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Solitary Fibrous Tumours of the Pleura

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Abstract

Solitary fibrous tumours of the pleura (SFTP) are rare neoplasms originating from one of the components of the sub-mesothelial connective layer underlying the pleura. They are the most common non-mesothelial primary pleural neoplasms but still remain relatively rare. Their behaviour is mostly indolent; however, some may de-differentiate into malignant and aggressive tumours. Surgical resection is the mainstay treatment for SFTP, even more so in case of voluminous masses, due to compression onto lung, mediastinum and great vessels. In this chapter, we discuss the disease characteristics reported in the literature with respect to clinical presentation, diagnosis and treatment; also, we will discuss the results of patients treated for SFTP who underwent a surgical treatment in our unit of thoracic surgery.

Keywords: solitary fibrous tumour of the pleura, pleura, surgery, resection, recurrence

1. Introduction

The pleura is composed of two sections: the mesothelium, a single layer of flattened cells, and a deeper sub-mesothelial layer formed by a matrix of collagen, elastic fibres, lymphatic and blood vessels.

Primary pleural tumours may originate from any of the pleural components.

Out of all the pleural neoplasms, 90% are malignant mesotheliomas, 5% are solitary fibrous pleural tumours (SFPT) and the remaining 5% consists of less frequent variants (**Table 1**) [1].

Solitary fibrous tumours of the pleura originate from one of the components of the sub-mesothelial connective layer; therefore, its origin is mesenchymal. It usually presents as a well-circumscribed mass of occasional finding at chest X-rays performed for other reasons, since it presents asymptotically.

SFTPs are the most common non-mesothelial primary pleural neoplasms, but still remain relatively rare. In fact, to date, <2000 cases have been reported in the literature [2]. They originate most frequently from the visceral pleura and have a benign course; only in a small percentage of cases (10–15%) their behaviour is

Benign Solitary fibrous tumour of the pleura Calcifying fibrous tumour Adenomatoid tumour Sclerosing pneumocytoma (hemangioma) Pleural lipoma Pleural Schwannoma
Malign Solitary fibrous tumour of the pleura Desmoplastic small round cell tumour Localized malignant mesothelioma Primary pleural thymomas Synovial sarcoma of the pleura Primary pleural liposarcoma Fibrosarcomas of the pleura and desmoid tumours
Vascular origin Epithelioid hemangioendothelioma Angiosarcoma Epithelioid angiosarcoma
Lymphatic Primary pleural lymphoma

Table 1.
Classification—rare pleural tumours.

malignant, presenting a de-differentiated pattern, aggressive clinical behaviour (invasion of adjacent organs or cardiac compression due to its huge mass) and a trend to relapse after several years, therefore requiring long-term follow-up.

Although surgery is the main approach to treating SFTPs, local and distant recurrences may be observed after a complete resection [3, 4].

In this chapter we will discuss the characteristics of the disease reported in the literature with respect to its clinical presentation, diagnosis and treatment; also, we will present the results of patients who underwent surgery for SFTP in our Department from 1989 to 2019.

2. Historical background

Lieutaud was the first to report a tumour of pleural origin in 1767 but the first report of what was thought to be a SFTP dates back to 1870 in the work of Wagner [5].

In 1931, Klemper and Rabin [6] provided the first pathological distinction for pleural tumours classifying them into diffuse and localised mesotheliomas. They assumed a sub-mesothelial mesenchymal origin for the localised type.

Eleven years later, Stout and Murray [7] described the typical histological feature of the fibrous tumour of the pleura, the so-called patternless pattern, initially thought to be a vascular neoplasm related to smooth muscle perivascular cells (pericytes), therefore naming it hemangiopericytoma.

Since its pathological features were first described, the nomenclature has become confused, and the disease has also been referred to as localised mesotheliomas, localised fibrous tumours, fibrous mesotheliomas, or pleural fibromas.

The introduction of electron microscope and immunohistochemistry clarified the hypothesis that SFTP does not originate from the mesothelial layer but from the sub-mesothelial, undifferentiated mesenchymal layer [8, 9].

SFTP is now recognised as occurring anywhere in the body, including soft tissue and viscera, albeit with a peculiar predilection for body cavity sites, including pleura, peritoneum, and meninges.

In recent studies, SFTPs distribution is as follows: 30% in the thoracic cavity (pleura, lungs and mediastinum); 30% in the peritoneal cavity, in the retroperitoneum or pelvis. When SFTP arise in the abdominal cavity it is mainly localised in the retroperitoneum followed by the pelvic soft tissue [10].

Nearly 20% of SFTPs are found in the head-neck district (including meninges). The remaining diseases develop in soft tissue of the trunk and extremities [11].

Data on presentation, clinical features and natural history of SFTPs are almost exclusively derived from retrospective series and case reports.

Since the discovery of SFTP, there has been some confusion in the classification by body site (pleural vs. extra-pleural), the histology (SFTP vs. hemangiopericytoma) and changes in diagnostic terminology has resulted in a fragmented and unsystematic approach to this uncommon neoplasm.

Robinson and Chmielecki's [12, 13] recent discovery of a common driver mutation for pleural and extra-thoracic SFTPs in 2013 drastically changed our understanding of SFTP pathogenesis and led to new opportunities for diagnosis, characterisation and treatment.

2.1 Clinical features

Usually, the SFTP is discovered in asymptomatic middle-aged adults (occasionally in children) and affects men and women equally. It is more common in the fifth and sixth decades of life. Some authors have reported that the tumour shows a slight predilection for women [2, 4, 14, 15].

It seems not to be associated with exposure to asbestos fibres exposure or tobacco smoke [16, 17].

Although the majority of SFTP are benign, it is reported that nearly 10–20% are malignant or show a malignant behaviour [18, 19].

Histologically, malignant tumours are classified according to England et al. [18] criteria:

- mitotic count with more than four mitosis/10 high power fields (HPF) ($\times 400$)
- presence of necrosis
- hyper cellularity as judged by nuclear crowding and overlapping
- presence of nuclear atypia

Mostly, patients are asymptomatic, but when they present symptoms, these usually include cough, chest pain, dyspnoea due to pleural effusion or the mass effect of the tumour. Haemoptysis and obstructive pneumonia may be observed as a result of airway obstruction. Chest pain has been reported more commonly with tumours arising from the parietal pleura.

A higher incidence of symptoms is also described in malignant variants [20], with a large variability of presentation varying from 43 to 73% [2, 14]; only few cases have been reported associated to paraneoplastic syndromes: 3% with hypertrophic pulmonary osteoarthropathy (HPO) and 2% with Doege-Potter syndrome [2].

2.2 Paraneoplastic syndromes

2.2.1 Hypertrophic pulmonary osteoarthropathy or Pierre Marie-Bamberger syndrome

Hypertrophic pulmonary osteoarthropathy (HPO) describes a rheumatoid like disease of the bones and joints. The symptoms include clubbing of the fingers and toes, stiffness of the joints, oedema over the ankles and occasionally the hands, arthralgia, and pain along the surfaces of the long bones, especially the tibia [20].

Finger pressure on the surface of the tibia can elicit pain before the onset of any radiographic evidence of SFTP.

When clubbing and HPO are attributed to a paraneoplastic syndrome, this is referred to as the Pierre Marie-Bamberger syndrome since they first described the symptoms in 1890 [21, 22].

This is reported in up to 20% of patients and it is more commonly associated with large tumours (>7 cm) [20].

Some authors have reported that these clinical features usually resolve within 2–5 months (or sometimes longer) after radical surgery and may reappear if the tumour relapses [3, 15, 18].

It is believed that local production of growth factors including PDGF and VEGF is implicated in the pathophysiology of HPO. In support of this, in a recent study the administration of zoledronate resulted in bone pain remission [23].

In another study, Hojo et al. suggested the abnormal production of hepatocyte growth factor as responsible for digital clubbing [24].

2.2.2 Hypoglycaemia (Doege-Potter syndrome)

The association between hypoglycaemia and a mesenchymal tumour has been reported for the first time in 1930 by Doege and Potter. This is present in <5% of patients affected by SFTP [25, 26].

Hypoglycaemia is equally distributed between benign and malignant SFTs albeit it occurs mostly in large peritoneal/pleural tumours [27].

Symptoms of hypoglycaemia include convulsions, syncope and coma and potentially death resulting from severe hypoglycaemia, if not corrected promptly.

Hypoglycaemia seems to be caused by an excessive production and secretion of a partially processed, high molecular weight form of insulin-like growth factor 2 (IGF-2) by the tumour [28]. The aberrant production of IGF-2 by the neoplasm is also the cause of refractory hypoglycaemia suppressing compensatory mechanism as gluconeogenesis in the liver and lipolysis in adipose tissue.

The paraneoplastic syndrome is generally cured after tumour's resection, with the return to normal levels of insulin within a few days after the operation [29].

2.3 Radiographic features

2.3.1 Chest X-ray

Generally, SFTPs are an occasional finding in chest X-ray performed for other reasons.

They appear as a solid, sharply marginated, well-circumscribed solitary lesion originating from the periphery of the chest or from a lung fissure. It may grow to remarkable dimensions, at times occupying the entirety of the hemithorax. It is very difficult, if not impossible, to distinguish them from other masses of the lung by means of a plain chest X-ray (**Figure 1**).

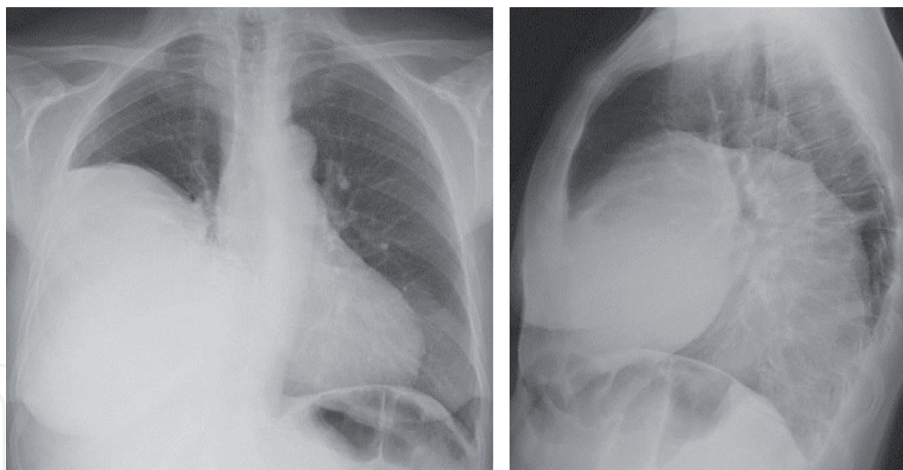


Figure 1.
Chest X-ray lateral view of a large SFTP located in the right hemithorax.

In particular, in neoplasms that reach a considerable size, areas of necrosis, haemorrhage and cystic or myxoid degeneration may be evident.

A pathognomonic radiological feature of pedunculated forms of SFTP originating from the visceral pleura is a change in shape and location of the mass during breathing or repositioning of the patient [30].

2.3.2 Computed tomography

At the computed tomography (CT) scan, SFTPs appear as a single lesion with well-defined margins arising from the chest wall (parietal pleura) or within a lung fissure (visceral pleura). They may grow up to reach remarkable dimensions, at times occupying the entire hemithorax and giving respiratory issues.

Distinctively, SFTP presents with its maximum diameter abutting the chest-wall. The lesion usually forms right or acute angles with a smooth tapering margin with the chest-wall (**Figure 2**).

Tumours arising in an interlobar fissure may be more difficult to differentiate from an intraparenchymal mass since they are surrounded by lung parenchyma.

A pathognomonic finding in pedunculated lesions is the mobility of the tumour with changes in patient position. However, this data is conditioned by the size of the tumour: the larger the tumour, the less mobile it is due to the greater number of adhesions it contracts with the surrounding tissues. It is important to evaluate the relationships with the surrounding tissues as SFTP usually presents with well-defined cleavage planes.

Another distinctive aspect of the fibrous tumour is its enhancement at the CT scan. Nearly 90% of lesions appear heterogeneous after administration of contrast, and in 75% of these a typical pattern may be recognised. Among these, the “geographic” one is the most represented. Small neoplasms tend to appear as sharp marginated masses with smooth margins, forming right or obtuse angles with the chest wall. Attenuation is homogeneous and similar to the adjacent musculature. This is a helpful feature to differentiate SFTPs from fatty lesions or saccular fluid collections. In regards to voluminous ones, they present as sharply marginated lesions with lobulated margins, creating acute angles with the chest wall. The contrast-enhanced CT evidences high attenuation of the mass due to its muscle fibres rich vascularisation, mainly and heterogeneous enhancement pattern (“geographic” the most common) with areas of necrosis, haemorrhages or cystic degeneration.

Absence of lymph nodal involvement and preservation of cleavage planes with adjacent structures provides evidence in support of the lesions’ benign nature.

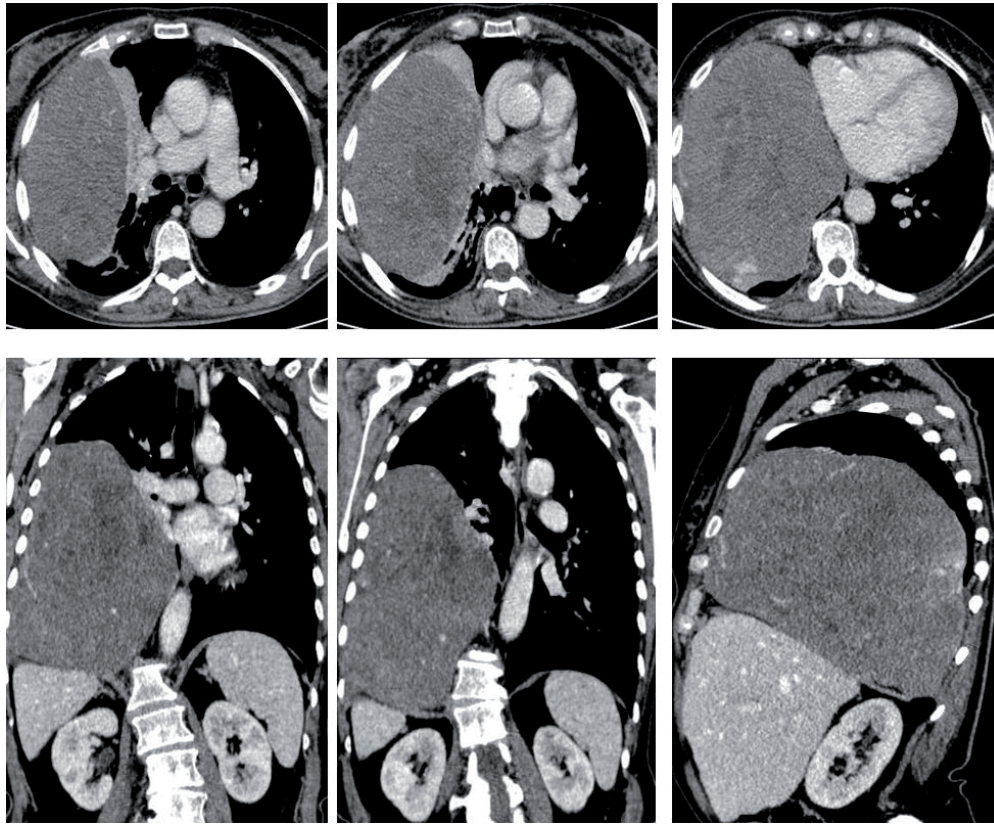


Figure 2.
Preoperative CT scan of a large SFTP in the right hemithorax.

For this reason, the presence of regional lymphadenopathy is suggestive of an alternative diagnosis.

CT therefore proves to be a very reliable imaging exam, especially when integrated with clinical and biopsy findings [30].

2.3.3 Magnetic resonance imaging

Magnetic resonance imaging (MRI) plays a limited role in the assessment of pleural disease. This exam proved to be superior to CT in studying the morphology and its relationship with the mediastinum, large vessels and diaphragm.

It is helpful in differentiating the tumour from other structures and in confirming intrathoracic localisation when the tumour abuts the diaphragm. Unfortunately, MRI patterns are quite variable in both benign and malignant SFTP [30].

2.3.4 F-18 fluoro-deoxy-glucose positron emission tomography

The role of F-18 fluoro-deoxy-glucose positron emission tomography (FDG-PET) in diagnosis of SFTP is limited and, to date, this exam is not able to discriminate between SFTP benign and malignant forms. However, it is reported its ability to identify areas of malignant transformation highlighting a focal increase of FDG uptake ($SUV_{max} \geq 3.0$) within a large, otherwise benign appearing SFTP.

So, it would appear that PET scan could be useful to predict a clinically aggressive behaviour of SFTP identifying areas of malignant histology within benign SFTP [31, 32].

2.3.5 Ultrasounds

The role of ultrasound (US) in the diagnosis of SFTP is limited. These tumours, at US appear as homogeneous and hypoechoic masses, manifesting respiratory movement along-with the chest wall.

US could be useful to define the origin, thoracic vs. abdominal, of tumours which originate in close proximity with the diaphragm.

In conclusion, we can assume that it is difficult to differentiate between benign vs. malignant SFTPs based on specific radiological signs alone, albeit some radiological features are more commonly associated with malignancy (large size, central necrosis and the presence of a pleural effusion).

It is important to underline the difficulty of making a diagnosis of certainty of SFTP with the sole aid of radiological imaging, for example, as described in a case report in which a giant ectopic pleural thymoma was pre-operatively diagnosed as an SFTP due to its radiological and clinical characteristics [33].

2.4 Pathologic characteristics

SFTP is an uncommon mesenchymal tumour, characterised by typical clinical presentation and variable biological behaviour.

It was first described arising from the pleura, but similar tumours can occur in the lung, in the mediastinum (in particular in the anterior one) and in other extra-thoracic sites.

The distinctive macroscopic and histological features overlap with many other soft tissue tumours, so over the years it has been given different and very heterogeneous names such as benign mesothelioma, localised mesothelioma, solitary fibrous mesothelioma or the most famous name of hemangiopericytoma [7].

In the last decades, advances in histological, molecular and genetic research studies led to the discovery of more reliable methods of differentiating this tumour, bringing all these lesions together under the name of SFTP.

A preoperative diagnosis is usually preferable and obtained by means of a biopsy. In order to obtain as much tissue as possible for diagnosis, a radiologic guided core needle biopsy or an open incisional biopsy by an experienced surgeon is recommended [34].

2.4.1 Macroscopic description

The tumour mass is usually solitary but may also be multiple. Typically, it is well circumscribed, solid in appearance and greyish in colour, often pedunculate and with variable dimensions (often larger than 10 cm). Cystic, haemorrhagic, necrotic and calcified areas can be found.

2.4.2 Microscopic appearance

SFTP typically displays a uniform spindle cell morphology, variable cellularity—without a specific growth pattern—a marked stromal hyalinisation and branching vascular pattern. The vascular pattern is characteristic and the vessels of different numbers and sizes are so-called “staghorn” and are very similar to those described for hemangiopericytoma [35].

The cells are characterised by having a tapered nucleus and a scarce and pale cytoplasm, the nuclear atypia is often minimal. Focally, a storiform or fascicular growth pattern could be present. The stroma could rarely be myxoid. Usually, <3 mitoses can be counted for 2 mm², and the count of four mitoses per 2 mm² seems

to correlate with greater aggressiveness. Necrosis is infrequent, but when present is associated with poorer prognosis (**Figure 3**).

2.4.3 Immunophenotype

Most lesions are positive for CD34 antigens but nevertheless this positivity lacks specificity in a conclusive way. Also, CD99 and Bcl2 positivity are not specific and therefore of little help. The most specific marker (>95% of cases), recently described, is STAT-6 [36] and in particular its strong and widespread nuclear reactivity (**Figure 4**). Since some de-differentiated liposarcomas can also express STAT-6, they should be kept in mind into differential diagnosis [37].

Some cases may be positive for smooth muscle actin and others for EMA (epithelial membrane agent), pancytokeratin, S100 or desmin.

2.4.4 Differential diagnosis

SFTP should be differentiated from synovial sarcoma, sarcomatoid mesothelioma, tumours of the nerve sheaths or type A Thymoma. The correct immunohistochemical reactions are necessary for a correct classification.

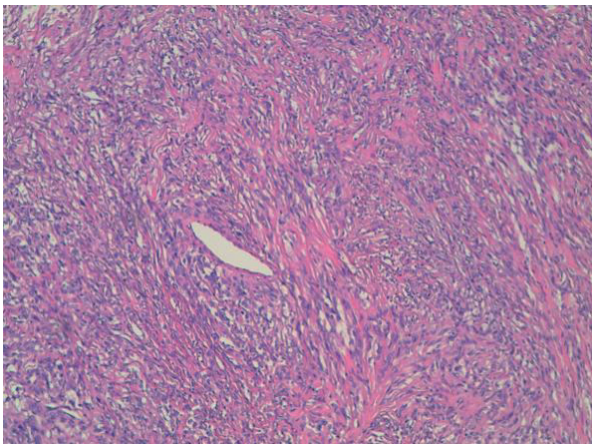


Figure 3.
Histologic features of SFTP. Morphological appearance of SFTP: typical spindle cell proliferation with low cytologic atypia (haematoxylin-eosin stain).

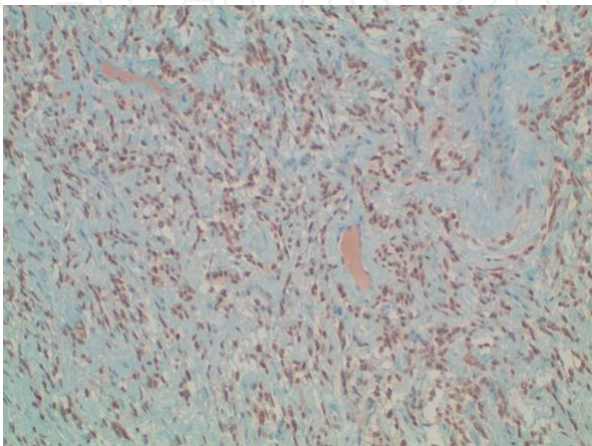


Figure 4.
Histologic features of SFTP. Immunohistochemical nuclear stain for STAT6 (IHC stain).

2.4.5 Genetic profile

SFTP harbours the gene fusion NAB2-STAT-6, which results from the intra-chromosomal inversion inv(12)(q13q13), which causes the over-expression of the protein STAT-6, found through the use of the specific antibody for the immunohistochemical reaction [12]. The over expression of IGF-2 found in some cases seems to be due to the loss of IGF-2 imprinting [38].

Telomerase reverse transcriptase (TERT) promoter mutations have been seen in 28% of SFT and are associated with high-risk pathologic characteristics and outcomes [39].

2.5 Diagnosis

The diagnosis of certainty of a SFTP is based on the histological examination of the specimen.

Usually, the first diagnostic step is a chest X-ray, performed for a different reason. The subsequent diagnostic procedure to further investigate the chest X-ray findings is a chest CT scan with contrast, which provides valuable information and orients the diagnosis towards a SFTP. As previously mentioned, this includes size and location of the tumour, the pleural origin or the presence of a stalk, areas of heterogeneity in larger lesions, an expression of the rich vascular network or intralesional haemorrhage or necrosis. These features also include the angle between the lesion and the thoracic wall which is useful when distinguishing between a pleural and a parenchymal lesion.

Larger tumours or tumours arising from the mediastinal pleura may be indistinguishable from mediastinal masses. In this case, the MRI scan is superior to the CT scan in studying the morphology and the relationship of the tumour with the mediastinum, large vessels and diaphragm. The MRI is also helpful in differentiating the tumour from other structures and better understanding margins and cleavages.

Fine needle aspiration biopsy (FNAB) is unreliable for providing a definitive diagnosis, which is mostly based on histological characteristics, as it provides insufficient tissue quantity [19], whereas a Tru-cut biopsy is more reliable. Weynand et al. reported a 100% diagnostic accuracy in determining a SFTP, using a transthoracic cutting needle [40].

2.6 Treatment

A complete surgical resection is the mainstay of the treatment of both benign and malignant SFTs, the absence of neoplastic residual (R0) being the main prognostic factor [41].

Due to the anatomical localisation and involvement, an anatomical resection (lobectomy, bi-lobectomy or a pneumonectomy) is seldom necessary, since offers no advantages over wedge resections, for which a free margin on healthy tissue of at least 1–2 cm is recommended. In order to guarantee an adequate free margin from disease, a frozen section analysis is sometimes very useful [29]. SFTs may occasionally require a lobectomy or a pneumonectomy when the lesion is not pedunculated but the base of implant is broad and sessile, or in case of an “inverted” tumour which grows inside the lung parenchyma.

When the tumour originates from the parietal pleura and adheres or invades the chest wall an extra-pleural dissection and a chest wall resection may be necessary [42].

Either a standard open thoracotomy or a video-assisted thoracic surgery (VATS) approach is valuable for the removal of an SFTP.

The standard open approach (posterolateral/anterolateral thoracotomy) is mandatory for patients with large tumours, multiple synchronous lesions or with obvious malignant tumours, while the VATS approach is feasible in small (up to 5.0 cm) lesions.

In case a VATS approach is preferred, it is necessary to avoid tumour dissemination using an endoscopic bag during the removal of the specimen, since contact metastases have been reported at the site of tumour extraction.

It is important to emphasise that the resection must be microscopically complete, in order to prevent late recurrence. Relapse of a benign SFTP lesion may, in fact, result in the development of a more aggressive or malignant tumour [43].

The role of adjuvant therapy in SFTP is quite limited and has not really been explored, but occasional clinical series have been reported. Suter et al. [3] studied one alive patient with no recurrence for more than 20 years after subtotal resection of the tumour followed by radiotherapy, while, Veronesi et al. [44] report the significant reduction of a recurrent fibrous tumour, not eligible for surgery, after chemotherapy with Ifosfamide and Adriamycin.

2.7 Prognosis and survival

As reported in a review [45], the overall survival of patients affected by a benign pedunculated SFTP is close to 100%. The percentage is reduced to about 92% in case of benign sessile tumour and lower in case of malignant pedunculated (85%) and malignant sessile tumour (37%). In a multicentre study, a clinicopathological staging system was presented in order to predict the clinical course or recurrences [46] with the recurrence rate distributed as reported in (Table 2).

Boddaert et al. [47] in their meta-analysis including over 700 patients reported a higher recurrence rate in patients with malignant histology (England’s criteria), sessile morphology and incomplete resection.

Despite a recurrence after a total resection is an uncommon event, recurrences are also reported after many years, especially subsequently an incomplete resection or excision of a malignant sessile SFTP.

The most important prognostic factor seems to be a disease-free resection margin (R0); in support of this statement, Van Houdt and colleagues [46] in their series of 81 patients reported that a positive resection margin after surgery with curative intent, was correlated with local recurrence. They also reported that a high mitotic rate and tumour size >10 cm are correlated with the development of metastasis.

Recurrences may be fatal due to mediastinal invasion and superior vena cava obstruction.

In case of relapse, the primary attempt should be surgical excision, if technically and oncologically feasible, for both benign and malignant tumours.

Most recurrences occur within 24 months from surgery and are localised in the pleural cavity while distant metastasis seems to be a late event [45]. For these reasons a long-term follow-up, more than 15 years is recommended [45].

In conclusion, despite the fact that SFTPs are considered benign tumours, they may express an aggressive behaviour which leads the tumour to relapse.

Pathologically benign, pedunculated	Stage 0	2% recurrence
Pathologically benign, sessile	Stage I	8% recurrence
Malignant pathology, pedunculated	Stage II	14% recurrence
Malignant pathology, sessile	Stage III	63% recurrence

Table 2.
De Perrot staging system.

2.8 Our experience

2.8.1 Introduction

The University Unit of Thoracic Surgery of San Luigi Hospital deals with the diagnosis, treatment and follow-up of a wide range of diseases of the lung, trachea and bronchi, mediastinum and chest wall, with a specific commitment to oncological procedures by means of open and minimally invasive approaches (VATS).

Patients are referred to our Department from the outpatient clinic and through a multidisciplinary team meeting (MDT) held weekly. The present study describes a series of 64 consecutive cases, surgically treated at our Department during a 30-year period.

2.8.2 Patients and methods

This is a single-centre retrospective analysis on prospectively collected data of patients operated on for a SFTP between December 1989 and March 2019 in our Unit of Thoracic Surgery. Data was retrieved from our surgical database and variables for each patient included: gender; age at operation; symptoms; smoking history; asbestos exposure; preoperative diagnosis; CT scan; PET scan (since 2003); bronchoscopy; preoperative diagnosis; tumour origin (visceral or parietal pleura) and side (right vs. left); tumour characteristics (implant on pleura—pedunculated vs. sessile—intrapulmonary growth; size); presence of associated paraneoplastic syndromes; comorbidities (Charlson Comorbidity Index); type of resection; postoperative complications; tumour histological characteristics (Ki67%; necrosis; mitotic count).

Surgical inclusion criteria included tumour resectability, no evidences of metastases or other tumours, a good performance status (PS < 3). All patients underwent a CT scan and a preoperative bronchoscopy was performed in case of voluminous tumours. Preoperative diagnosis was attempted by means of a fine needle aspiration biopsy (FNAB) in all patients.

Postoperatively, all patients had a chest X-ray performed in post day one and after chest drain removal. Chest drains were removed when there was no air-leak detected and <250 ml of pleural fluid drained in 24/hour (**Figure 5**).

Patients' follow-up was updated by contacting all those patients known to be alive at the time of their most recent outpatient clinic attendance. Information of patients lost at follow-up was retrieved through the General Register Office. The follow-up ended on the 1 March 2019.

2.8.3 Results

A total of 64 patients were operated on for a SFTP. Twenty-eight patients were males (43.7%) and 36 females (56.3%). Mean age at surgery was 61.7 years (range 35–83 years). Thirty-one (48.4%) patients were smokers or had a history of smoking.

Thirteen patients (20.3%) were symptomatic at diagnosis with predominant symptoms being cough and chest pain. No patients reported a history of asbestos exposure (**Table 3**).

All patients underwent chest X-rays and CT scans of the chest. Positron emission tomography was performed in 12 cases (18.8%).

Fifty tumours (78.1%) were based on the visceral pleura and 14 (21.9%) arose from the parietal pleura. Thirty-five tumours (54.9%) were pedunculated while 29

(45.3%) were broad based. Among tumours arising from visceral pleura, five (7.8%) showed a prevalent intrapulmonary growth (“inverted fibroma”).

The tumour was right-sided in 30 patients (46.8%) and left-side in 34 (53.2%). The lesions had a median diameter of 60 mm, the smallest tumour was 10 mm at maximum diameter and the largest was 380 mm (interquartile range: IQR-40–130 mm) (**Figure 6**).

The Charlson comorbidity index (CCI) is reported for all patients in **Table 3**.

Local excision of the pleural tumour was accomplished in 57 patients (89%). In two (3.1%) cases a wedge resection was performed and in seven patients (10.9%) an anatomical resection was required (three lobectomies, one pneumonectomy and one segmentectomy).

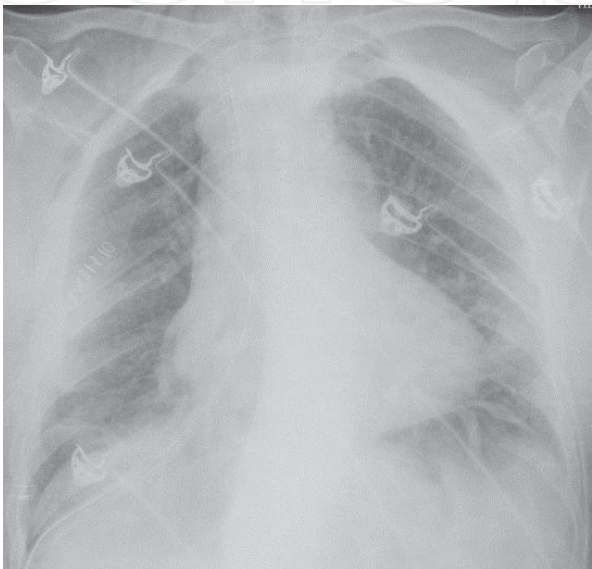


Figure 5.
Postoperative chest X-ray after radical excision of voluminous SFTP in the right hemithorax.

Age (mean, year)	61.7
Sex	
Male	28 (43.7%)
Female	36 (56.3%)
Presenting symptoms	
Cough	3
Chest pain	3
Fever	1
Dyspnoea	1
Weight loss	1
Hypoglycaemia	2
Smokers	31 (48.4%)
Charlson comorbidity index	
CCI = 0	43
CCI = 1	12
CCI = 2	7
CCI = 3	1
CCI = 4	1

Table 3.
Patient characteristics.

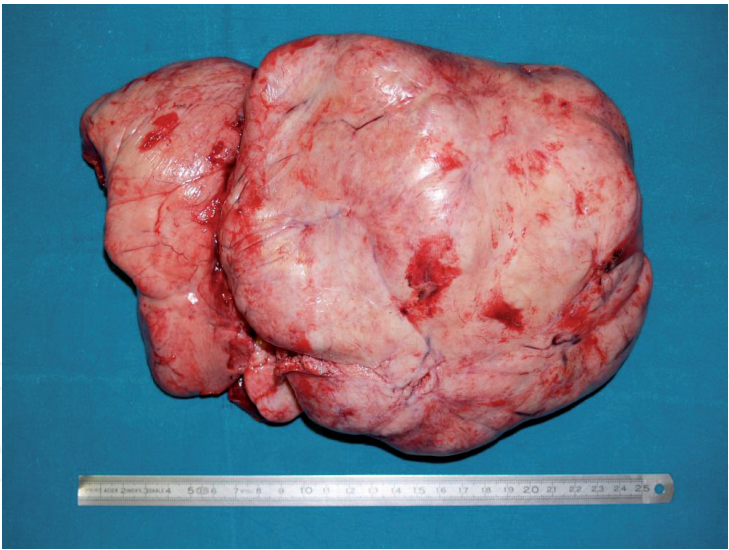


Figure 6.
Surgical specimen after a radical excision of voluminous SFTPs located in the right hemithorax.

Resection of the SFTP was performed through a thoracotomy in 51 cases (79.7%); VATS in nine cases (14.1%), and sternotomy in four cases (6.2%).

Histologically free margins were obtained in 63 cases (R0 residual disease). No patient was administered a neo-adjuvant or an adjuvant treatment.

Major postoperative complications included two atrial fibrillations, both treated with amiodarone, severe anaemia (two patients) with requirement of blood transfusions, one acute respiratory failure. Minor complications included subcutaneous emphysema (one patient), persistent air-leak from the chest drain (one patient) and atelectasis (one patient).

The histological analysis of the tumours, including Ki67% and mitosis is reported in **Table 4**.

All patients were evaluated as part of postoperative and oncological follow-up with clinical examination and chest X-ray after one and 6 months. Chest CT scan was performed every year for the first 5 years after surgery. After the first 5 years, an annual chest X-ray was recommended, or at the discretion of the general practitioner in the event of a new onset of symptoms. The annual examination is generally extended up to 15 years due to possible late onset of recurrences.

After a median follow-up of 135 months (IQR 49.2–198), 22 patients died (34.4%) and 42 are alive (65.6%). The mean disease-free interval (DFI) was 28.9 months (range: 8.7–106.1 months). In eight patients (12.5%) a single recurrence was reported while, in one patient two consecutive recurrences were identified.

Ki67	
>10%	8 (25%)
<10%	24 (75%)
N° mitosis × HPF	
>10	7 (20.6%)
<10	27 (79.4%)
Necrosis	
Present	6 (19.4%)
Absent	25 (80.6%)

Table 4.
Histology.

3. Conclusions

Solitary fibrous tumours of the pleura are rare pathological entities and are mostly discovered incidentally. Their behaviour is mostly indolent; however, some may de-dedifferentiate into malignant and aggressive tumours. Surgical resection is the mainstay treatment for SFTP, even more so in case of voluminous masses, due to compression onto lung, mediastinum and great vessels. Surgery should be carried out after a complete radiological assessment and a preoperative diagnostic attempt (FNAB), however, the diagnosis of certainty is obtained only with the definitive histological examination on surgical specimens. A long follow-up is recommended due to possible tumour recurrence.

Conflict of interest

The authors declare no conflict of interest.

Appendices and nomenclature

SFTP	solitary fibrous tumours of the pleura
HPO	hypertrophic pulmonary osteoarthropathy
IGF-2	insulin-like growth factor 2
HPF	high power fields
PDGF	platelet-derived growth factor
VEGF	vascular endothelial growth factor
CT	computed tomography
MRI	magnetic resonance imaging
FDG-PET	F-18 fluoro-deoxy-glucose positron emission tomography
US	ultrasounds
TERT	telomerase reverse transcriptase
EMA	epithelial membrane agent
FNAB	fine needle aspiration biopsy
VATS	video-assisted thoracic surgery
MDT	multidisciplinary team meeting
CCI	Charlson comorbidity index

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