Intrapulmonary solitary fibrous tumor

Aleksandra Lovrenski, Aleksandra Ilić, Ivan Kuhajda, Dragana Tegeltija, Jovan Lovrenski

University of Novi Sad, Faculty of Medicine, Novi Sad, Serbia

SUMMARY

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

Case outline We report a case of an 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 a finding suspicious for spindle cell tumor. Consequently, right anterolateral thoracotomy with right lower lobectomy was performed. On gross examination, the lower right lobe was almost completely replaced with abnormal, white-yellow, well-demarcated solid nodule measuring 13.5 cm in its largest diameter surrounded by a pseudocapsule. After histological examination and applied immunohistochemical analysis, a diagnosis of intrapulmonary solitary fibrous tumor of low malignant potential was set. Due to the presence of unfavorable prognostic parameters (tumor size, as well as the presence of hypercellularity), more frequent follow-up check-ups were recommended. Eighteen months after surgery, the patient remained 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

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, an abnormal nodule about 13 cm in the largest diameter in the lower right lung lobe was detected. There was no mediastinal and hilar lymphadenopathy. The patient did not have a history of cough, shortness of breath, chest pain, fever, loss of weight and appetite, smoking, drinking alcohol, nor 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 a moderately cellular smear with the 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 a pseudocapsule (Figure 2). The nodule was not attached to the overlying slightly thickened and whitish visceral pleura.

INTRODUCTION

Soft tissue tumors represent a diverse group of neoplasms that are of mesenchymal origin, and are classified according to the tissue of origin and histological differentiation. These tumors rarely occur within lung parenchyma, and one of the rarest primary soft tissue tumors in the lung described 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
Histological examination revealed a hypercellular tumor tissue, composed of spindle-to-oval-shaped cells with elongated nuclei with tapered ends and without prominent nucleoli. The tumor cells showed overlapping with a fascicular and “patternless” 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 (Figure 3).

Immunohistochemically, the tumor cells showed diffuse positivity for vimentin, CD34, bcl-2 and CD99 (Figure 4), 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 the presence of hypercellularity), more frequent follow-up was recommended. Eighteen months after surgery, the patient has been 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% 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 everyday work and demonstration of CD34 immunoreactivity in these tumors (tumor cells in these tumors correspond to a distinctive subset of fibroblasts characterized by CD34-positivity and the 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 the lung parenchyma, when it is termed an intrapulmonary SFT. This tumor may derive from the 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 an 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 highly improves the management of soft tissue tumors. Microscopic examination usually shows moderately cellular smears composed of small, oval-to-polygonal-shaped 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 ropy 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]. However, 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, 9]. 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, 10]. Other markers which exhibit positivity in these SFTs are bcl-2 and CD99; however, these markers are also not specific and can be positive with many other tumors. These neoplasms are generally vimentin-positive and negative for epithelial markers (epithelial membrane antigen, cytokeratins), smooth muscle markers (actin, desmin), neural markers (S-100, neuron-specific enolase) and other specific markers of differentiation [1, 10]. 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 diagnosing this tumor [11, 12].

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 SFTs. A 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, 10]. According to England et al. [13], the criteria for malignancy are hypercellularity, pleomorphism and overlapping of nuclei, the presence of necrosis or hemorrhage, and more than four mitoses per 10 HPF. However, only 55% of SFTs with these characteristics showed aggressiveness in the form of infiltration, recurrence, and metastasis [13]. Vallat-Decouvelaere et al. [14] found that the histological characteristics of SFTs were not always consistent with their behavior, showing that there are SFTs that have exhibited invasion of bone and chest soft tissue structures and recurrence, without fulfilling any of the abovementioned criteria for malignancy. On the other hand, Fletcher [15], one of the greatest names in modern pathology, believes that only the presence of more than four mitoses per 10 HPF can be considered a valid criterion for malignancy.

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

Since primary intrapulmonary SFT is a relatively rare condition, a small number of case reports and case series has been reported in the literature [16–19]. The largest series ever reported were published by Rao et al [19]. In their study of 24 cases of intrapulmonary SFTs, the patients’ ages ranged 44–83 years (mean being 58 years), and none of the patients had a history or evidence of a similar tumor in another location. The tumors ranged in size 2.3–22 cm in the greatest diameter (mean being 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 [19]. As in our case, 21 cases showed features of a solitary fibrous tumor of low malignant potential with low mitotic activity (< 5 mitoses per 10 HPF), the absence of cytologic atypia, nuclear pleomorphism, and necrosis. One case showed intermediate malignant potential (increased cellularity with plump, pleomorphic nuclei, and 5–10 mitoses per 10 HPF), 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

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18 patients showed that 14 were alive and well without evidence of disease from one month to 14 years after the initial diagnosis. Three patients died within seven years after surgery; one patient had a tumor with high-grade malignant potential, and in the other two, the initial tumor had been of low-grade malignant potential, but the recurrences and/or metastases showed a 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 a reliable predictor of tumor behavior [19].

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. A helpful feature of intrapulmonary SFTs, which distinguishes 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.

**REFERENCES**

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 литературин. Приказ болесника Приказујемо случај болеснице старе 63 године код које је случајно током припреме за ергометријско испитивање на рендгену плућа откривена велика, добро ограничена туморска формација. Компјутеризованом томографијом 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 вретенацелјски тумор, после чега је изведена десна антеролатерална торакотомија са десном доњом лобектомијом. Макроскопски, десни доњи режа је скоро потпуно 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 са малом могућношћу малигнитета. Због присуства неповољних прогностичких параметара (величине тумора и хиперцелуларности), препоручене су чешће контроле. Годину и по дана после операције болесница се добро осећа и нема знакове 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 на то да морфолошка слика није укључена у претсказатељ понашања тумора, неопходне су редовне и доживотне контроле.
Кључне речи: солитарни фиброзни тумор; интрапулмонални; дијагноза; цитологија; имунохистохемија