors, which often complicate the resection. Complications including bleeding may occur occasionally with resection, but the surgical mortality is low in the later series, ranging from 0%⁹ to 1.5%.¹⁰

Adjuvant Therapy

Due to the rarity of these tumors, there is no systematic assessment of the role of adjuvant therapy in SFTP.^{2,17} Anecdotal reports describe long-term survivals with postoperative radiotherapy in patients with incomplete resection of the tumor.² Responses to ifosfamide and doxorubicin have been reported for recurrent, inoperable SFTP. Nevertheless, recurrent benign or malignant tumors should be strongly considered first for repeat surgical resection. Following resection, adjuvant therapy should be considered for recurrent tumors, particularly the sessile, malignant variety, although little experience is described in the literature with postoperative treatment.²

Neoadjuvant therapy has been suggested for large malignant tumors, but the utility of this technique is limited by the difficulty in obtaining a definite preoperative diagnosis and the lack of any described successes in the literature for this technique. Additional therapy such as brachytherapy or photodynamic therapy, which have been described in the treatment for

malignant pleural mesothelioma, could be applied for SFTP, but reports of this are rare and the effectiveness is uncertain.²

Pathology

Grossly, the tumor is a firm, encapsulated lobular mass with a characteristic whorled appearance in the benign variety and a more homogeneous appearance in the malignant neoplasm. On cut section, there may be areas of hemorrhage and necrosis in both, although calcifications are usually confined to the benign tumors. The size may vary from 1 to 36 cm in diameter, with a mean of 6 to 8 cm, and can weigh as much as 5.2 kg.^{16,18} Size bears no relation to whether the tumor is benign, malignant, resectable, or curable.

Microscopically, the smaller benign tumors (less than 8 cm in diameter) tend to be poorly vascularized with few visible mitoses and with uniform elongated spindle cells with variable amounts of collagen and reticular fibers. Larger benign tumors often have more pleomorphism but usually less than 4 mitoses per 10 high-power fields. Malignant SFTPs show an increased cellularity with crowding and overlapping nuclei, cellular pleomorphism, and a high mitotic count (more than 4 mitoses per 10 high-power fields). The malignant tumors commonly have areas of hemorrhage, necrosis, myxomatous change, and vascular or stromal invasion.^{2,5,7,19}

Immunohistochemistry may be quite useful in differentiating the SFTP from mesotheliomas and sarcomas.^{2,7,19} SFTP generally is vimentin-positive and cytokeratin-negative, as opposed to mesothelioma, which is cytokeratin-positive and often vimentin-negative. In addition, both the benign and malignant varieties of SFTP are CD34-, CD99-, and bcl-2-positive. SFTPs are also generally S-100-, carcinoembryonic antigen-, and smooth muscle actin-negative. A description of the comparative immunohistochemistry of SFTP and other neoplasms is outlined by de Perrot et al.²

Results of Treatment

Localized benign SFTPs are almost always cured with complete surgical resection, although recurrences have occurred as long as 17 years after the initial resection.¹⁰ The unpredictability of local recurrences even in this group mandates a generous resection with histological-proven clear margins. More sessile benign tumors appear deceptively localized but deserve liberal resection margins because of up to an 8% recurrence rate in this group. Reresection of benign recurrences is usually curative.^{2,5,7} In contrast, the malignant SFTP has a relatively poor outlook despite a complete resection. In a series by Okike et al,¹⁰ all patients had a recurrence

Table 2. — Characteristics of Benign and Malignant Solitary Fibrous Tumors of the Pleura

	Benign	Malignant
Gross		
Pedunculated	+++	+
Sessile	+	+++
Atypical location	++	+++
Size >10 cm	+	++
Necrosis and hemorrhage	+	+++
Calcification	++	+
Microscopic		
Cellular pleomorphism	+	+++
High mitotic count (> 4 per 10 high-power fields)	—	+++
High cellularity with crowding and overlapping nuclei	+	+++
Necrosis	+	+++
Stromal or vascular invasion	—	+++
Data from References 2, 5, 7, 19.		

or distant metastasis with only a 12% long-term survival. However, in a series by England et al⁵ involving 82 malignant SFTPs, results were somewhat better; 45% were cured by excision alone, although most of these survivors had a pedunculated or well-localized tumor. Solitary fibrous tumors also occur rarely in a wide variety of extrathoracic locations, as reviewed by Gold et al.²⁰ The clinical and pathologic features of these extrathoracic tumors are similar to those of the SFTP.

Histologic characteristics are useful in estimating the risk of recurrence in SFTP.^{2,21} Table 2 lists the gross and microscopic characteristics that help differentiate benign and malignant tumors, thereby aiding in assigning recurrence risk. Based on their review of multiple patient series relating recurrence to histologic and morphologic indicators, de Perrot et al² provide a classification of SFTP according to tumor characteristics and prognosis: (1) benign pedunculated tumors had a 2% recurrence rate, (2) benign sessile tumors had a 8% recurrence rate, (3) malignant pedunculated tumors had a 14% recurrence rate, and (4) malignant sessile tumors had a 63% recurrence rate and a 30% mortality, with most deaths occurring within 24 months.

Conclusions

Solitary fibrous tumors of the pleura are rare neoplasms that fortunately are benign 80% of the time. They are readily curable with careful, complete resections. Although the less common malignant variety of SFTP has a higher recurrence rate and higher tumor-related mortality, aggressive surgery and careful postoperative surveillance may still permit long-term survivals in as many as 70% of these patients.

In general, after complete resection in all patients, chest CT scans should be used to monitor for recurrence every 6 months for the first 2 years and then yearly. Most recurrences, particularly of the sessile malignant tumors, occur within 24 months of the initial resection. Nevertheless, all SFTP patients need long-term follow-up of 15 to 20 years due to the possibility of late recurrences. If a local recurrence is detected in any patient, strong consideration should be given for resection, which may well be curative.^{2,21}

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