

# PLEURAL SOLITARY FIBROUS TUMOR: A CASE REPORT

*Tumor fibroso solitário pleural: um relato de caso*

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## ABSTRACT

**Objectives:** To report a case of a pleural solitary fibrous tumor, a rare soft tissue neoplasm, demonstrating its clinical complexity and diagnostic difficulties, seeking to raise awareness about the disease. **Methods:** The patient underwent total tumor resection, and samples were obtained for anatomopathological and immunohistochemical studies. Additional information was obtained by analyzing the medical records made available by the Hospital Geral de Carapicuíba, after approval by the institution's ethics committee and literature review. **Results:** The patient had a good clinical outcome and is being followed up at the outpatient clinic to screen for possible recurrences. **Conclusion:** Knowledge about the clinical and anatomopathological features of solitary fibrous tumors is essential for the correct diagnosis and favorable outcomes, including lower risk of recurrence and higher survival rates.

**Keywords:** Solitary Fibrous Tumor, Pleural.

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## INTRODUCTION

Solitary fibrous tumor (SFT) is a neoplasm of mesenchymal origin, which presents a low incidence and corresponds to less than 2% of all soft tissue tumors<sup>1</sup>. There is no risk factor associated with this pathology, such as environmental exposure to radiation, tobacco, asbestos or other toxic substances<sup>2</sup>. Due to its rarity, despite having been described in 1931, SFT is still a relatively little-known tumor, which represents a challenge for its diagnosis and treatment<sup>1</sup>. In addition, the diagnostic difficulty is compounded by the indolent clinical

course and nonspecific symptoms of most STFs. As a result, most cases are diagnosed only after an incidental finding on radiological imaging<sup>2-5</sup>.

Another feature that contributes to the clinical complexity of SFT is that it can affect almost all anatomic sites of the body, including the skin, meninges and gastrointestinal tract, among others. Originally described as a pleural tumor, it is currently known that only 30% of cases have a pleural origin<sup>6</sup>. On the other hand, different case series differ regarding the other most frequently affected sites, as some studies report the

meninges in second place, with 27% of cases<sup>6</sup>, while others point to the peritoneal cavity (abdomen and pelvis)<sup>7</sup>. Within the thoracic cavity, in addition to the pleura, SFT has also been described in the lung parenchyma, mediastinum and pericardium<sup>8</sup>. Other less common sites include the extremities, oral cavity, orbits and paranasal sinuses<sup>1</sup>. The mean age of patients with pleural SFT is around 60 years<sup>9</sup>, but the tumor has been reported in younger individuals, including children<sup>4</sup>. Extra-pleural SFT, on the other hand, tends to occur in younger patients, with a mean age of 50.3 years<sup>10</sup>.

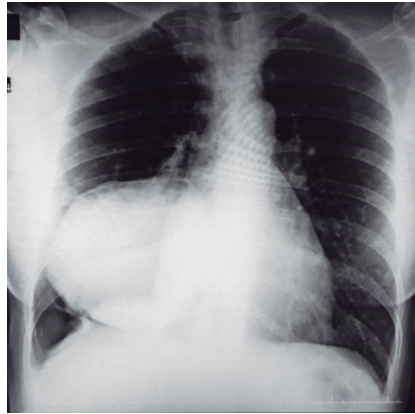
SFT also has histological characteristics in common with other soft tissue tumors, which led to several nomenclature changes in the past, such as the denomination hemangiopericytoma, widely used in the past<sup>1</sup>. With the advances in molecular, immunohistochemical and genetic techniques, the understanding of SFT is improving, and now it is possible to better characterize this neoplasm. This case report aims to raise awareness of this rare disease by discussing its clinical presentation and treatment, in light of its complexity and recent advances in its understanding.

### CASE REPORT

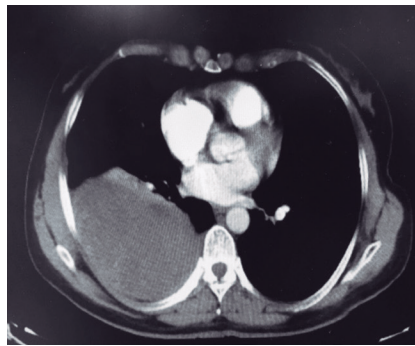
The patient is a 47 year old non-smoker female patient with no relevant medical history, complaining of dry cough and pleuritic chest pain for nine months, without associated infectious symptoms. The patient had already been treated with antibiotic therapy on two occasions, without improvement. On physical examination, she was in good general condition, well-nourished, with absent breath sounds at the base of the right hemithorax on lung auscultation, dullness on percussion and increased vocal remits at the same location.

The initial chest X-ray (figure 1) shows a homogeneous opacity at the base of the right lung, which remained radiographically stable during follow up. Computed tomography (CT) of the chest was then performed (Figure 2), which showed a hypodense lesion measuring 11.8 x 8.3 cm occupying the right middle lung field, apparently with pleural origin, and without significant enhancement after intravenous contrast. The lesion was compressing the adjacent lung parenchyma, causing passive atelectasis. A basal posterior laminar pleural effusion on the right could also be seen.

The etiological investigation was performed with a video-assisted thoracoscopy biopsy, which was inconclusive. Then, a decision was made to perform thoracotomy with resection of the mass located in the chest wall. This time, the gross surgical pathology analysis of the piece revealed a mass weighing 710 grams and measuring 16 x 14 x 5 cm, with a smooth, brownish external surface. Upon cuts, a whitish and firm tissue was noticed. The microscopic examina-



**Figure 1. Chest x-ray performed before surgical resection of the tumor.**



**Figure 2. Chest CT with IV contrast performed before surgical resection of the tumor.**

tion, in turn, revealed a spindle cell neoplasm without atypia and with extensive collagenous areas in-between. The circumferential margin was positive.

The immunohistochemical study was positive for actin (in vessels), BCL-2 and CD34 (strong and diffuse), with positive Ki-67 in 1% of neoplastic cells. The observed mitotic index was low. The diagnosis was consistent with a solitary fibrous tumor of the chest. Figure 3 illustrates the chest X-ray performed after tumor resection.

### DISCUSSION

This report illustrates a case of SFT that manifested with nonspecific respiratory symptoms, although previously published case series have reported that only a minority of patients (about 23%) have any symptoms<sup>7</sup>. However, tumors that reach large volumes, in particular, can cause symptoms resulting from local compression, such as cough, chest



**Figure 3. Chest x-ray performed after surgical resection of the tumor.**

pain, dyspnea and hemoptysis<sup>2</sup>. Cases of paraneoplastic syndromes associated with SFT have also been reported, especially Doege-Potter syndrome, characterized by hypoglycemia of unknown origin, resulting from the production of insulin-like growth factor 2 (IGF-2) by SFT cells<sup>11</sup>. Cases of secondary hypertrophic osteoarthropathy associated with SFT have also been described<sup>2,12</sup>.

However, SFT is often asymptomatic and only incidentally diagnosed by imaging tests<sup>5</sup>. Thus, it is essential to know this pathology and the radiological findings associated with it as a first step towards the correct diagnosis. The initial investigation can be done with a simple chest X-ray, which typically shows a single nodule or mass with well-defined contours that originate from the pleura, with or without a pedicle<sup>1</sup>. The next step involves performing a chest CT with contrast, which also shows the nodule or mass with regular contours, but sometimes lobulated. The tumor is hypervascular and may have, especially if large, areas of necrosis. T2-weighted MRI scans may reveal foci of hyperintense signal associated with areas of necrosis, which give the lesion a non-homogeneous appearance<sup>1</sup>.

Investigation with chest CT is useful for differentiating from other thoracic masses<sup>2</sup>, since SFT accounts for less than 5% of pleural tumors<sup>2</sup>. Examples of differential diagnoses are malignant pleural mesothelioma, neurogenic mediastinal tumors, synovial tumor, fibrosarcoma, malignant fibrohistiocytoma and, in the case of anteriorly located masses, thymic pathologies and germ

cell tumors. The definitive diagnosis, however, is made through anatomic pathology, immunohistochemical and molecular analyses.

SFT histology shows areas of alternating cellularity, with areas rich in tumor cells and other that are hypocellular, but, rather, rich in stromal collagen. Tumor cells vary from ovoid to spindle-shaped<sup>1</sup>, with rounded to oval nuclei and small cytoplasm<sup>1,5</sup>. They are usually low-grade neoplasms, with minimal nuclear pleomorphism, and generally rare or absent mitoses<sup>1</sup>. Conventional immunohistochemical markers include CD34 expression in about 79% of cases, but this is a nonspecific marker, as neoplasms such as gastrointestinal stromal tumors (GIST) can also express it. Other markers that can be expressed by TDS include Bcl2, CD99, vimentin in the absence of actin, and epithelial markers, such as the epithelial membrane antigen<sup>1,13</sup>.

A barrier to the immunohistochemical diagnosis of SFT, however, arises from other tumors with similar histology expressing these same markers<sup>13</sup>. Examples of differential diagnoses are monophasic synovial sarcoma, leiomyomas and desmoid tumors, which also express CD34<sup>14</sup>. The specificity of these markers is therefore relatively low<sup>13</sup>, which, added to the histological complexity and possibility of SFT affecting several anatomic sites, contributes to the diagnostic challenge. SFT can also be mistaken for other tumors, such as other soft tissue

neoplasms, such as schwannomas, spindle cell lipomas, dermatofibrosarcoma protuberans, liposarcomas, GIST, malignant peripheral nerve sheath tumors, and synovial sarcomas<sup>13</sup>.

To minimize diagnostic challenges and better differentiate SFT, molecular techniques have emerged as a useful tool for this purpose<sup>13</sup>. One of the molecular markers that are known to be highly sensitive and specific for SFT is the NAB2 and STAT6 gene fusion, which is present in more than 90% of the samples, whereas it is absent even in histologically similar tumors. It is also possible to investigate the nuclear expression of STAT6 using immunohistochemical techniques. Studies have shown that a strong and diffusely positive result for STAT6 in the nucleus is highly specific for SFT, although weakly positive results can be observed in other tumors<sup>1,13</sup>. Thus, such tools contribute to the challenging diagnosis of SFT, which requires integrating clinical, anatomic pathology, immunohistochemical and molecular features<sup>13</sup>.

The World Health Organization Classification of Tumors of Soft Tissue and Bone, fifth edition, classifies SFT as intermediate tumor (rarely produces metastases)<sup>13</sup>, since most cases have a benign behavior, although it can be locally aggressive. Overall survival rates reflect this classification, ranging from 59-100% at one year and 40-89% at ten years, depending on the case series<sup>1</sup>.

However, several cases present a malignant behavior, reportedly between 10% and 20%<sup>15</sup>, which may recur and metastasize. At least three important studies have identified risk factors associated with malignant behavior and worse prognosis. They are: size > 10 cm (15 cm in one of the studies), age > 55 years, more than 4 mitoses/10 high-power fields, high nuclear pleomorphism, high cellularity, presence of necrosis, hemorrhage and/or a malignant component on the anatomic pathology analysis (e.g. stromal or vascular invasion)<sup>16-18</sup>. The presence of paraneoplastic syndromes, such as Doege-Potter's, is also associated with malignant tumors (up to 70%) and, consequently, with a worse prognosis<sup>1,19</sup>. Molecular markers were also observed more frequently in tumors with malignant behavior, such as the presence of mutations in the promoter region of telomerase reverse transcriptase<sup>1</sup>. The loss of CD34 expression was also associated with malignant tumors<sup>13</sup>. Table 1 summarizes the characteristics associated with malignant behavior of SFT.

The treatment of SFT is surgical and can be performed by open thoracotomy or videothoracoscopy (recommended for tumors smaller than 5 cm)<sup>20</sup>. Regardless of the technique, the objective of surgery should be the total resection of the tumor and obtaining free margins, which is associated with a lower rate of local recurrence and higher chance of survival<sup>1,20</sup>. The presence of a pedicle

**TABLE 1 - Features associated with malignancy in Solitary Fibrous Tumors**

<b>Clinical and demographical features</b>	<ul style="list-style-type: none"> <li>• Age &gt; 55 years;</li> <li>• Paraneoplastic syndromes, such as Doege-Potter's.</li> </ul>	Adapted from Davanzo et al., <i>Transl Gastroenterol Hepatol</i> 2018 <sup>1</sup> ; Tariq et al., <i>Diagn Pathol</i> 2021 <sup>13</sup> ; Demicco et al., <i>Mod Pathol</i> 2012 <sup>16</sup> ; England et al., <i>Am J Surg Pathol</i> 1989 <sup>17</sup> ; Gold et al., <i>Cancer</i> 2002 <sup>18</sup> ; Herrmann et al., <i>Exp Clin Endocrinol Diabetes</i> 2000 <sup>19</sup> .
<b>Anatomopathological features</b>	<ul style="list-style-type: none"> <li>• Size &gt; 10 cm (15 cm in one of the studies);</li> <li>• &gt; 4 mitoses/10 high-power fields;</li> <li>• High nuclear pleomorphism;</li> <li>• High tumor cellularity;</li> <li>• Necrosis and/or hemorrhage;</li> <li>• Malignant component on anatomopathological examination.</li> </ul>	
<b>Molecular markers</b>	<ul style="list-style-type: none"> <li>• Telomerase reverse transcriptase promoter region mutations</li> </ul>	
<b>Immunohistochemical markers</b>	<ul style="list-style-type: none"> <li>• Loss of CD34 expression.</li> </ul>	

makes resection easier, but larger, invasive and sessile tumors can represent a surgical challenge. Some cases, such as large tumors attached to the lung or with parenchyma invasion, may require lobectomy to obtain free margins. The same applies to tumors that adhere to and/or invade the diaphragm, parietal pleura, and pericardium, which may require more extensive surgery<sup>20</sup>.

SFT recurrence can occur during late follow-up, as far as 17 years after the initial resection, even when complete resection is achieved, with free margins, and even when the tumor is benign<sup>1,21</sup>. The recurrence rate reported in large case series varies from 10 to 18.2%<sup>21,22</sup>, but may vary depending on the follow-up time and the characteristics of patients<sup>1</sup>. As for tumors with malignant characteristics, however, recurrence rates can be as high as 63%<sup>1,22</sup>. In a literature review, de Perrot *et al.* described a risk stratification system for SFT recurrence, based on histological and morphological characteristics of the tumor. According to the study, the tumors can be classified based on the presence of malignant in histological features (the same ones described above) and according to their gross morphology, which can be pedunculated or sessile. The risk of recurrence ranged from less than 2% in benign pedunculated tumors to 63% in sessile malignant tumors<sup>22</sup>. However, obtaining clear margins is the most important consideration after surgical resection to predict the risk of recurrence<sup>2</sup>.

Adjuvant radiation therapy is indicated only in patients with sessile tumors with malignant features, whose risk of recurrence is high, as proposed by de Perrot *et al.*<sup>22</sup>. However, in other patients, when complete resection with negative margins is possible, radiation therapy in the treatment of SFT is not indicated, as it is a rare and indolent tumor, for which there are no controlled studies<sup>1</sup>. In cases of local recurrence, a new resection can be attempted<sup>1,22,23</sup>. The role of adjuvant radiation therapy in these cases, as well as when the margins are compromised, is not well established, due to the lack of controlled studies<sup>1</sup>. Only isolated case reports have shown a significant response of recurrent SFTs to radiation therapy<sup>24</sup>.

SFT metastases are usually hematogenous and occur mainly in the liver,

central nervous system, spleen, peritoneum, adrenal glands, gastrointestinal tract, kidneys and bones<sup>22</sup>. However, the ideal treatment for metastatic SFT, as well as for locally advanced and unresectable tumors, is not well established, as controlled studies are lacking, given the rarity of the tumor<sup>1</sup>. Most of the studies performed to date are retrospective, including the use of cytotoxic chemotherapy based on doxorubicin, which has shown low response rates<sup>1</sup>. Some studies also evaluated the effectiveness of targeted therapy in SFT, including drugs such as antiangiogenics (pazopanib, sorafenib, sunitinib, regorafenib and axitinib). Results were poor, and controlled studies are still needed to determine whether such drugs are effective or not<sup>1</sup>.

After the surgery, the patient should be followed up periodically, focusing on the early identification of recurrences and metastatic disease. However, there are no well-defined guidelines on how such monitoring should be done, due to the lack of studies and the rarity of the disease. In general, the risk criteria described above (Table 1) are used to identify patients at higher risk of recurrence and metastatic disease<sup>1,16-18</sup>. De Perrot *et al.* proposed that high-risk patients (sessile tumors with malignant characteristics) should be followed up every six months for the first 24 months after resection, with CT and chest X-rays, as relapse occurs within this time interval in most of these patients<sup>22</sup>. Follow-up can be done annually thereafter. It is also possible to consider the guidelines for the follow-up of soft tissue sarcomas proposed by the National Comprehensive Cancer Network (NCCN), which recommend follow-up with imaging tests every six months for three years in low-risk patients, followed by annual follow-up until the fifth year. For intermediate and high risk patients, the interval is shorter, every three to four months for the first two years and then every six months until the fifth year<sup>25</sup>. However, it is prudent to continue monitoring these patients for several years, as recurrences have been described up to 17 years after resection of the primary tumor<sup>1</sup>.

In summary, pleural SFT is a rare neoplasm with no known risk factors. The clinical course of most cases is indolent, and the diagnosis is generally made af-

ter incidental imaging findings. Diagnosis can be difficult due to the histological and immunohistochemical features shared by other soft tissue tumors, but advances in molecular techniques now allow better characterization of SFT. The patient of this case underwent total resection of the tumor, presented with good clinical outcomes, and has maintained outpatient follow-up to monitor for possible recurrences. These are the recommended treatments and the evolution of most cases, but up to 20% of patients may have tumors with malignant features, which indicate a worse prognosis and higher risks of recurrence. Due to the rarity of the disease, there are no controlled studies that validate the use of adjuvant radiation therapy or chemotherapy. Generally, adjuvant radiation therapy is reserved for cases with a high risk of recurrence. Also due to its rarity, clinical complexity and diagnostic difficulty, good knowledge about SFT is essential to obtain favorable results and good survival rates, as most tumors have benign features.

## CONFLICTS OF INTERESTS

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