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**Intrapulmonary solitary fibrous tumor**

Интрапулмонални солитарни фиброзни тумор

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## Intrapulmonary solitary fibrous tumor

### Интрапулмонални солитарни фиброзни тумор

#### SUMMARY

**Introduction** Solitary fibrous tumor is a neoplasm that arises most commonly from the pleura, but can occur at other sites. Intrapulmonary solitary fibrous tumour has been rarely reported and therefore is not well recognized.

**Case outline** We report a case of asymptomatic 63-year-old woman in whom a large, well-circumscribed mass was incidentally revealed on chest X-ray during preparation for ergometric cardiac testing. Chest computed tomography revealed an abnormal nodule in the lower right lung lobe. Mediastinal and hilar lymphadenopathy was not detected. After transthoracic fine needle aspiration, cytology showed finding suspicious for spindle cell tumor. Consequently, right anterolateral thoracotomy with right lower lobectomy was performed. On gross examination, lower right lobe was almost completely replaced with abnormal, white-yellow, well-demarcated solid nodule measuring 13,5 cm in its largest diameter surrounded with pseudocapsule. After histological examination and applied immunohistochemical analysis, diagnosis of intrapulmonary solitary fibrous tumor of low malignant potential. Due to the presence of unfavorable prognostic parameters (tumor size, as well as presence of hypercellularity) more frequent follow-up was recommended. One and half year after surgery, patients is uneventful with no evidence of tumor recurrence.

**Conclusion** Intrapulmonary solitary fibrous tumor is a rare entity challenging for diagnosis, because variegated histology and variability of its growth patterns can resemble other soft tissue tumors. The treatment of choice is complete excision with clear surgical margins, but since morphology cannot be a reliable predictor of clinical behavior, the patients need a long-term follow-up.

**Keywords:** solitary fibrous tumor, intrapulmonary, diagnosis, cytology, immunohistochemistry

#### САЖЕТАК

**Увод** Солитарни фиброзни тумор је неоплазма која најчешће води порекло из плеуре, али се може јавити и у другим органима. Интрапулмонални солитарни фиброзни тумор је редак ентитет недовољно описан у медицинској литератури.

**Приказ болесника** Приказујемо случај пацијенткиње старе 63 године код које је случајно током припреме за ергометријско испитивање на рендгену плућа откривена велика, добро ограничена туморска формација. СТ прегледом грудног коша описана је туморска промена доњег десног режња, без присутне медијастиналне или хиларне лимфаденомегалије. Цитолошком анализом материјала добијеног трансторакалном пункцијом постављена је сумња на вретенастоћелијски тумор, након чега је изведена десна антеролатерална торакотомија са десном доњом лобектомијом. Макроскопски, десни доњи режањ је скоро у потпуности био замењен беложутим, солидним туморским ткивом окруженим псеудокапсулом, највећег промера 13,5 cm. Хистолошким прегледом и имунохистохемијском анализом постављена је дијагноза интрапулмоналног солитарног фиброзног тумора ниског малигног потенцијала. Због присуства неповољних прогностичких параметара (величине тумора и хиперцелуларности), препоручене су чешће контроле. Годину и по дана након операције, пацијенткиња се добро осећа без знакова рецидива болести.

**Закључак** Интрапулмонални солитарни фиброзни тумор је ретка неоплазма која због шаролике хистолошке слике може да имитира друге мекоткивне туморе, те представља значајан дијагностички изазов. Императив у лечењу је комплетна ексцизија тумора, али с обзиром да морфолошка слика није поуздан предиктор понашања тумора, неопходне су редовне и доживотне контроле.

**Кључне речи:** солитарни фиброзни тумор, интрапулмонални, дијагноза, цитологија, имунохистохемија

#### INTRODUCTION

Soft tissue tumours represent a diverse group of neoplasms that are of mesenchymal origin, and are classified according to the tissue of origin and histological differentiation. These tumor rarely occur within lung parenchyma, and one of the rarest primary soft tissue tumor described in the lung is intrapulmonary solitary fibrous tumor.

Solitary fibrous tumors (SFTs) are rare, slow-growing spindle cell mesenchymal tumors whose behavior cannot be accurately predicted by histological findings. These neoplasms are

ubiquitous, can arise in many different organs, but most often they arise from visceral pleura leading the origin of the mesenchymal tissue cells that are found in the submesothelial layer of pleura [1]. Intrapulmonary SFT has been rarely reported and is therefore not well recognized. We report a case of a 63-year-old woman with an abnormal nodule in the lower right lung detected on chest X-ray during preparation for ergometric cardiac testing. Histological examination revealed an intrapulmonary solitary fibrous tumor.

## CASE REPORT

A 63-year-old woman was admitted to hospital after a large, well-circumscribed mass was revealed on chest X-ray during preparation for ergometric cardiac testing. On chest computed tomography (CT) an abnormal nodule about 13 cm in largest diameter in the lower right lung lobe was detected. There was no mediastinal and hilar lymphadenopathy. Patient did not have a history of cough, shortness of breath, chest pain, fever, loss of weight and appetite, smoking, drinking alcohol, as well as prior malignancy. Her past medical history revealed hypertension and hypertensive cardiomyopathy. Clinical and imaging studies did not reveal evidence of tumor elsewhere.

A diagnostic transthoracic fine needle aspiration cytology was performed, and cytological analysis showed moderately cellular smear with presence of small, oval-to-polygonal cells with uniform bland nuclei and scant cytoplasm, as well as rare spindle cells with moderately abundant pale cytoplasm and fusiform nuclei suspicious for spindle cell tumor (Figure 1.). The patient was referred to the Department for thoracic surgery where right anterolateral thoracotomy with right lower lobectomy was performed.

On gross examination, lower right lobe was almost completely replaced with abnormal, white-yellow, well-demarcated solid nodule measuring 13,5 cm in its largest diameter surrounded with pseudocapsule (Figure 2.). Nodule was not attached to the overlying slightly thickened and whitish visceral pleura.

Histological examination revealed a hypercellular tumor tissue, composed of spindle to oval cells with elongated nuclei with tapered ends and without prominent nucleoli. Tumor cells showed overlapping with a fascicular and "patternless pattern" appearance. Focal areas displayed dense hyalinized "ropey" stromal collagen, while others showed myxoid changes in

the stroma. Blood vessels were branched, "staghorn-like", focally with thickened and hyalinized walls. Some of the tumor cells showed mild atypia. No mitotic figures or necrosis were seen (Figures 3a, 3b, 3c and 3d.).

Immunohistochemically, the tumor cells showed diffuse positivity for vimentin, CD34, bcl-2 and CD99 (Figures 4a, 4b, 4c and 4d.), and negative reaction for EMA, SMA, desmin and S-100.

The final diagnosis was an intrapulmonary solitary fibrous tumor of low malignant potential. Due to the presence of unfavorable prognostic parameters (tumor size as well as presence of hypercellularity) more frequent follow-up was recommended. A year and a half after surgery, patient is feeling well with no evidence of tumor recurrence.

## DISCUSSION

Solitary fibrous tumors are uncommon soft tissue tumors that mostly arise within the thorax, where more than 80% all of cases originate from the visceral pleura. For many years, SFTs were believed to be restricted to the pleura, but after implementation of immunohistochemistry in every day work and demonstration of CD34 immunoreactivity in these tumors (tumor cells in these tumors correspond to distinctive subset of fibroblasts characterized by CD34 positivity and presence of elongated, dendritic cytoplasmic processes), extrapleural SFTs started to become recognized [2,3]. These tumors may occur in various anatomical sites, including the head, neck, breast, abdomen, pelvis, extremities, as well as within lung parenchyma when it is termed an intrapulmonary SFT. This tumor may derive from invagination of the visceral pleura, from interlobar septal connective tissue, or from pulmonary parenchymal fibroblasts [4].

Most of these tumors behave as slow-growing neoplasms. More than 50% of the patients with intrapulmonary SFT are asymptomatic, but organ compression by the tumor sometimes result in chest pain, cough, fever and dyspnea. One of the most prominent clinical features is hyperinsulinism. Patients usually present with severe hypoglycemia caused by production of insulin-like growth factor released by large tumors, as a part of paraneoplastic syndrome [4,5]. Our patient was completely asymptomatic, without any clinical signs present at the time of diagnosis.

The detection of these tumors is often incidental and the definitive diagnosis requires an integrated approach including clinical, histological, immunohistochemical and molecular findings [4,6].

The use of fine needle aspiration cytology (FNAC) highly improves the management of soft tissue tumors. Microscopic examination usually shows moderately cellular smears composed of small, oval-to-polygonal elements with uniform bland nuclei; evenly distributed and finely granular chromatin; and scant cytoplasm. When a spindle cell population is present in the sample, the spindle cells have pale and relatively well-defined cytoplasm and fusiform or ovoid and basophilic nuclei with finely dispersed chromatin and without nucleoli. The cells are widely dispersed separately, but smears usually contain some irregular, loose aggregates of cells enmeshed in a collagenous matrix. The background contains irregular roopy fragments of collagen and a few inflammatory elements [7].

Histologically, they typically display zones of both hypercellular and hypocellular collagenized stroma in a so-called “patternless” architecture, focal zones of myxoid changes within tumor stroma and branched hemangiopericytoma-like blood vessels which are all in accordance with our case [8]. But, these tumors can show tremendous degree of variability in histologic growth patterns including fascicular, storiform, herringbone, neural-like, angiofibromatous etc [1,2].

Immunohistochemistry is the most important method used to differentiate SFTs from spindle cell carcinoma, melanoma, sarcomatoid mesothelioma, peripheral nerve sheath tumors, sclerotic and cellular variant of sclerosing pneumocytoma, and a wide variety of primary and metastatic soft-tissue neoplasms, including thymic neoplasms and lymphomas [1,3,19]. Specifically, CD34 is positive in most SFTs, although CD34 positivity can be seen in a variety of other spindle cell neoplasms as well as in non-spindle cell lesions. On the other hand, recent studies have demonstrated that this marker may not be expressed in SFTs in up to 40% of cases. One should always keep in mind that in the appropriate context positive staining for CD34 support a diagnosis of SFT, while negative staining does not rule it out [4,5,9]. Other markers which exhibit positivity in these SFTs are bcl-2 and CD99, however these markers are also not specific and can be positive in many other tumors. These neoplasms are generally vimentin positive and negative for epithelial markers (EMA, cytokeratins), smooth muscle markers (actin, desmin), neural markers (S-100, NSE) and other specific markers of differentiation [1, 9]. Recent molecular studies showed

intrachromosomal rearrangement on chromosome 12q13 due to paracentric inversion of two overlapping genes, NAB2 and STAT6, producing a NAB2/STAT6 fusion gene. This fusion can be demonstrated using commercially available STAT6 monoclonal antibody which is, at the moment, the most specific and highly sensitive marker for diagnosis of this tumor [10,11].

Although SFTs are tumors with a benign course, about 10–20% of them are locally aggressive or malignant. There are no unanimous criteria of malignancy for these tumors. Therefore, it is not always easy to make differential diagnosis between benign and malignant SFT. Malignant SFT is usually characterized by the presence of infiltrative margins, large size (usually over 10 cm), pleomorphism, hypercellularity, mitotic index >4/10 high-power field (HPF), necrosis, hemorrhage and stromal or vascular invasion [7,9]. According to England et al. criteria for malignancy are hypercellularity, pleomorphism and overlapping of nuclei, presence of necrosis or hemorrhage and more than 4 mitoses per 10 HPF. However, only 55% SFTs with these characteristics showed aggressiveness in the form of infiltration, recurrence and metastasis [12]. Vallat-Decouvelaere et al. found that the histological characteristics of SFT were not always consistent with their behavior, showing that there are SFTs that have shown an invasion of bone and chest soft tissue structures and recurrence, without fulfilling any of the above mentioned criteria of malignancy [13]. On the other hand, Christopher Fletcher, one of the greatest names in modern pathology, believes that only the presence of more than 4 mitoses per 10 HPF can be considered as valid criteria of malignancy [14].

The clinical, histological, and immunohistochemical features do not appear to differ between pleural SFT and intrapulmonary SFT. The malignancy rate of intrapulmonary SFT is reportedly 12.5%, although the precise rate is difficult to determine because of the small number of patients diagnosed with intrapulmonary SFT [7].

Since primary intrapulmonary SFT is a relatively rare condition, small number of case reports and case series have been reported in the literature [15-18]. The largest series ever reported were published by Rao et al. In their study of 24 cases of intrapulmonary SFT, the patients' ages ranged from 44 to 83 years (mean 58 yrs), and none of the patients had a history or evidence of a similar tumor in another location. The tumors ranged in size from 2.3 to 22 cm in greatest diameter (mean 8.5 cm). They were histologically classified as low, intermediate and high-grade lesions based on the degree of cytologic atypia, nuclear

pleomorphism, necrosis and mitotic activity [18]. As in our case, 21 cases showed features of solitary fibrous tumor of low malignant potential with low mitotic activity (<5 mitoses per 10 high-power fields), absence of cytological atypia, nuclear pleomorphism and necrosis. One case showed intermediate malignant potential (increased cellularity with plump, pleomorphic nuclei and 5 to 10 mitoses per 10 high-power fields), while two cases showed high grade malignant potential (presence of areas resembling a pleomorphic high-grade sarcoma admixed with foci of conventional, low-grade SFT). Clinical follow-up in 18 patients showed that 14 were alive and well without evidence of disease from 1 month to 14 years after initial diagnosis. Three patients died within seven years after surgery; one patient had tumor with high grade malignant potential, and in other two initial tumor had been of low grade malignant potential, but the recurrences and/or metastases showed transformation to a high grade tumor. This study indicated that beside tumors with obviously malignant features, tumors with low grade malignant potential can behave in an aggressive manner, and that in many cases morphology cannot be reliable predictor of tumor behavior [18].

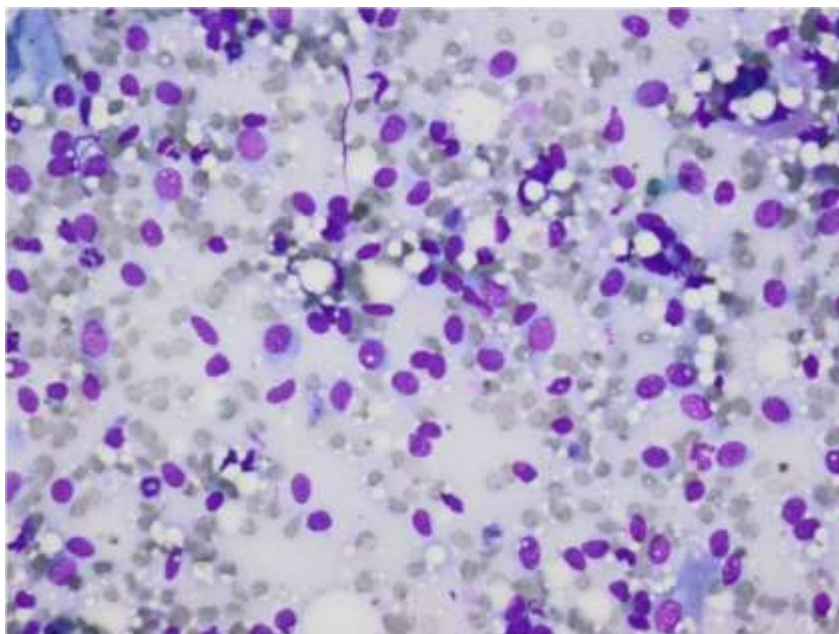
In conclusion, intrapulmonary SFTs can present a challenge for diagnosis, because of their variegated histology and variability of growth patterns due to which these tumors can resemble other soft tissue tumors. Helpful feature of intrapulmonary SFTs, which differ these tumors from other soft tissue tumors, is the fact that an admixture of different growth patterns is usually present. Therefore, in samples taken from different areas of the lesion the tumor may show variable histologic appearance. The treatment of choice is complete excision with clear margins and with additional chemotherapy and radiotherapy for metastatic or locally recurrent tumors. These tumors have unpredictable clinical behavior, so the patients need a long-term follow-up.

**Conflict of interest:** None declared.

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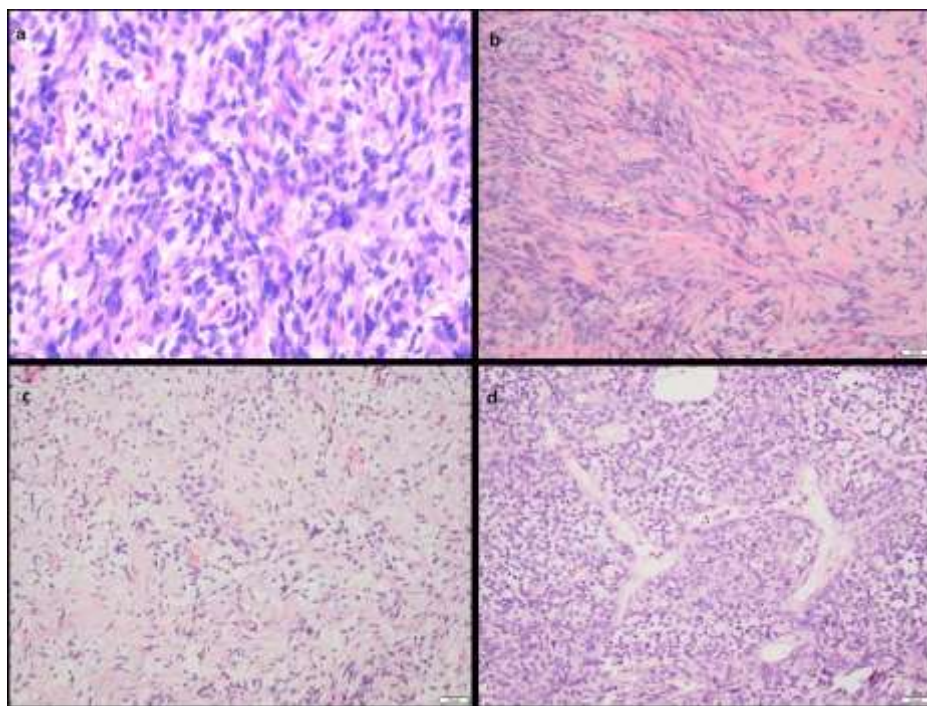
**Figure 1.** FNAC – moderately cellular smear composed of small, oval-to-polygonal cells with uniform bland nuclei and scant cytoplasm, as well as sparse spindle cell population with fusiform basophilic nuclei with no nucleoli

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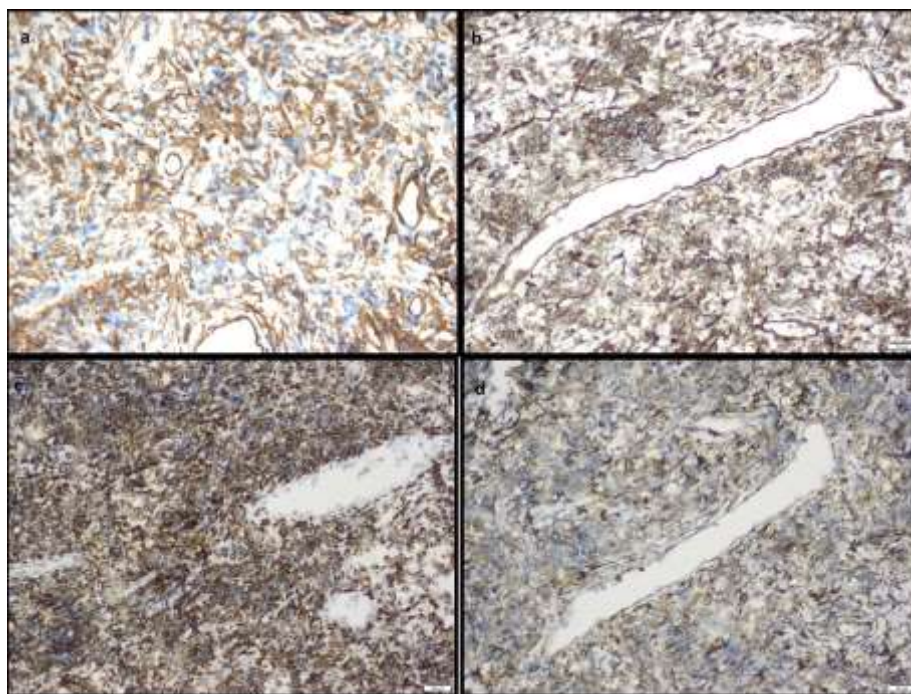


**Figure 2.** Right lower lobectomy - white-yellow, well-demarcated solid nodule surrounded with pseudocapsule and without not abutting visceral pleura

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**Figure 3.** a) hypercellular tumor tissue composed of spindle to oval cells arranged in “patternless pattern” with elongated, somewhat overlapping nuclei; b) focal areas with dense hyalinized “ropy” stromal collagen; c) myxoid changes within the stroma and d) branched, “staghorn-like” blood vessels



**Figure 4.** Positivity of tumor cells for: a) vimentin; b) CD34; c) bcl-2 and d) CD99