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# SOLITARY FIBROUS TUMOR OF THE LUNG: CASE REPORT AND LITERATURE REVIEW

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**Abstract:** Solitary fibrous tumor is a rare neoplasm originating in mesenchymal tissue, with fibroblastic differentiation, with the potential to form throughout the body, and is notable for its rarity. It has an excellent prognosis but caution should be exercised due to its unpredictable biological behavior and course. In addition, most patients are asymptomatic or present with nonspecific symptoms of the pathology. The objective of this study was to report the case of a patient with a solitary fibrous tumor of the lung and to review the scientific literature on the subject. The bibliographic search was conducted over a period of time in databases of scientific journals and articles, using studies in Portuguese, English, and Spanish, and addressing the importance of early diagnosis, aiming at better treatment by the medical profession and a favorable prognosis for patients.

**Keywords:** neoplasm, lung, fibrous tumor, solitary fibrous tumor of the lung.

## **Introduction**

Solitary fibrous tumor (SFT) of the serous cavity was first described by Lietaud in 1767 and later by Klemperer and Rabin in 1931.<sup>1,2,3,4</sup> The cause of the tumor remains unexplained. Exposure to and trauma from asbestos have been implicated, but there is still considerable doubt as to the etiological significance of these factors.<sup>1,5</sup> There are two theories about its origin: (a) These tumors may arise from the subpleural mesenchyme in continuity with interlobular septa and (b) arise from the submesothelial elements of the lung parenchyma.<sup>3,4,6</sup> Although metastasis is rare, this possibility should always be considered.<sup>7,8</sup>

Solitary fibrous tumors are spindle cell tumors that can form anywhere in the body but often form in the visceral pleura.<sup>5,18,10,11</sup> It is believed that the origin of these tumors is not mesothelial, as was previously thought, but rather submesothelial, based on histological and immunohistochemical studies. SFTs located entirely in the lung are extremely rare and have been little described in the literature.<sup>1,5,6,12</sup>

In addition to pleural involvement, they can also be found in the head and neck region, as well as in the kidney, prostate, spinal cord, vertebrae, mediastinum, pericardium, peritoneum, heart, lung, bladder, breast, thyroid, orbit, oral cavity, salivary gland, epiglottis, nasopharynx, nasal cavity, paranasal sinuses, parotid gland, skin, and meninges, among others.<sup>2,5,9,1,3,4,6,13,14,15,16</sup> Only about 20% are malignant. These tumors grow slowly and tend to be asymptomatic until they become very large, which can cause compression of adjacent organs, initiating the clinical picture of the pathology.<sup>3,5,15,13,14</sup>

Its estimated incidence is 2.8 cases per 100,000 hospitalizations.<sup>1,9,17</sup> Intraparenchymal presentation has been associated with aggressive or malignant behavior, with malignancy reported in 13% to 23% of cases.<sup>6</sup> It occurs mainly in adults between the ages of 20 and 70,<sup>9</sup> most commonly during the fifth and seventh decades of life<sup>11,5</sup> affecting men and women equally.<sup>9,4,6</sup> The literature describes the cases of an 8-year-old patient and a 20-year-old patient.<sup>9</sup>

The tumors varied in size, generally from 1.0 to 15.0 cm, with an average of 5.0 cm.<sup>4,6,14</sup> Surgical treatment in cases of localized disease has a 5-year survival rate of over 90%<sup>4,19</sup> and a 10-year survival rate of between 54% and 89%.<sup>3,9,18</sup> The recurrence

rate in benign forms is 1.4%, and between 9% and 19% in malignant forms.<sup>4,19</sup>

Benign SFT originates from CD34+ dendritic stromal cells and differentiates into fibroblasts. The origin of malignant TFS is still controversial. One hypothesis is that high-grade malignant tumors transform from benign TFS or low-grade malignant TFS, as observed by Yokoi.<sup>20</sup> The pathogenesis of this condition is not yet fully understood.

Patients with pulmonary TFS have a very limited clinical picture, with absent or nonspecific signs and symptoms. Approximately half of patients with this type of tumor are asymptomatic. However, in some cases, tumor growth results in compression of pulmonary structures, which can lead to nonspecific signs and symptoms, such as chest pain, chronic cough, dyspnea, hemoptysis, or may be accompanied by systemic manifestations such as hypoglycemia, fever, and clubbing.<sup>1,3,4,6,14,15,16</sup> Compression can also drastically affect nearby structures, such as the bronchi, pulmonary hilum, carina, and superior vena cava, obstructing these structures.<sup>13</sup>

On physical examination, chest auscultation may reveal wheezing, with marked decrease in vesicular murmur, dullness to percussion, and decreased thoracovocal fremitus in the affected hemithorax.<sup>21</sup>

These tumors are also related to several paraneoplastic syndromes. Some of them are: refractory hypoglycemia (Doege-Potter syndrome [DPS]), pulmonary hypertrophic osteoarthropathy, and elevated human chorionic gonadotropin. In addition to being related to the poor prognosis of TFS.<sup>16,22</sup>

SFTs, being a pathology that fluctuates between asymptomatic patients and nonspecific symptoms, are usually disco-

vered incidentally through imaging tests during investigation for other comorbidities.<sup>4,17</sup> Diagnostic imaging tests may consist of the following: posterior-anterior and profile chest X-ray, chest ultrasound (USG), chest computed tomography (CT), chest magnetic resonance imaging (MRI), and positron emission tomography (PET-CT).<sup>25</sup>

Emphasizing the two imaging exams most reported in the literature: chest X-ray and CT. Chest X-ray reveals a solitary ovoid mass, in most cases with no pleural effusion, with or without areas of atelectasis.<sup>22</sup> Chest CT generally shows a homogeneous soft tissue lesion, clearer, often in contact with the chest wall, with a heterogeneous uptake pattern after intravenous contrast infusion, with or without calcifications<sup>21,14,19,23</sup> in addition to similar findings on chest radiography. Nevertheless, X-ray, CT, and MRI examinations of TFSs are defined as nonspecific.

The definitive/specific diagnosis of the lesion is confirmed by histopathology with immunohistochemical staining of the tumor after surgical excision or percutaneous biopsy.<sup>9,2,6,13,10,14,22</sup> Histologically, the tumors are composed of rounded and spindle-shaped cells with dense collagen, arranged in a variable context, containing circumferentially hyalinized vessels.<sup>22</sup> Tumor cells are arranged in a so-called “*patternless*” pattern, which is characterized by a random distribution of spindle cells and fibrous stroma, mixed with hypocellular and hypercellular areas.<sup>21,10,19,24</sup> TFSs are classified as benign or malignant based on histological findings: pleomorphism, cellularity, mitotic activity, invasive growth, or presence of necrosis.<sup>17,24</sup> The malignant form of this tumor is defined histopathologically as hypercellular (increased cellularity), with high mitotic activity

(more than 4 mitoses per 10 high-power fields), with the presence of atypia or cellular pleomorphism, size greater than 10 cm, hemorrhage, necrosis, and/or infiltrative margins.<sup>15,17,26</sup>

In some cases, because there is no histological distinction, immunohistochemical examination is of great value. The final diagnosis is often made with immunohistochemical findings, being positive for CD34 antibodies in 100% of cases, CD99 antibody in 70% of cases, Bcl-2, SMA, and epithelial membrane antigen in 20%, and vimentin in 90% of cases, in addition to being negative for cytokeratins, actin (α-SMA), desmin, and S100 protein.<sup>3,10,11,19,24</sup> However, some authors consider these studies to be relatively nonspecific, and recently there have been more studies on genotyping (avoids confusion with histological imitations). Thus, intrapulmonary TFS is positive for STAT6, a very sensitive and specific marker, and reverse transcription polymerase chain reaction reveals a NAB2-STAT6 fusion gene, confirming the final diagnosis of malignant TFS.<sup>16,17,26</sup>

In addition, the histological evaluation of these tumors based on immunohistochemistry is enhanced by CD100 antibody staining, which is positive in TFS and, according to some authors, is a specific characteristic of this tumor.<sup>6,14</sup>

Complete resection surgery with clear margins is the first-line treatment for localized disease, with 10-year survival rates ranging from 54% to 89%. It is the best and most reliable treatment for both malignant and benign tumors, and the type of surgery used to remove an STS depends on where the tumor is located.<sup>9,3,19</sup> The effectiveness of treatment depends on the quality of tumor resection, which can prevent recurrence.<sup>13</sup>

Radiotherapy and chemotherapy are not first-line therapies for TFS.<sup>27</sup> There are no international recommendations regarding the role of adjuvant therapies, but RT is often used in cases of unresectability to reduce the tumor when there is no evidence of distant metastasis, or for local control when resection is incomplete, while CT is usually an option in cases of distant metastasis.<sup>5,19</sup> Some chemotherapeutic agents have begun to be used in the treatment of advanced SFTs, namely: Bevacizumab (Avastin), Sunitinib (Sutent), Pazopanib (Votrient), and Sorafenib (Nexavar).<sup>3</sup> The target of this therapy is to act on vascular endothelial growth factor and other tyrosine kinase signaling pathways, thereby interrupting the tumor's blood supply.

The prognosis of the disease after surgical resection with clear margins is excellent. Five-year survival is over 90%. The recurrence rate in benign forms is 1.4%, and among malignant forms it is 9% to 19%. Generally, patients are discharged from the hospital a few days after surgery.<sup>4,19</sup> Due to the biological behavior and unpredictable course of fibrous tumors, long-term follow-up after surgical resection is essential.<sup>19</sup> Chest CT scans should be performed to monitor for recurrence every six months for the first two years and then once a year for 15 to 20 years.<sup>3</sup>

## Materials and Methods

This is a descriptive, cross-sectional, case report study of a female patient diagnosed with pulmonary SFT, initially treated for nonspecific symptoms. The bibliographic search was conducted over a period of time, using studies in Portuguese, English, and Spanish, found in databases such as

Scielo, Pubmed, Revista de Biologia e Ciências da Terra, Revista CIEZT Clínica e Cirurgia, Official Journal of The Society of Thoracic Surgeons and the Southern Thoracic Surgical Association, using the keywords “neoplasia, lung, fibrous tumor, solitary fibrous tumor, solitary fibrous tumor of the lung,” with the Boolean operator “and” to select the articles most relevant to the proposed theme.

## Objective

The study aims to report the case of a patient with a solitary fibrous tumor and her treatment, as well as to review the literature on the subject.

## Case Report

Patient N.M.C., 77 years old, married, homemaker, with systemic arterial hypertension and hypothyroidism, presented with a tumor in the lung parenchyma found through imaging.

In 2017, she sought medical attention, reporting a dry cough for about 45 days, and was prescribed antibiotic therapy with Amoxicillin and Potassium Clavulanate 875 mg + 125 mg (Clavulin BD) twice a day for 7 days, with no improvement in symptoms. A PA and profile chest X-ray was then requested, showing a large, partially defined oval opacity with soft tissue density, located in the projection of the right middle/lower lobes. (Figure 1 and Figure 2).



Figure 1 - PA chest X-ray



Figure 2 - Profile chest X-ray

After the results, a chest CT scan was requested (June/2017) for further evaluation, revealing an expansive lesion with defined borders and a lobulated contour, loca-

ted in the anterior portion of the lower third of the right hemithorax, at the level of the cardio-phrenic recess (Figure 3 and Figure 4).

Immediately afterwards, a chest MRI was performed (June 2017), revealing the tumor, closely related to the mediastinal, diaphragmatic, and anterior parietal pleura, measuring 8.6 x 8.0 x 6.8 cm, with soft tissue density, hypointense signal on T2, with foci of calcification in between, and slight heterogeneous contrast enhancement, causing slight parietal indentation in the right atrium, with no signs of invasion (Figures 5, 6, and 7).

The set of findings described above suggested the possibility of a pleural nature, with the following diagnostic hypotheses being considered: pulmonary SFT and pleural fibroma.

For diagnostic confirmation, a CT-guided percutaneous biopsy was performed. The material was analyzed by Pathology, confirming the diagnosis of Solitary Fibrous Tumor. After diagnostic confirmation, surgical risk assessment and preoperative tests were requested:

# Spirometry, using a portable One Flow device, showing obstructive ventilatory parameters, moderate obstruction (chronic obstructive pulmonary disease). Absence of bronchodilator test in flow, and volume with 400 mcg of Salbutamol Sulfate Spray. Reduced forced vital capacity and peripheral capillary O<sub>2</sub> saturation of 92%.

# Transthoracic Doppler echocardiogram, which showed no significant changes.

# Surgical risk, with the patient classified as ASA III and NYHA I.

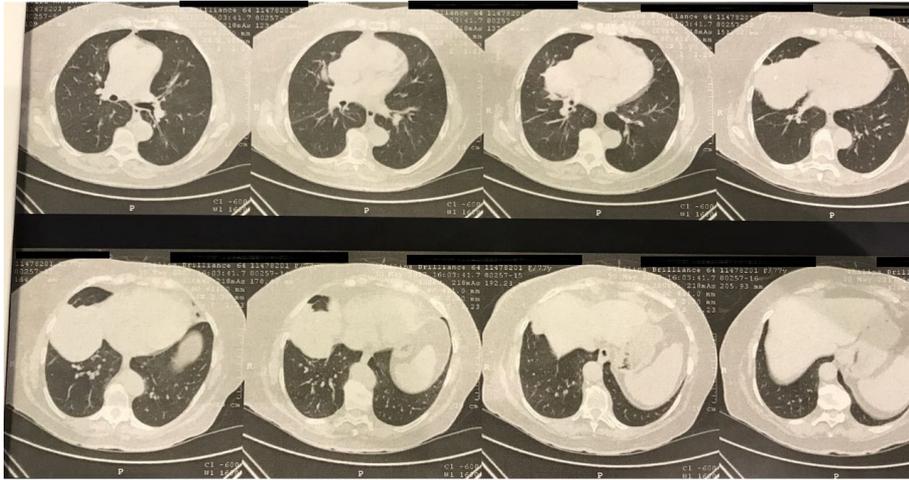


Figure 4 - Sagittal chest CT scan



Figure 3 - Coronal Chest CT Scan



Figure 5 - Sagittal chest MRI



Figure 6 - Coronal section of chest MRI

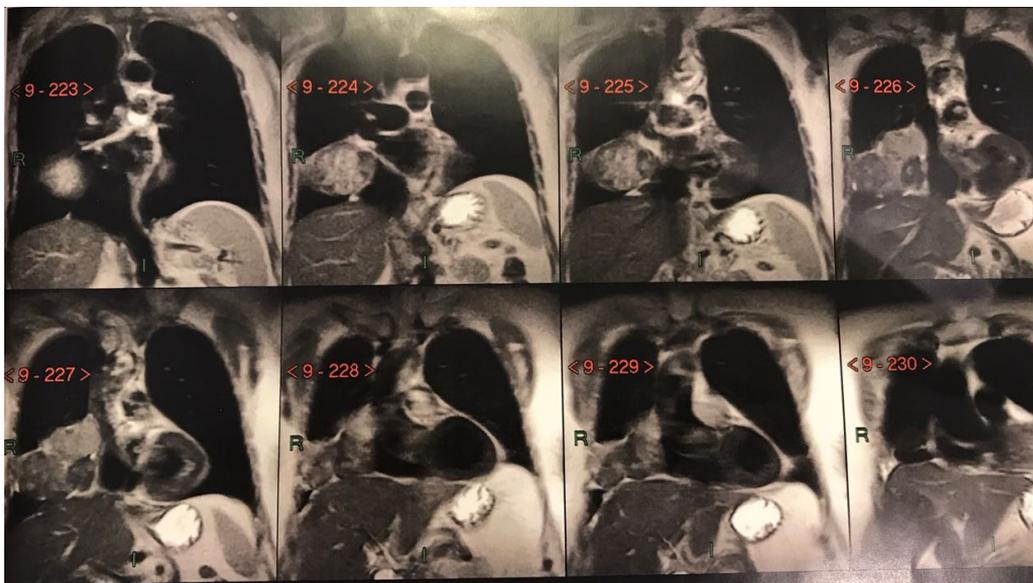


Figure 7 - Coronal chest MRI

The patient underwent surgery on September 12, 2017, in which a right posterolateral thoracotomy was performed, revealing a large tumor adhered to the right middle lobe of the lung. It was decided to perform a right middle lobectomy (Figure 8 and Figure 9).



Figure 8 - Surgical specimen

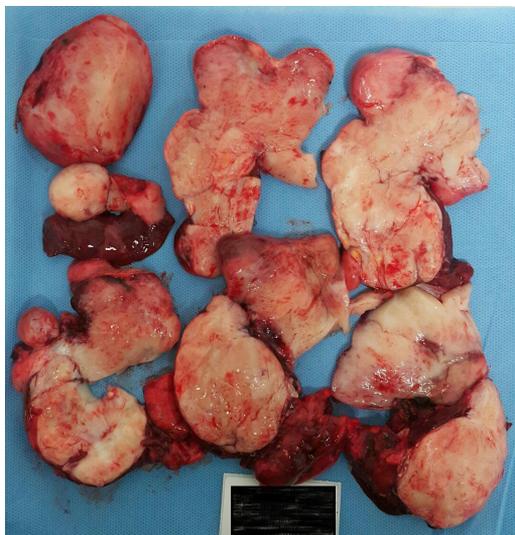


Figure 9 - Sectioned surgical specimen

Perioperative freezing confirmed the diagnosis of SFT. The histopathological report showed: Solitary Fibrous Tumor measuring 12.0 x 9.0 x 7.5 cm.

Right thoracic drainage and surgical wound closure were then performed. The patient was transferred to the ICU for postoperative follow-up. On the second postoperative day, the patient developed difficult-to-control atrial fibrillation, which delayed her discharge from the hospital until the 10th postoperative day. The patient remained under periodic follow-up every 6 months, presenting partial and total remission.

## Discussion

This study presents a case report of a 77-year-old patient with a large intraparenchymal and pleural TFS, as well as its diagnosis and successful treatment. It is recognized that lobectomy can lead to postoperative complications<sup>28</sup>, but the care measures taken for the surgery were fundamental for the complication-free outcome.

The results of fluorodeoxyglucose PET (FDG/PET) or PET/CT of TFSs have rarely been reported. Few case reports have shown that benign TFSs had little or no FDG uptake. Hypercellular tumors and those with less collagen area may show relatively greater FDG uptake than hypocellular tumors and those with more collagen area. One case of malignant TFS with low FDG uptake has been reported in the literature. In another case, a benign tumor histologically showed intense FDG uptake, which may be due to the abundance of lymphatic cells.<sup>15</sup>

Therefore, PET-CT was not performed in the patient in this study because, as explained above, it is not reliable for differentiating benign from malignant tumors and is unnecessary in this case. These cases indicate that the clinical behavior of this type of tumor can be unpredictable based solely on histological characteristics and the

degree of FDG uptake. The use of FDG/PET in cases of TFS still requires further evaluation.<sup>15</sup>

Another important issue, which may generate some conflict in the medical field, is the fact that therapies such as RT, in this type of tumor, are classified as second-line, with undefined benefits, even ineffective, with complete resection with free margins being the only first-line therapy.<sup>6</sup> However, there are reports in the literature of cases of large, unresectable TFS without a cleavage plan due to compression of important adjacent structures, such as the bronchus, carina, superior vena cava, trachea, esophagus, among others, and, having employed a neoadjuvant radiotherapy regimen, reducing the tumor area, with a considerable reduction in its dimensions, and subsequently using resection, resulting in complete excision of the expansive process. In the patient in the case report in question, the tumor was significant in size and neoadjuvant RT was not performed because respiratory function tests were satisfactory and the tumor had a free cleavage plane. If the patient had a higher surgical risk, RT could be useful to reduce the tumor size, making it unnecessary to perform a mediastinal lobectomy, but rather only excision of the tumor. Therefore, its applicability should be further studied and consequently more widely used as a possibility for inclusion in first-line treatment in cases of larger, unresectable tumors with extensive distant metastases, severe cardiopulmonary dysfunction, severe liver or kidney damage, severe bleeding disorders, and cachexia, as well as for those who cannot tolerate surgery.<sup>15</sup> In this sense, while chemotherapy has shown little progress, immunotherapy has been promising with

molecules against VEGF and other tyrosine kinase pathways<sup>27</sup>.

As a final question, even with an extensive review of the literature, the existence of risk factors related to the onset of TFSs has not been proven.<sup>4,6,29</sup> Some articles mention the relationship with smoking or exposure to asbestos, as it is related to possible causes of pleural SFTs<sup>30</sup>. However, in the case report in question and in the literature review of this intraparenchymal tumor, the patients in question, who have intrapulmonary TFS, are not smokers (also no history of smoking), and there is no personal history of exposure to asbestos. The relationship between these exposures and the genesis of the pathology in question must be analyzed in greater depth in order to reach a more scientifically sound conclusion.

## Conclusion

Intrapulmonary TFS is an extremely rare pathology that is rarely described in the literature. It can form throughout the body. It generally affects older patients, with no gender predominance. The subject addressed is extremely peculiar, due to its diversity of presentation and evolution, making it unpredictable. While it has an excellent prognosis due to its high incidence of benignity, malignant TFSs can be similar to benign ones in terms of histological and histopathological characteristics, contrast uptake, among others, while benign TFS itself can become malignant, that is, a functionally undefined tumor. The case presented was challenging, first because of the nonspecificity of the symptoms (in addition to more than half of the patients being asymptomatic), and second because of the size of the tumor and the difficulty of resection, which

could lead to negative perioperative repercussions. However, the postoperative repercussions were not directly related to the surgery. In this sense, although successful in most cases, other less invasive and promising alternatives, such as immunotherapy, are being researched as alternatives to surgical treatment.

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