CASE REPORT

Ordinary symptom for a serious pathology – giant solitary fibrous tumor of the pleura

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Abstract
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. From an epidemiological standpoint, solitary fibrous tumors of the pleura account for less than 5% of primary pleural tumors, and commonly affect patients in the sixth and seventh decades. We presented the case of a 38-year-old woman, without any significant pathological history, who presented at the emergency room for unspecific respiratory symptoms. Imagistic investigations showed a giant opacity in the upper half part of the left hemithorax. The patient underwent surgery and en bloc resection of the tumor (30/25 cm) in oncological limits was performed. Definite diagnosis – solitary fibrous tumor of the pleura – was obtained through histological examination and immunohistochemistry. Even if SFTP are benign tumors, a long follow-up period is mandatory as even patients with complete resection are at risk of recurrence several years after surgery.

Keywords: fibrous tumor, pleura, immunohistochemistry, surgery, recurrence.

Introduction
First described in 1931 by Klemperer and Rabin [1], solitary fibrous tumor of the pleura (SFTP) is a very rare benign tumor representing less than 5% from the total cases of primary pleural tumors [2]. Primary pleural tumors are usually divided into two major categories: diffuse and localized tumors. The diffuse pleural tumor is a mesothelioma known to be associated with exposure to asbestos and has a generally poor outcome. Solitary/localized tumors are far less common than the diffuse ones. Over the years, this type of tumor has been cited in the literature under different names, such as localized fibrous tumor of the pleura, fibrous mesothelioma, benign mesothelioma, localized mesothelioma, subpleural fibroma, benign fibroma and other, reflecting the controversy related to their histogenesis. In the latest years, electron microscopy and immunohistochemistry have demonstrated that these tumors have a mesenchymal rather than a mesothelial origin and the term solitary fibrous tumor of the pleura has been implemented [3].

Because of its rarity, data regarding symptoms, management and prognosis of SFTP come from case reports, case series or from the few retrospective analysis done to date. The first teams to sense the need for a comprehensive study of this pathology were Briselli et al. (1981) [4] and England et al. (1989) [5], who reviewed in total 368, and 223 cases respectively. This subject has received significant attention ever since from enthusiastic researchers in order to complete a new chapter on tumor pleural pathology.

Patient, Methods and Results
We report the case of a 38-year-old woman who presented at the emergency room for a five-day history of irritative cough. She also reported a three months history of fatigue, but with a good exercise capacity considering her recent mountain climbing holiday. The patient never smoked and denied any exposure to asbestos or other hazardous material.

Clinical examination revealed a slightly underweight patient (body mass index of 18.8 kg/m²), normal body temperature, increased volume of the right thyroid lobe, dullness to percussion of the upper half of the right hemithorax, with no breath sounds at this level, normal oxygen saturation on room air (98%), blood pressure of 100/70 mmHg, hepatomegaly with normal spleen and an otherwise normal exam. Hematological and biochemical findings were unremarkable.

Chest X-Ray showed a giant opacity in the upper half part of the left hemithorax displacing the trachea towards the right (Figure 1).

Computed tomography (CT) (Figure 2) revealed a large, relatively well delimited, mass of 20/13 cm in the left-anterior mediastinum starting immediately under the left part of the upper thoracic aperture compressing the aortic arch and its branches, the pulmonary trunk and
the left pulmonary artery with the lower limit at the left pulmonary hilum, displacing the whole mediastinum to the right. The mass had septa and areas of necrosis alternating with areas of increased contrast captation. CT examination pointed out also hepatomegaly but without any focal lesions inside.

Figure 1 – Chest X-ray at admission: a giant opacity in the upper half part of the left hemithorax displacing the trachea towards the right hemithorax.

Figure 2 – Chest computed tomography scan: a large, well-delimitated mass in the left-anterior mediastinum compressing different intrathoracic structures and displacing the whole mediastinum to the right. The mass had septa and areas of necrosis alternating with areas of increased contrast captation.

Spirometry showed a restrictive ventilatory dysfunction with a 39.9% reduction in vital capacity and 40.5% of forced expiratory volume in one second. Results of blood gas analysis were within normal limits.

Bronchoscopy was performed and revealed a displaced and deformed trachea in its upper half due to posterolateral compression, left bronchial tree with erythematous and edematous mucosa and important compression on the upper left pulmonary lobe. There were no masses found inside the respiratory tree.

Bronchoscopic cytology revealed no abnormal findings and no signs of bronchitis. Ziehl–Neelsen staining did not reveal any acid-alcohol resistant bacillus and cultures for Koch bacillus were negative.

To complete the differential diagnosis, pulmonary tumor biomarkers were assessed, i.e., α-fetoprotein, carcino-embryonary antigen (CEA) and cytokeratin-19 fragments (CYFRA 21-1), and were all within normal range.

In this setting, considering the imagistic examination suggested an extrapulmonary intrathoracic tumor, the decision was to proceed to surgery, which would also allow biopsy and histological diagnosis.

Total sternotomy and left anterior thoracotomy through the fifth intercostal space was performed for the resection of the tumor. Upon entering the pleura, the surgeon found a giant polyllobulated tumor of 30/25 cm extended over the upper half of the left hemithorax causing right mediastinal displacement (Figure 3). Dissection of the tumor was performed and several very large feeder vessels from the parietal pleura were revealed along with the hypervascularization of the parietal pleura. There was a relatively large blood loss (around 2500 mL) during surgery, which lead to multiple blood transfusions.

Histologically, Hematoxylin–Eosin (HE)-stained cross-sections, the tumor consisted of short spindle-shaped cells, with a predominant storiform and hemangiopericytomatous pattern, with very rare mitoses. Inside the tumor proliferation, there were multiple vessels with a hyaline wall and the adjacent pulmonary parenchyma showed several areas of condensations (Figures 4–6). The immunohistochemistry study (Table 1) showed immunoreactivity to vimentin, CD34 and Ki67 within the tumor cells, with negative reactivity to actin (Figures 7–9). The pathological examination established the diagnosis of solitary fibrous pleural tumor solitary.

Table 1 – Antibodies used for the immunohistochemical study

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Manufacturer</th>
<th>Clone</th>
<th>Dilution</th>
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<tbody>
<tr>
<td>CD34</td>
<td>DAKO</td>
<td>QBEnd 10</td>
<td>1:50</td>
</tr>
<tr>
<td>Actin</td>
<td>DAKO</td>
<td>1A4</td>
<td>1:100</td>
</tr>
<tr>
<td>Ki67</td>
<td>DAKO</td>
<td>MIB-1</td>
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Postoperative evolution was generally uneventful, with the exception of the development of a residual anterolateral pleural cavity (Figure 10). The patient was discharged 17 days after surgery.

Serial chest X-rays (Figure 11) showed no recurrence of the tumor and at this moment the patient is clinically asymptomatic and has resumed her usual activities.

Figure 3 – Solitary fibrous tumor of the pleura: operative specimen. The tumor measured 30×25 cm.

Figure 4 – Tumor proliferation with spindle-shaped cells and multiple elongated, angulated and ramified blood vessels. HE staining, 200×.
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Figure 5 – Tumor proliferation limited by cubic and flattened benign mesothelial cells. HE staining, 200×.

Figure 6 – Tumor proliferation with spindle-shaped cells and no mitotic activity. HE staining, 400×.

Figure 7 – Intense and diffuse positive CD34 within the tumor cells and positive within the vascular endothelial cells. Immunohistochemistry staining for CD34: (A) 200×; (B) 400×.

Figure 8 – Ki67 was nuclear positive within 2–3% tumor cells. Immunohistochemistry staining for Ki67, 400×.

Figure 9 – Actin was negative within the tumor cells and positive within the blood vessels. Immunohistochemistry staining for actin, 200×.

Figure 10 – Postoperative chest X-rays showed the development of a residual anterior-lateral pleural cavity: (A) Five days after surgery; (B) 14 days after surgery.

Figure 11 – Serial chest X-rays showed no recurrence of the tumor: (A) Three months after surgery; (B) Six months after surgery.
Discussion

The solitary fibrous tumor of the pleura is a rare primary tumor arising from mesenchymal cells in the areolar tissue subjacent to the mesothelial-lined pleura. It is benign in approximately 80% of cases. According to the review by De Perrot et al. [6], until 2002, there were only 800 cases reported in the literature and an additional 960 cases of SFTP were collected by Cardillo et al. [2] between 2002 and 2012, adding to a total of approximately 1760 cases over the years. Although SFTP occurs in a wide age range, it predominantly affects patients in the sixth and seventh decades of life, with a fairly equal frequency in both sexes [7]. The common presentations are relatively small tumors less than 10 cm in diameter in an asymptomatic patient, discovered incidentally on a routine chest X-ray. Tumors larger than 10 cm, occupying a large area of the thorax and compressing other thoracic structures may cause symptoms such as dyspnea, chest pain, cough, and fatigue as seen in the case presented above. Pain usually appears when the parietal pleura is involved [6].

Patients with SFTP can display paraneoplastic syndromes such as pulmonary hypertrophic osteoarthropathy known as Pierre-Marie–Bamberger syndrome in 10–20% of cases, or refractory hypoglycemia, the Doege–Potter syndrome, in 5% of cases [5, 8]. These result from an abnormal secretion of hyaluronic acid or hepatocyte growth factor and an excess secretion of insulin-like growth factor 2 in the tumor, respectively [9].

Imaging tests are helpful in localizing the tumor and to establish its size. Even though the tumor can be incidentally discovered on the chest X-ray, chest CT is an important imaging modality, which more clearly defines 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. In case of small SFTP, CT more frequently typically demonstrates a homogeneous well-defined, non-invasive, lobular, soft-tissue mass whereas larger lesions are typically heterogeneous and may not exhibit CT features suggestive of pleural tumors and can be misdiagnosed as peripheral lung cancer [10].

Differential diagnosis should take include lung cancers, all anterior mediastinal tumors including thymoma and teratoma, posterior mediastinal masses like neurogenic tumors; mesothelioma should also be considered, even though the well circumscribed and localized aspect of the SFTP usually rules out mesothelioma on the imaging test. Definite diagnosis is only confirmed after both imaging and histological tests are available.

Definite diagnosis can be made before surgery by obtaining histological material through percutaneous transthoracic needle biopsy or fine needle aspiration (FNA). Sung et al. [11] have shown a success rate for definite diagnosis by FNA of 43%. In this setting and because surgical resection involves simultaneous diagnosis and treatment, preoperative FNA is not always mandatory. Surgical resection for diagnosis and treatment is acceptable as long as operability is carefully assessed before intervention.

The macroscopic appearance is of an encapsulated firm lobular mass with a characteristic white and whorled appearance in the benign variety and a more homogeneous appearance in the malignant neoplasm. Many are pedunculated on pleural-based pedicles that contain hypertrophic arteries and veins. On cut section, there may be areas of hemorrhage and necrosis in both, although calcifications are usually confined to the benign tumors. The size and weight may vary, with no relation to the resectability, curability or the malignant/benign nature of the tumor [7].

The histological origin of SFTP has been for a long time a matter of debate. Initially, this type of tumor was considered a localized mesothelioma, thus arising from the mesothelial cells of the pleura. Subsequently, it was proven that SFTP originated in the submesothelial, non-committed mesenchymal layer [4].

The microscopic appearance is of cellular areas with packed fusiform nuclei and fibrillar collagen alternating with sclerotic areas of fibrous collagen and infrequent nuclei. Sometimes cells can be organized as bundles or palisades. Spindle-shaped cells typically have minimal nuclear pleomorphism and rare or absent mitoses. Nuclei are intensely basophilic, with tapered endings in transverse section and round or polygonal endings in cross section. Numerous thin-walled vessels constitute an additional feature of large tumors [3, 4].

SFTPs can be clearly diagnosed by means of specific immunohistochemical staining techniques and thus differential diagnosis with mesotheliomas or pulmonary sarcomas can be easily made.

Solitary fibrous pleural tumors typically staining positive for vimentin, a marker of mesenchymal cells, CD34 antigen and Ki67 and negative for cytoplasmic keratins, which are found in mesotheliomas [12]. The CD34 antigen, found in normal and neoplastic endothelial cells, is present in nearly all occurrences of these tumors, whether they are benign or malignant [13]. Antiapoptotic proto-oncogene bcl-2 stains intensively positive in the case of SFTP and can be used to confirm or dismiss the diagnosis in CD34-negative tumors [14]. The conversions of a SFTP from a CD34-positive mass to a CD34-negative lesion can suggest malignization [3, 4].

Histological attributes have been described in an attempt to predict the malignant potential. In his series, England et al. [5] (1989) established the following features suggestive of malignancy: mitotic counts exceeding 4/10 high-power fields, necrosis, hemorrhage, pleomorphism, stromal or vascular invasion, and size exceeding 10 cm. These pathological features are helpful, but the absence of these characteristics is not completely predictive of benign behavior.

De Perrot et al. [6] described a staging system based on pedunculated versus sessile attachment and malignant versus benign histology that predicted recurrence:

- stage 0: pedunculated tumor without signs of malignancy (<2% recurrence);
- stage I: sessile or “inverted” tumors without signs of malignancy (<8% recurrence);
- stage II: pedunculated tumor with histological signs of malignancy (14% recurrence);
- stage III: sessile or “inverted” tumor with histological signs of malignancy (63% recurrence); and
• stage IV: multiple synchronous metastatic tumors.

Outcome predictors are morphological and histological factors as stated before, however, the most reliable predictor remains the complete surgical resection of the tumor [15].

The curative treatment of patients with SFTPs is complete surgical excision. Aggressive surgery is recommended due to the high probability of their recurrence [16]. Small pedunculated tumors located on the visceral pleura can be excised through video assisted thoracic surgery (VATS) [17]. However, great care must be taken 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.

The type of surgical resection differs according to the size of the tumor, its location and extent of invasion to adjacent structures. Complete, en bloc surgical resection is the mainstay therapy for all benign and malignant SFTPs and is the one recommended by most authors [3].

SFTPs develop in 80% of cases on the visceral pleura with the remainder on the parietal pleura [18]. In case of sessile tumors involving the visceral pleura or fibrous tumors of the pulmonary parenchyma, it is necessary to excise a large part of the affected lung to reduce the recurrence rate [19]. Massive intraoperative bleeding may occur due to either vascular adhesion to adjacent tissues or highly vascular tumors. Moreover, technical difficulties may arise related to the large size of the tumor or large insertion area on the lung, diaphragm, mediastinum or thoracic wall. Nonetheless, the surgical mortality is low, ranging from 0% to 1.5% [20].

According to De Perrot et al. [6], the recurrence rate is around 8% for the sessile SFTP, whereas in the case of pedunculated tumors, the rate is of 2%. Curative treatment of recurrences is represented by surgical re-intervention and complete excision of the tumor [19].

The follow-up plan after the intervention consists in chest X-rays every six months in the first two years and annually thereafter. SFTP prognosis after surgery is very good but close follow-up is mandatory as recurrences can appear even after 15–20 years and the biological behavior can be unpredictable even with subsequent malignization [21].

Conclusions

We presented the case of a young female patient with a very rare primary pleural tumor – a giant solitary fibrous tumor of the pleura. Even though the tumor was very large and compressed a series of intrathoracic structures, the patient’s only symptom was an irritative cough and had only a mild decrease in exercise capacity (she could very well climb a mountain in the recent period). We successfully managed to surgically remove the giant SFTP via sternotomy and thoracotomy. Although SFTP are benign tumors, a long follow-up period is mandatory as even patients with complete resection are at risk.

References