Solitary fibrous tumor: A center's experience and an overview of the symptomatology, the diagnostic and therapeutic procedures of this rare tumor

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ABSTRACT

Solitary Fibrous Tumor of the Pleura (SFTP) is a rare tumor of the pleura. Worldwide about 800 patients diagnosed with this oncological entity have been described in the existing literature. We report our center’s 13 year experience. During this time three patients suffering from this rare disease have been treated in our department. All patients were asymptomatic and their diagnosis was initially triggered by a random finding in a routine chest x-ray. The diagnosis was set preoperatively through a needle biopsy under computer tomography (CT) guidance. The tumors were resected surgically though video-assisted thoracoscopic surgery (VATS) or thoracotomy. Because of the lack of specific guidelines due to the rarity of the disease a long-term, systematic follow-up was recommended and performed. Parallel an overview of the diagnostic and therapeutic procedures of the rare tumor is made.

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1. Introduction

The tumors of the pleura are an important nosological entity of the thoracic cavity. The most known tumor of the pleura is the mesothelioma. However, other tumors of the pleura have also been described. A less known and less common tumor is the solitary fibrous tumor of the pleura (SFTP). SFTP is a rare localized mesenchymal tumor which was initially thought to be a mesothelial pleural lesion [1]. Solitary fibrous tumors can arise from visceral organs or mesothelial tissues [1,2]. Solitary fibrous tumors have also been described in other localizations such as the pelvis, abdomen, retroperitoneum, buccal space, maxillary sinus, liver, pancreas, suprarenal region, and kidneys. It is believed that these tumors originate from extrapleural sites of these anatomical cavities and organs [3]. As far as the pleural solitary fibrous tumors are concerned, about 800 cases of SFTP have been described in the literature. Historically several terms have been used to describe this tumor, such as benign mesothelioma, localized mesothelioma, localized fibrous mesothelioma, localized fibrous tumor of the pleura, sub-pleural fibroma, pleural fibroma, localized benign fibroma, and sub-mesothelial fibroma [1,4,5]. The first description of the tumor is chronologically debatable. The first description of this entity is contributed to Lieutaud in 1767, while in other reports

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suggest that it was first described by Wagner in 1870. The first official description of the tumor’s pathology was however made by Klemperer and Rabin. The majority of tumors are benign, but 10–20% of the tumors are malignant [1,4,6].

The tumor often presents no symptomatology and is usually randomly discovered during a routine chest x-ray. During the period of the last six years (2010–2016) three patients with SFTP were treated in the Department of thoracic and cardiovascular surgery in Kaiserslautern. The preoperative diagnosis was made through needle biopsy under computed tomography guidance. The patients underwent surgical excision and a subsequent long term follow-up. In this article we attempt to describe our experience in this field as well as to present a general overview of the existing literature regarding the diagnostic and therapeutic procedures of this rare tumor.

2. Cases presentation

2.1. 1st case

A 56-year-old female was presented to our outpatient clinic with a mass in the area of the lower lobe of the left lung that was incidentally revealed by a chest x-ray performed due to influenza symptoms. No other symptoms or physical signs implying malignancy existed. Patient’s past medical history revealed COPD, hypothyroidism, type 2 diabetes mellitus and heavy smoking of thirty pack years (py). The chest computer tomography (CT) revealed a pleural mass having a size of 4 × 7 × 5 cm. A needle biopsy under CT guidance was performed and histology showed a SFTP. A further staging with bronchoscopy and Positron Emission Tomography - Computed Tomography (PET-CT) revealed no further pathological findings. A left postero-lateral thoracotomy was performed. A tumor arising from the lower lobe with no infiltration of the thorax wall was found. A complete tumor resection with apical lung parenchyma wedge resection was performed. The histopathological examination of the mass revealed a large SFTP of 11 cm diameter with circumscribed subcapsular necrosis, sometimes moderately granular nuclear pleomorphism and with 3 mitoses to 10 HPF (high-power field). The examination findings partially fulfilled the England’s criteria for the characterization of a malignant SFTP (described below) [7]. For this reason, the tumor was characterized semi-malignant. In addition the histological examination showed tumor free margins of the resected tissue. In immunohistochemical analysis cells were positive for CD34 and negative for CD117. A long-term follow-up was also recommended.

2.2. 2nd case

A 50-year-old female appeared in our outpatient clinic with a detected mass in the area of the upper lobe of the left lung. This patient’s tumor was also revealed incidentally during a chest x-ray examination. She presented no other symptoms. The patient’s past medical history revealed hypertension, thrombocytopenia and thyroidectomy because of multinodular goiter and smoking. A CT scan revealed the mass (diameter: 3 cm) and the final diagnosis of SFTP was also set through a CT needle biopsy. Because of a patient’s denial for surgical treatment a follow-up was alternatively suggested. After a three years follow-up time and because of a significant increase of the mass diameter in the last CT (5.3 cm) a VATS was finally performed. Intraoperatively the tumor presented no infiltration of the chest wall. A tumor excision was performed through a wedge lung parenchyma resection. The finding of a benign SFTP with a diameter of 6 cm was showed histologically. In immunohistochemical assay cells were positive for CD34, positive for less than 2% of cells for KI-67 and negative for CD117, D2-40 and TTF1. The patient was discharged on the 4th postoperative day without having any complications. A systematic follow-up was in this case also recommended.

2.3. 3rd case

A 77-years-old male patient aged was incidentally diagnosed with a mass in the left hemithorax and a lung nodule in right hemithorax. Patient’s past medical history revealed only arterial hypertension. The CT scanning showed a mass of 9 cm in diameter in the left hemithorax. The staging procedures with bone scintigraphy and CT showed no sign of metastases. A diagnostic CT guided needle biopsy showed a SFTP. A thoracoscopic wedge resection of the middle lobe showed an old tuberculosis. Because of the size of the tumor an excision through thoracotomy was finally conducted. Intraoperatively the SFTP presented adhesions to the visceral pleura of the lower lobe. The patient’s postoperative course was uncomplicated. The patient was discharged on 5th postoperative day after the second surgery. Histology revealed a SFTP sized 9 × 5.5 × 4.0 cm. In immunohistochemical analysis cells was clearly positive for CD34 and negative for CD117. A long-term follow-up was also recommended to this patient as well.

3. Discussion

SFTP is a very rare tumor [1,4], which has gained appropriate recognition in the last two decades as a discrete pathologic entity [9]. It represents 5% of the tumors of the pleura. Only 800 such cases have been described in the literature between 1931 and 2002 [1,4,6,10]. However, Cardillo et al. reported that the number of the SFTP can possibly be about 960. The patients with SFTP are 2.8 per 100,000 hospitalized patients. The number of SFTP seems to increase, but it is significantly smaller than the commoner tumor of mesothelioma [6]. The age of the tumor diagnosis varies from 5 to 87. However, the most common age of diagnosis is the sixth and seventh decade of life [1,5,6]. The tumor also occurs with the same frequency in men and women [1]. Sook et al. however described a light deviation of frequency to the side of the females [11]. There is no evidence of heredity. A case with a tumor in mother and daughter has however been described in the literature [10]. The association with asbestos exposition, nicotine effusion or exposure to another environmental factor has been reported [1,5,8,9,11]. In our three treated cases two of the patients were females and no hereditary among relatives was reported.

SFTPs often present no special clinical signs and no special symptomatology that could lead the clinical physician to a secure
tumor diagnosis. The most common sign can be clubbing which is unspecific and can appear in many other lung and heart diseases, is therefore not pathognomonic. Clubbing can be accompanied with hypertrophic pulmonary osteoarthropathy (HPO). The etiology of clubbing in SFTP is currently unknown. Clubbing may subside after surgical removal of the tumor [1].

The clinical course of the disease is unpredictable [6]. Often there is no symptomatology. For this reason, the tumor is in most cases randomly diagnosed. Nevertheless, the tumor can appear with various symptoms, but its symptomatology consists of ordinary symptoms of the respiratory tract [1,5,6,12,14]. For example, cough [6,13], thoracic pain, fever, dyspnea, weight reduction have been described [1,6,11,12,14]. Hemoptysis und pneumonitis may be observed in some rare cases [1,6,15]. Thoracic pain can occur if for example the tumor arises from or infiltrates the parietal pleura. A large tumor may also press the bronchus, and in that case pneumonitis and atelectasis can consequently occur. A large number of cases of the malignant type of the tumor can be symptomatic [1,5,6,15,16]. Thus, patients with benign tumors may have symptoms in 54–67% of the cases. Symptoms in malignant tumors are oftenar and occur in approximately 75% of the cases [1]. In our three cases, no symptomatology was preoperatively reported. Signs which may lead to the suspicion of a tumor malignancy can be the existence of clinical symptoms of a mean tumor’s diameter greater than 10 cm, fibrous adherences, pleural effusion and a positive histology for Ki67 10% or greater [5].

Interesting paraneoplastic syndromes have also been described in patients with SFTP [6]. These syndromes are often described in large SFTPs [1]. The hypertrophic pulmonary osteoarthropathy (HPO) is the most common. It occurs in 22% of SFTP [1,5,6,14,17,18]. However, it can also occur in 5% of cases of lung carcinoma. Regarding the clinical symptomatology of HPO it can be described as swelling of the legs and pain along the long bones. The etiology of the syndrome remains unknown [1]. A cause of the syndrome can be the excessive release of hyaluronic acid by the tumor [6]. HPO can be a good indication of the tumor’s progression. The symptoms may be drastically reduced after a successful operative care. This postoperative disappearance or reduction of the syndrome can occur within a few hours [1] to three months [6] after surgery. The syndrome can also appear in cases of a tumor recurrence. Based on the findings, the hypothesis that HPO occurs due to hormonal factors (probably somatropin) produced by the tumor is possible [1,6].

An additional interesting paraneoplastic syndrome is hypoglycemia (Doege–Potter syndrome). However, paraneoplastic hypoglycemia is not often in SFTPs [1]. The hypoglycemia is probably most common. It occurs in 22% of SFTP [1,5,6,14,17,18]. However, it can also occur in 5% of cases of lung carcinoma. Considering the clinical symptomatology of HPO it can be described as swelling of the legs and pain along the long bones. The etiology of the syndrome remains unknown [1]. A cause of the syndrome can be the excessive release of hyaluronic acid by the tumor [6]. HPO can be a good indication of the tumor’s progression. The symptoms may be drastically reduced after a successful operative care. This postoperative disappearance or reduction of the syndrome can occur within a few hours [1] to three months [6] after surgery. The syndrome can also appear in cases of a tumor recurrence. Based on the findings, the hypothesis that HPO occurs due to hormonal factors (probably somatropin) produced by the tumor is possible [1,6].

The initial approach to diagnosis and subsequently surgical surgery is made after appropriate radiological examination. The preoperative diagnosis of the tumor is a difficult challenge [6]. The definitive diagnosis of SFTP will be however histologically made after the surgical resection of the tumor [3,6]. Chest x-ray has of course a leading role in the first diagnostic approach of the disease, as in most cases of thoracic disease. The chest x-ray will provide as with signs which lead to the initial suspicion of the tumor. The actual size of the tumor may be significantly different compared to that seen in the x-ray. The tumor borders are still clear. The tumors that arise from the thoracic wall and the parietal pleura may form a corner with the lung parenchyma. However the exact percentage of tumors that present such a radiological morphology varies [1]. The information provided through ultrasound examination is limited and its use is not usually reported in analyses of the cases in the literature [6].

The computed tomography (CT) of the thorax is considered to be the most important examination in the diagnostic pathway of the disease. The performance of the CT scan can give the clinicians valuable information concerning the tumor size, the tumor morphology and its relationship with the other organs of the thoracic cavity. In addition, it can also be a great aid in the careful preoperative planning of surgical therapy [1,5,6]. CT scans usually demonstrate a well-defined and occasionally lobulated mass with soft tissue attenuating appearance on the pleural surface, and the displacement of the surrounding structures [6]. Sook et al. reported that in most cases the findings were presented as tumors arising from the pleura. However, there also exists the possibility that they appear as intrapulmonary or mediastinal tumors [11]. The exact position of the tumor arise can also possibly be detected in CT. As a result, the SFTP can be detected in all arising from the parietal pleura, the lung fissure or the visceral pleura [1,6]. However, it is not always possible to decide between intrapulmonary tumors the differential diagnosis from lung cancer can be very difficult [6]. This should be taken into consideration during the planning of the operation in order to avoid unpleasant intraoperative surprises. The majority of the tumors mostly arise from the visceral pleura and seldom from the parietal pleura. Intratumoral necrosis, hemorrhage [1,6,20], neangiogenesis with increased tumor’s blood supply network [6,20] could also be detected in CT scan. These findings may be indicative of malignancy [1,6,20]. A tumor’s diameter bigger than 10 cm may also imply the malignant character of the tumor. However, Hélage et al. reported that the presence of intratumoral calcifications and maximum post-contrast enhancement value are not significant for the recognition of a benign or a malignant SFTP [20]. In case of a large SFTP or a tumor arising from the mediastinal pleura it can be sometimes difficult to preoperatively distinguish the mass from a mediastinal tumour. In some rare cases SFTP can be seen as multiple nodules in CT. Also, pleural effusion can be detected in CT accompanying a SFTP in up to 12% of the cases. In our case in all patients a CT always followed the detection of the mass in chest x-ray. The diagnostic value of CT can be also seen in the guided needle biopsy of the tumor, which provides us with valuable preoperatively information concerning the tumor’s nature and may even set the diagnosis. However, this method is controversial. The majority of the investigated literature regarded that a preoperative CT fine needle aspiration (FNA) should not be performed as diagnostic routine examination [6]. In this way, Boddaert et al. suggested that CT-guided FNA does not influence the therapeutic approach to SFTP and should be considered only in patients who require extended procedures, with high surgical risk, or unresectable tumors [5]. Cardillo et al. have recommended a Tru-cut biopsy if the preoperative diagnosis is necessary [6]. Chunlai Lu et al., on the other hand, suggested ultrasonography-guided core needle biopsy combined with immunohistochemical analysis as it might be a safe and rapid method to provide a diagnosis before the planned tumor resection [21]. However, preoperative diagnosis using needle biopsy has been reported in 5 cases by Weynand et al. [22]. In our cases needle biopsy under CT was performed in all three patients and offered us the ability to preoperatively assess the tumor’s nature. However, in the case of the semi-malignant SFTP it was not able to distinguish the tumor’s malignancy that was later histologically diagnosed. Magnetic resonance imaging (MRI) has a limited use in the
can be successfully performed by an experienced surgeon without and the size of the tumor and not depending on the suspicion that margins so that no tumor recurrence occurs [1,6]. For this reason a minimal as possible, but wide enough to ensure free resection performed. The lung parenchyma resection should be kept as but pleural tumors and as a result a careful tumor resection must be performed. The benign subtypes of the disease [1]. If the tumor is benign, of oncological SFTP resection is the same both for the malignant and section analysis of the margins is suggested [6,27]. The approach of the resection and the resection margins, an intraoperative frozen sec-
chyma is recommended. If there are still doubts concerning the R0 tumor excision with margins of 1 stage III, sessile or sessile or pedunculated tumor without signs of malignancy [2]; stage I, proposal a fi
morbidity and mortality [11]. Preoperatively the surgical treatment course, a limited lung parenchyma resection should be performed.

As far as the genetic background of the disease is concerned NAB2-STAT6 gene has been accused to be involved in the pathogenesis of SFTP [26]. Immunohistochemistry plays a key role in terms of the distinction of SFTP from mesotheliomas and sarcomas. SFTP were positive for vimentin, but they lacked cytokeratin expression. In addition, the positivity of most SFTP for CD34 helps clinicians to distinguish them from mesothelioma. Both benign and malignant varieties of SFTP are CD34+, CD99+, and bcl-2-positive [1]. Concerning the characterization of such a tumor as malignant England et al. have suggested that a SFTP could be characterized as malignant when at least one of the following criteria is met: 1. high mitotic activity; 2. high cellularity; 3. necrosis; 4. hemorrhage; 5. Pleomorphism. Otherwise if none of these criteria is met the SFTP can be considered as a benign tumor [7]. In addition, De Perrot proposed a five-stage classification for the SFTP [1]: stage 0, pedunculated tumor without signs of malignancy [2]; stage I, sessile or “inverted” tumor without signs of malignancy [3]; stage II, pedunculated tumor with histologic signs of malignancy [4]; stage III, sessile or “inverted” tumor with histologic signs of malignancy; and [5] stage IV, multiple synchronous metastatic tumors [2].

The therapy of both benign and malignant types of the SFTP is the complete en bloc surgical resection with free resection margins [1,5,6,11]. The surgical approach has also an indication for diagnostic purposes as long as this thoracic surgical approach has low morbidity and mortality [11]. Preoperatively the surgical treatment can be suitably planned according to radiological findings [1,6]. However, the exact surgical approach will be based on the location and the size of the tumor and not depending on the suspicion that the tumor might be a SFTP [11]. The surgical resection of the tumor can be successfully performed by an experienced surgeon without any complications [1]. These tumors are not primary lung tumors, but pleural tumors and as a result a careful tumor resection must be performed. The lung parenchyma resection should be kept as minimal as possible, but wide enough to ensure free resection margins so that no tumor recurrence occurs [1,6]. For this reason a tumor excision with margins of 1–2 cm of healthy lung parenchyma is recommended. If there are still doubts concerning the R0 resection and the resection margins, an intraoperative frozen section analysis of the margins is suggested [6,27].

Fig. 1. The 3rd patient. The preoperative chest x ray with the mass in the left lower lobe. The tumor can be seen in the Ct that followed. The Ct scan showed a 9cm tumor diameter. The tumor was approached with an anterolateral thoracotomy.

Smaller tumors can be removed through video-assisted thoracoscopic surgery (VATS) [1,6,9,11,28]. However, a large SFTP could also be resected thoracoscopically. Mazzella et al. have reported the oncological resection of a large SFTP via a single port VATS [29]. Caution is needed so that no spread of tumor cells occurs through the surgical trocar of the VATS. For larger or gigantic tumors a resection through thoracotomy is recommended. A lobectomy or a pneumonectomy could finally be carried out in larger tumors or in intraparenchymal tumors. If the tumor arises from the parietal pleura a thoracic wall resection could be considered [1]. In a case of thoracotomy attention should also be paid to avoid the intraoperative spread of the tumor [6]. In case of malignancies that infiltrate adjacent structures en-block surgical resection could be performed involving the adjacent structures [1]. Lu et al. for instance reported two cases of partial lung resection and thymus resection [9]. In some cases that the mass gave the impression of a thymus tumor a sternotomy was used as surgical approach [9,11,30]. As expected the hospitalization time is longer in case of thoracotomy than VATS [6]. The most often perioperative complication is bleeding [1,6]. In larger tumors the risk of bleeding is greater [6]. The fact that the tumor commonly arises from the visceral pleura should also be taken into consideration as the tumor develops adhesions with the parietal pleura. However these adhesions are not well perfused and can be carefully prepared without causing a significant bleeding. In addition, in order to avoid this risk of intraoperative bleeding every surgeon should always pay attention to the vascular pedicle that can arise from the parietal pleura [27]. In addition, in cases of large tumors a preoperative embolism of the tumor can be performed in order to reduce the
intraoperative bleeding risk [6]. The most common postoperative complication is the tumor recurrence. The tumor’s perioperative mortality is rather low and ranges from 0 to 1.5% [1] (See Figs. 1–4).

Due to the rarity of the tumor adjuvant chemotherapy is not widely used [1,6,11]. However, chemotherapy could be useful in some selected cases. For example, it could be used in uncompleted resected tumors, malignant sessile SFTPs or in cases of chest wall invasion and concurrent pleural effusion [6]. Unfortunately, there is still no great experience in this field and only few literature reports because of the rarity of the tumor [1]. However, as far as SFTP recurrence after surgical treatment is concerned the tumor’s recurrence is a clear indication for a new operation. In addition there is no data to support the use of neo adjuvant chemotherapy. On the contrary, due to the difficulty and the uncertainty of the preoperative diagnosis neo adjuvant chemotherapy is not recommended [1,6]. Hyperthermic cisplatin chemotherapy and brachytherapy, which are usually used in the treatment of malignant pleural mesothelioma, could also be applied in cases of SFTP, but their efficacy is still uncertain [3]. Radiotherapy has also been reported to have been performed after incomplete tumor resection. There are however also no data to support its efficacy [1,6] (see Table 1).

After the surgical treatment of a SFTP an extensive follow up is always recommended. This long term follow up is suggested due to the lack of specific guidelines regarding the treatment of SFTP and the high risk of SFTP recurrence after surgical resection. A postoperative follow-up with computer tomography is also recommended every 6 months for 2 years and then annually. The follow up, however, may be needed to be longer as a SFTP recurrence has been reported fifteen years after the surgical treatment [6]. The malignant and larger SFTP are more likely to develop metastases. For this reason, in high risk cases for postoperative metastases a long-term follow up is necessary [6,11,31]. Metastases from SFTP have been observed to bones, brain, lungs and in intra-abdominal lymph nodes [11]. Ricciuti et al. have reported a thyroid gland metastasis because of a malignant giant SFTP [31]. In addition, Takuya Inoue et al. have reported a patient’s case that SFT, in which the disease recurred locally with malignant transformation 2 years after wedge resection of the primary tumor [32]. This could probably also be an additional argument for a long-term follow-up [24,33]. In our case the proposed risk assessment model of Elizabeth Demicco that ranged from 0 to 6 was followed [8].

Table 1

| Characteristics/ Patients | 1st patient | 2nd patient | 3rd patient |
|--------------------------|------------|------------|------------|
| Age                      | 58         | 60         | 77         |
| Symptoms                 | No specific symptoms | No specific symptoms | No specific symptoms |
| Preop. Diagnosis Therapy | CT-Puncture | CT-Puncture | CT-Puncture |
| Lobe of the lung Histology | Left lower lobe SFTP | Left upper lobe SFTP | Left lower lobe SFTP |
| Size | 11.5 × 11 × 7cm | 6cm in diameter | 9 × 5.5 × 4cm |
| Postop. Complications    | Pneumony    | No         | No         |
| Postop. Day of discharge | 8th p.d.   | 4th p.d.   | 5th p.d. of the second surgery |

The second patient. Female. The chest x-ray finding. An upper lobe SFTP. The tumor was treated thoracoscopically.

Fig. 3.

1st Patient. A left lower lobe SFTP. Because of the growth of the tumor was approached with posterolateral thoracotomy. Histologically semi-malignant SFTP. As in all cases a long term follow up is recommended.

Fig. 4.
addition, in 2012 Tapias et al. proposed a new scoring system for the recurrence of resected SFTP based on the pleural origin, the morphology, the size of the tumor, the presence of hypercellularity, necrosis and mitotic activity ≥4/HPF [34]. In our case a post-operative follow up was recommended to all patients, especially to the patient who initially denied surgery.

4. Conclusion

SFTP is a rare tumor of the pleura. These tumors are often asymptomatic. As in most lung diseases the CT provides us with useful information. The preoperative diagnosis of the tumor is a difficult challenge. In our case the diagnosis was made preoperatively through CT-guided needle aspiration. The tumor's treatment is surgical. A long term follow up is in all cases highly recommended.

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