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Solitary Fibrous Tumor of the Pleura: A Case Report and Review of the Literature

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ABSTRACT

Solitary fibrous tumor of the pleura (SFTP) is a rare mesenchymal cell tumor that can be benign or malignant. The best treatment of this tumor is a complete surgical resection. We present clinical and histopathologic characteristics of the 4 patients and their outcomes. (Tanaffos 2009; 8(3): 69-76)

Key words: Solitary fibrous tumor, Pleura, Tumor

INTRODUCTION

Pleuropulmonary solitary fibrous tumor of the pleura (SFTP) is a rare mesenchymal cell tumor, which has gained increasing recognition during the last two decades as a discrete pathologic entity (1). SFTP represents less than 5% of all neoplasms involving the pleura (2) and can histologically be differentiated into benign and malignant forms (3).

SFTP occurs at all ages but peaks in the sixth and seventh decades of life with equal incidence between men and women. About 40% of the cases are incidentally diagnosed while investigating an unrelated pathology (4). The presentation of this tumor is nonspecific (1, 3) and the majority of patients are asymptomatic at presentation (5-7).

In order to define the clinical behavior of SFTP more precisely, we reviewed the clinical presentation and histopathological characteristics of these tumors.

The selection of appropriate treatment depends on the preoperative diagnosis (1) but complete pleural resection with adequate safe margins can achieve a satisfactory outcome in a majority of cases (7-9).

We retrospectively reviewed clinical data of four cases who were consulted with the oncology department between 2002 and 2007. The histological specimens were reviewed again by two pathologists and the diagnosis of SFTP was confirmed. The clinical and para-clinical findings of the patients are as follows:

CASE SUMMARIES

Case 1

A 68-year-old man presented with symptoms of cough, dyspnea, fatigue, and weight loss for about 4 months. He had no positive past medical history

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including alcohol consumption or cigarette smoking. On physical examination, the percussion test at the base of the left lung was dull and breath sounds were also absent in this area, the rest of the general examination and chest examination were normal. Baseline laboratory investigations (renal and liver function tests, and complete blood counts) were normal except erythrocyte sedimentation rate (ESR) and serum alkaline phosphatase which were 46 mm/hr and 405 IU/L, respectively.

The chest x-ray revealed a mass in the left lung base with left-sided pleural effusion (Figure 1). Pleurocentesis was done and the pleural fluid appeared bloody with cytologic analysis consistent with a transudative fluid.

Pleural fluid analysis demonstrated: sugar=90 mg/dl, LDH=108 Units, protein=2.4 mg/dl, WBC=2700 cells/ml (polynuclear and mononuclear cells were 10% and 90%, respectively), and RBC=many.

The CT-scan of the chest showed a large soft tissue mass in the left hemithorax causing compression atelectasis of the underlying lung with a shift of the mediastinum toward the right side (Figure 2). The mass was enhanced homogenously with intravenous contrast without infiltration of the underlying lung.



Figure 1. Chest x-ray showed a mass in the left lung base with left-sided pleural effusion.



Figure 2. A large soft tissue mass located in the left lower hemithorax.

The bronchoscopic study was normal. A CT-guided biopsy reported spindle cell tumor. Therefore, the patient was a candidate for tumor resection. A pre-operative work-up was completed including pulmonary function tests which showed a restrictive effect.

Intra-operatively, the tumor was arising from the dorsal pleura of the left chest and had an adhesion to the left lower lobe.

Finally, total resection of the tumor was completed without leaving any tumor remnants.

Histopathological examination showed bland-appearing spindle cells with bands of collagenized stroma. Mitotic figures were present but rare in number. Immunohistochemistry was positive for CD34, BCL2, MIC2, and negative for cytokeratin and calretinin, which was consistent with SFT (Figure 3 A, B).

He has been on regular follow-up for about 24 months with no evidence of recurrence.

Case 2

A 73-year-old man presented with progressive dyspnea for 6 months. He had no other remarkable sign or symptoms such as chest pain, cough, fever, or weight loss. He had a past history of cigarette smoking (30 yr×1/2 pack) and diabetes mellitus (type 2) for 20 years. On physical examination, the percussion test at the base of the left lung was dull

and breath sounds were also absent in the corresponding area. The rest of the general examination was normal. Baseline laboratory investigations (renal and liver function tests and complete blood counts) were normal. The chest x-ray revealed a mass lesion in the base of the left lung. CT-scan showed the location of the mass to be in the left lower lobe with minimal extension to the left upper lobe. This was followed by a CT-guided biopsy that reported spindle cell tumor (Figure 4 A, B). The immunohistochemistry was negative for cytokeratin, EMA, S100, and CD34.

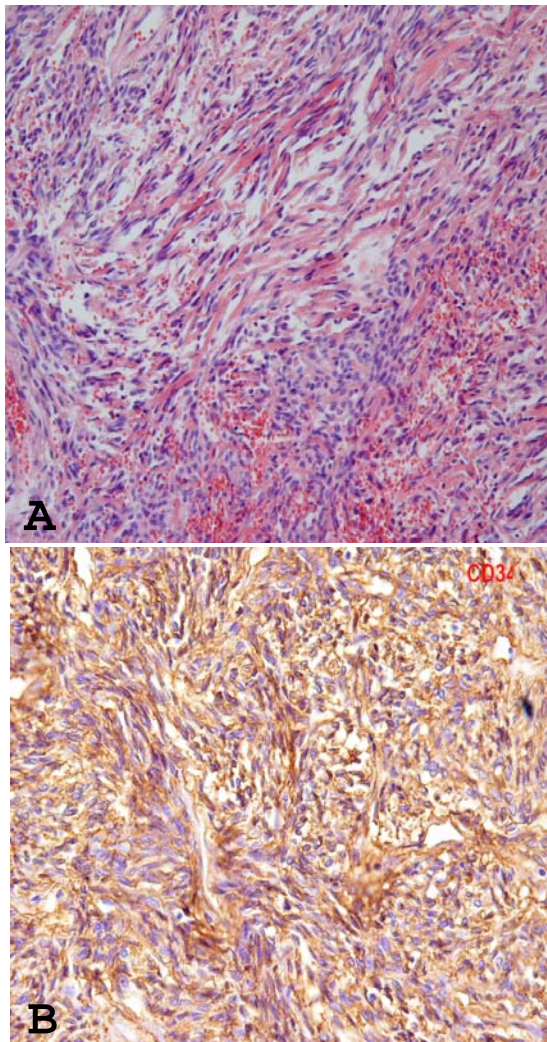


Figure 3 (A, B). Proliferated bland-appearing spindle cells with rope-like collagen deposition (H&E stain). B. Strongly CD 34-positive cells (IHC stain)

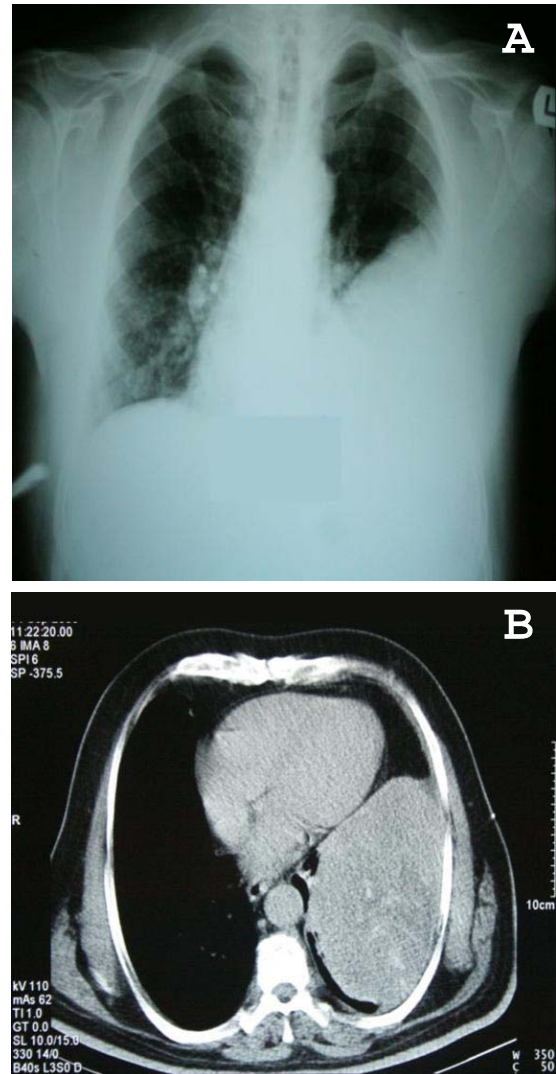


Figure 4 (A,B). A mass at the base of the left hemithorax adjacent to the pleura.

Eventually, the patient was scheduled for surgery. Pulmonary function tests showed a restrictive effect. The patient underwent thoracotomy and left lower lobectomy with wedge resection of the left upper lobe and partial pleurectomy. Intra-operatively, the tumor was arising from the left lower lobe with the greatest diameter being 16 cm, and was attached to the parietal pleura with minimal extension into the left upper lobe. The histopathological examination showed proliferated spindle cells arranged in some areas as short ill-defined fascicles as well as

pericyclic vascular pattern with mild pleomorphism of nuclei within collagenized stroma. The mitotic activity was practically rare. Areas of calcification and necrosis were also seen. Immunohistochemical staining showed absence of reactivity for keratin, desmin, actin, and S100 protein, but the tumor cells were diffusely positive for CD34. Due to the large size of specimen (more than 10 cm) and presence of necrosis, the case was considered as SFT with feature of malignancy according to some references. The patient has been on regular follow-up for about 21 months without evidence of recurrence.

Case 3

A 45-year-old woman presented to our hospital with a 2-month history of pleuritic left hemithorax pain. The patient's past medical history was unremarkable. The physical examination was normal. Since the pain had not responded to the outpatient managements, a chest x-ray was done which revealed a mass lesion in the external middle area of the left hemithorax. The CT-scan revealed the location of the mass to be in the external surface of the mid left lung with adhesion to the chest wall.

Although biopsy was not done, the patient was a surgical candidate with the diagnosis of lung mass and the probability of malignancy. The pre-operative bronchoscopy was normal. A pre-operative diagnostic video-assisted thoracoscopy was done by making a port in the 5th intercostal space which demonstrated a tumor mass in the upper lobe with a majority of it being out of the lung with adhesion to the chest wall. Therefore, the patient underwent a thoracotomy in the 5th intercostal space and the tumor was resected along with a wedge of the adhered left upper lobe. The parietal pleura was also resected in the location of the chest wall adhesion. The intra-operative frozen section was negative for malignancy and in the surgeon's judgment this was a benign tumor with a visceral pleural source.

Histopathological examination showed a spindle cell tumor with myxo-hyalin degeneration. The immunohistochemistry was positive for CD34, BCL2, and MIC and negative for S100, and CD31 which was consistent with SFT.

Case 4

A 57-year-old man presented with a history of pleuritic chest pain in the region of the right hemithorax for 2 months. On physical examination, the only remarkable finding was decreased respiratory sounds in the right lung. The patient was initially managed conservatively, but due to no response, he underwent radiographic examinations. The chest x-ray revealed a large mass in the right hemithorax. On CT-scan, a large and homogenous well-defined mass without any invasion to the chest wall was noted in the right hemithorax.

CT-guided biopsy was done and the histopathological examination showed small cell carcinoma, which was also confirmed by immunohistochemistry. In another center, the patient received 2 cycles of chemotherapy without any radiographic response. The patient was referred by his oncologist to our thoracic surgery department for further assessment. Meanwhile, the pathologic specimens were sent to the United States and the result of the pathologic examination was reported to be SFT. Thus, the patient was scheduled for thoracotomy and tumor resection. The pre-operative bronchoscopy was normal, while the intra-operative data revealed a large solid tumor with minimal chest wall adhesions which were then freed. The tumor had a severe adhesion to a part of the parenchyma of the upper and middle lobes of the right lung and it seemed to be originated from the visceral pleura of this part of the lung. The tumor and the involved areas of the lung were resected by lobar or wedge resection. Histopathological examination revealed a spindle cell tumor in favor of SFTP. No

Immunohistochemistry data was found in the patient's file. He has been on regular follow-up for about 24 months with no evidence of recurrence.

DISCUSSION

Primary tumors of the pleura were divided into diffuse and localized forms by Klemperer and Rabin in 1931(10). Diffuse pleural tumors are mesotheliomas which are more common than localized or solitary forms. They arise from mesothelial tissue, are associated with asbestos exposure, and almost always have a fatal course. Solitary tumors are less common, of mesenchymal origin, not related to asbestos exposure, and have a better prognosis than the diffuse variety. The origin of these tumors is controversial, and their nomenclature is inconsistent, with names such as fibroma, neurofibroma, fibrosarcoma, myxosarcoma, localized fibrous mesothelioma, submesothelial fibroma and benign fibrous mesothelioma (11). The preferred term is solitary fibrous tumor of the pleura (12). There is no relation between SFTP and mesothelioma but SFTPs are frequently confused with mesothelioma.

These uncommon tumors could occur at both intrathoracic and extrathoracic areas such as the meninges, nose, oral cavity, pharynx, epiglottis, salivary glands, thyroid, breast, kidneys, bladder, and spinal cord (13, 14).

In our study 3 of the 4 patients were men, the ages ranged between 45 and 73 with a mean age of 60.7 yrs, which was consistent with the literatures (4).

SFTP may remain asymptomatic but about 60% of patients are symptomatic at the time of diagnosis with the most common symptoms being dyspnea, cough, and chest pain (4,15). In one study only thirteen percent of cases had an aggressive clinical behavior with local infiltration or local recurrence and in some cases even distant metastases. The

majority of cases (about 87%) had a benign clinical behavior (16). Extrathoracic manifestations include clubbing of fingers in the form of hypertrophic pulmonary osteoarthropathy and hypoglycemia (4, 5).

In our study, all 4 patients were symptomatic of which 2 presented only with chest pain and the other 2 with dyspnea. One patient also suffered from generalized signs such as malaise and weight loss, but no extrathoracic manifestation was detected.

A chest x-ray may be very helpful for diagnosis by providing the initial clue, but the CT-scan remains the modality of choice due to its ability to assess resectability of the tumor and its relationship to the neighboring structures. MRI is the most sensitive test for detection of invasion into the adjacent structures and is more useful than CT-scan when cost is not a constraint. Fine needle aspiration cytology is inconclusive in most cases as the tumor contains acellular as well as hypocellular areas and the material obtained is not representative. Definitive diagnosis is usually obtained by histopathological examination after surgery as in our cases (9).

Radiologic evaluation usually reveals a solitary circumscribed and homogeneous lesion. Rarely, it may occupy the entire hemithorax, but the average size is about 6 cm (16). In one study, most of the masses had an atypical appearance for pleural-based tumors that form an acute angle with the chest wall on radiographic examinations. This may be due to the size of the lesions and their tendency to hang from a pedicle into the lung (17). In some cases the mass may be mobile due to the pedicle, and occasionally movement can be documented using decubitus views. CT-scan may reveal heterogeneous areas of enhancement in some larger tumors that correlate pathologically with vascularity, and areas of low attenuation that correlate with cystic necrosis and hemorrhage. All have contours that are smooth

and lobulated without evidence of invasion into the underlying tissues. Occasionally dense calcification is seen (18). MRI findings are consistent with a fibrous tumor, with low signal on T1- and T2-weighted images (19, 20). There is little information regarding the use of PET to differentiate solitary fibrous tumors from malignant mesothelioma (21,22).

In our study two of the cases had a homogenous pattern on CT-scan. Only in one case the tumor was adhered to the chest wall and in the remaining three, no invasion to the chest wall was detected.

Macroscopically, 80% of tumors arise from but do not invade the visceral pleura. Half the tumors are pedunculated and half are sessile. On sectioning, they are grey-white in color and harbor areas of necrosis and hemorrhage. In our study only one case had arisen from parietal pleura, and the others were from visceral pleura.

Microscopically, most of the tumors are composed of spindle cells, which are arranged in interlacing fascicles or have a short storiform arrangement, a so-called patternless pattern. Myxoid, fibrotic, and hyalinized changes have also been described (23). In some cases, SFTP may have vascular features of hemangiopericytoma (24). Immunohistochemically, most of the tumors are positive for CD34. Some of the tumors are also positive for BCL-2, O-13, smooth muscle actin, desmin, Leu-7, and vimentin (25-27). A new study reported significantly higher expression of nestin in malignant tumors compared to benign tumors especially in CD34 negative ones (1). In our study, all tumors were composed of spindle cells, out of which 2 were positive and one was negative for CD-34 on immunohistochemical staining.

Some benign SFTPs may transform into the malignant form even after several years (3,9,28). Malignant SFTPs are characterized by high

cellularity, pleomorphism, hemorrhage, and mitotic activity (more than 4 mitotic figures per 10 high-power fields), and necrosis (5). Some authors believed that malignant tumors were usually greater than 10 cm in diameter (29) but in another study size of the tumor bore no relation to whether the tumor was benign or malignant (30). In the most extensive series of thoracic solitary fibrous tumors reported from a single institute, an atypical location (e.g., parietal pleura, parenchyma, mediastinum, or endophytic growth into the lungs) was also a feature associated with malignancy (31). Complete excision of the tumor at primary surgery is the most important single indicator of clinical outcome and the best prognostic factor (5, 29,32,33).

Other important prognostic factors are the presence of a benign histological variant, a pedunculated, and a small size (<10 cm) tumor (24,29,34). However, other studies have not found such correlation (35,36). The malignant form of SFT still remains enigmatic. Indeed, the tumor's behavior is often unpredictable and does not always correlate with histological findings (5).

On our limited number of cases we had no recurrence of the tumor after complete resection. Complete pleural resection with adequate safe margins can achieve satisfactory outcomes in the majority of cases (1). Five-year survival rates as high as 97% have been reported in cases with adequate excision. However, with incomplete resection or malignant transformation, the median survival is only 24 to 36 months (9). Sometimes, return of a paraneoplastic syndrome can accompany a recurrence of the solitary fibrous tumor (37). Outcome of malignant SFTP is less favorable, and death related to local invasion, recurrence, or metastases has been reported in the literature (13). There are only a few cases described in the literature concerning adjuvant radiotherapy or chemotherapy in

malignant SFTP and their effectiveness needs to be established (32).

Clinical and radiological follow-ups are indicated for both benign and malignant SFTPs.

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