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Case report

Endobronchial solitary fibrous tumors: An enigma for diagnosis

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ABSTRACT

Solitary fibrous tumors (SFTs) are rare mesenchymal neoplasms constituting less than 2% of all soft tissue tumors. They typically originate in the thoracic cavity, mainly in the pleura, but can also occur in other various sites such as lung parenchyma, pericardium, and bronchus. In this study, a 49-year-old non-smoking female with a history of allergies presented to our pulmonary clinic with a chronic cough. An explorative bronchoscopy revealed an intrabronchial mass in the left superior bronchi, and a 68 Ga-DOTATOC positron emission computed tomography suggested a carcinoid tumor. Subsequent pulmonary segmentectomy unveiled a well-circumscribed polypoid lesion diagnosed as a low-grade bronchus SFT through histopathological and immunohistochemical assessments. The patient was asymptomatic after surgical excision and showed no other lesion during the 6-month follow-up. The endobronchial location of SFT is uncommon, with only a few reported cases in the literature, underscoring the necessity of considering various differential diagnoses, including carcinoid, mucoepidermoid carcinoma, endobronchial pleomorphic adenoma, hamartoma, leiomyoma, and metastasis, depending on location and imaging features. This report underscores the importance of careful histological and immunohistochemical evaluation in understanding and appropriately stratifying the risk associated with polypoid lesions.

1. Introduction

Solitary fibrous tumors (SFTs), classified as rare mesenchymal neoplasms [1], have emerged as intriguing entities within the realm of oncology, particularly when they manifest in the bronchus. Constituting less than 2% of all soft tissue tumors [2], these enigmatic growths predominantly originate in the thoracic cavity, mainly in the pleura, but can manifest at diverse sites, including the lung parenchyma, pericardium, and rarely, within the bronchial tree [3]. This article comprehensively explores the clinical status of bronchial SFTs, expanding on the related diagnostic challenges, treatment modalities, and the pivotal roles of histological and immunohistochemical evaluations in the process of unraveling the intricate anatomical subtleties of these tumors. As we will go into detail throughout the present case study, the rarity of endobronchial SFTs will become apparent, reinforcing the importance of recognizing subtle differentiations amidst a spectrum of mimicking pathologies. In our quest for understanding, we shed light on the diagnostic dilemma presented by bronchial SFTs, emphasizing the imperative role of meticulous evaluation for accurate diagnosis and subsequent risk stratification. This article aims at serving as a guide for clinicians, pathologists, and researchers, urging them to pay detailed attention to the complexities surrounding SFT in the bronchus.

2. Case presentation

A 49-year-old non-smoker female with a previous history of autoimmune disorders was referred to our pulmonology department with wheezing and progressive difficulty in breathing. She was treated with inhaled corticosteroids and bronchodilators without significant beneficial effects. Pulmonary function tests revealed a mixed pattern (FVC

Abbreviations: SFTs, Solitary Fibrous Tumors; CT, Computed tomography; PET, Positron emission tomography; VATS, Video-assisted thoracic surgery.

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65%, FEV1 57%, FEV1/VC 75%). She underwent a chest computed tomography (CT) scan which showed an endobronchial lesion with smooth margins characterized by high contrast enhancement in the left upper bronchus (Fig. 1).

A subsequent exploratory bronchoscopy confirmed the presence of an intrabronchial vegetative mass in the left upper bronchus. A multidisciplinary team discussion led to the conclusion that the clinical and radiological features were highly suggestive of a carcinoid. A 68 Ga-DOTATOC positron emission computed tomography (PET/CT) was consequently performed. The lesion showed significant uptake of radiotracer, supporting the suspected diagnosis (Fig. 1).

The patient underwent video-assisted thoracic surgery (VATS) with left upper lobectomy and wedge bronchial resection. An intramucosal, well circumscribed 19-mm polypoid lesion with a grayish white color was detected. Pathological examination revealed a low-grade mesenchymal neoplasm arranged in a short wavy bundle. In some areas, the tumor showed a storiform pattern, thin-walled large branching, and "staghorn"-shaped (hemangiopericytoma-like pattern) blood vessels, without necrosis (Fig. 2). The tumor cells had mild atypia with a low mitotic index (1 mitosis/mm2). The immunohistochemical study revealed negativity for cytokeratin (AE1/AE3), S100 protein, smooth muscle actin, and neuroendocrine markers (chromogranin and synaptophysin). The neoplastic cells were positive for STAT6, CD34, and BCL2. The proliferation index (Ki-67) was 5%. Histological features were consistent with the diagnosis of a low-risk SFT, as defined in the WHO 2021 classification [1]. After surgery, the patient was followed up for six months. Although not enough to predict behaviour of tumour, no lesion was detected during this short period.

3. Discussion

SFTs are rare mesenchymal tumors, typically arising from the mesenchymal tissue underlying the mesothelial pleural layer [1]. Although the pleura is the most common site, accounting for around 30% of the cases, SFTs have been reported at almost every anatomic site [2]. Indeed, SFTs of the meninges, abdominal cavity, trunk, extremities, head, and neck have been described, but endobronchial SFTs in particular are extremely rare [2]. To the best of our knowledge, only six cases have been described in the literature [4–9] (Table 1). Epidemiologically, SFTs account for less than 2% of soft tissue tumors, the age range is 40–70 years, and there is no gender predilection. Because SFT lesions grow slowly, in general patients with intra-thoracic SFTs are often asymptomatic and the diagnosis is incidental [10].

Diagnostic imaging is crucial for detecting and diagnosing SFTs. In cases where the lesions are located in the pleura, chest radiography can often reveal well-defined opacities [10]. However, for endobronchial lesions, radiographs mainly identify the effects of bronchial obstruction, such as distal parenchymal atelectasis. CT scans are more accurate in characterizing tumor features, including hyperdensity due to collagen content, contrast enhancement, calcifications, or areas of necrosis in larger lesions [4–9]. When dealing with endobronchial lesions, other benign and malignant tumors detected through imaging—such as mucoepidermoid carcinoma, hamartoma, leiomyoma, and rarely, metastases—should be considered as primary differential diagnoses [11]. In our case, the primary hypothesis initially suggested by the vivid enhancement of the lesion was bronchial carcinoid which account for 1–2% of all pulmonary cancers and are endobronchial in the majority of cases [12,13]. While PET/CT was not used in any of the reported endobronchial SFT cases in the literature, 18 F-fluorodeoxyglucose PET/CT can help distinguish between malignant and benign lesions [14]. Additionally, a few cases of 68 Ga-DOTATOC PET/CT positive SFTs have been described, indicating that these lesions may express somatostatin receptors and resemble neuroendocrine tumors [15,16]. SFTs typically present as spindle cell lesions with a characteristic patternless architecture [1]. Alternating hypercellular and hypocellular areas, along with prominent staghorn-shaped blood vessels within a collagenous stroma, are a hallmark of SFTs [1]. Specific immunohistochemical markers aid in the diagnosis of SFTs. CD34 is one of the most

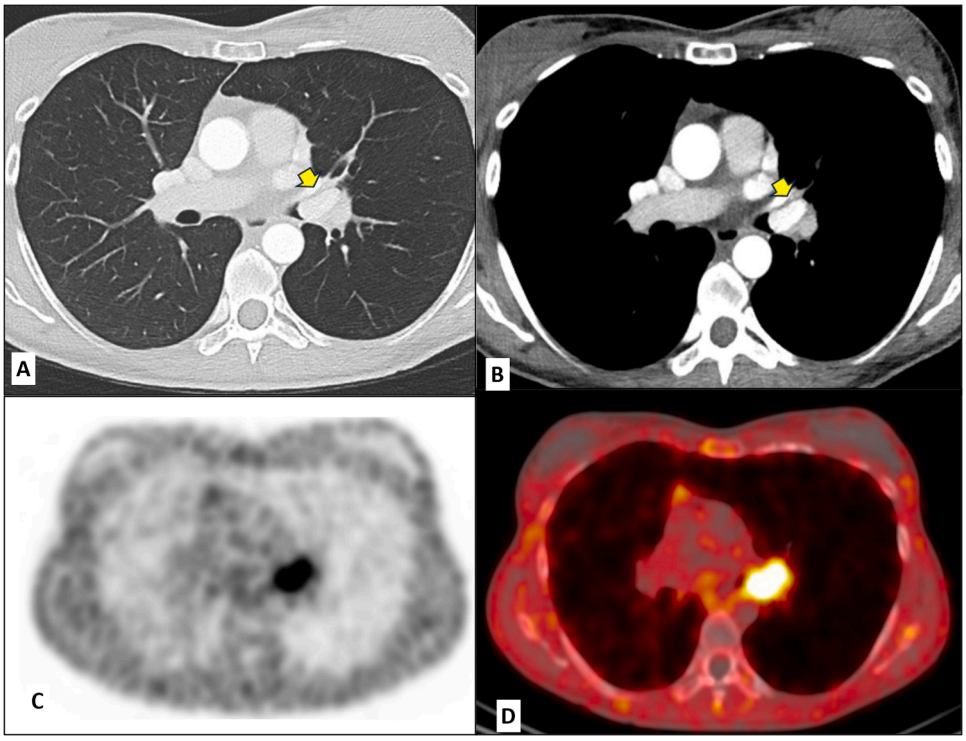

Fig. 1. (A,B) Axial chest computed tomography showing an endobronchial lesion in the left upper bronchus (yellow arrow in A) with significant contrast enhancement (yellow arrow in B). **C,D)** Axial 68 Ga-DOTATOC PET/CT showing the strong tracer uptake of lesions in the left upper bronchus in the axial PET (C) and the PET/CT fused image (D).

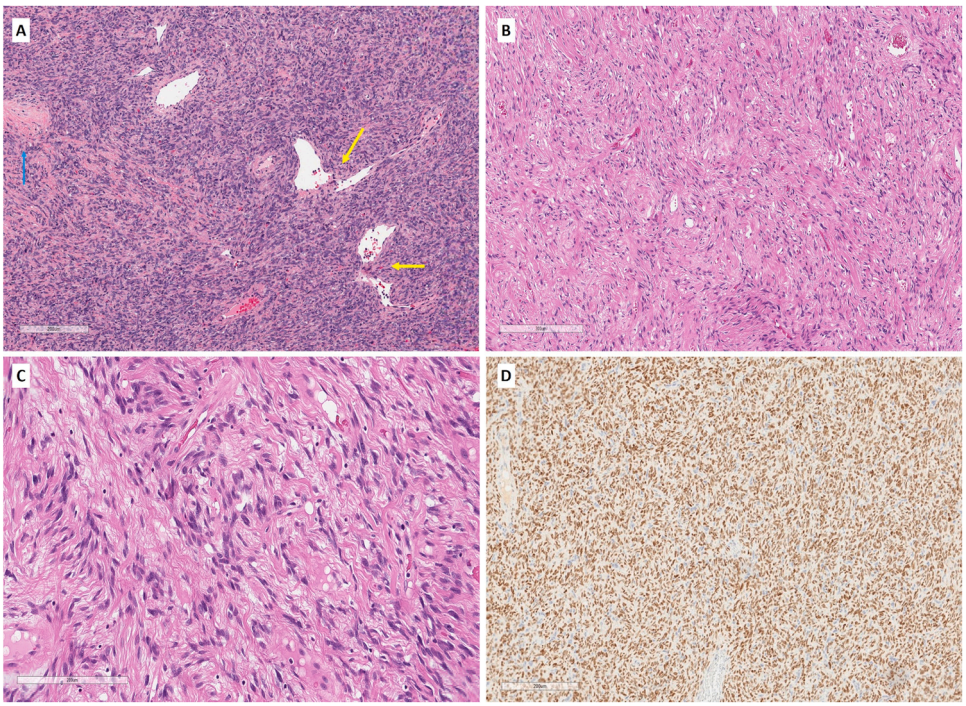

Fig. 2. Explanatory histological images of the tumor. The mass consisted of haphazard, storiform, fascicular spindle cells (blue arrow, A), with dilated, branching, staghorn-like vessels (yellow arrows, A), alternating with hyalinized and collagenous stroma (B) (haematoxylin and eosin, scale bar: 200μm) Tumor cells showed a mild atypia (C, haematoxylin and eosin, scale bar: 200μm) and were strongly and diffusely positive for STAT6 (immunohistochemistry for STAT6, scale bar: 200μm) (D).

Table 1
List of Cases of Endobronchial Solitary Fibrous Tumors reported in the Literature.

	Source	Year	Age	Gender	Symptoms	Diagnostic	Morphological details	Immunohistochemical positivity	Treatment
1	Pak et al. [8]	2010	55y	Female	Recurrent pneumonias	CT scan and bronchoscopy	No details	CD34	Bloc sleeve resection
2	Okereke et al. [6]	2014	86y	Female	Dyspnoea and fatigue	CT scan and bronchoscopy	Increased cellularity and mitoses	CD34, BCL2	Lobectomy
3	Liu et al. [4]	2015	49y	Male	Cough and short of breathing	CT scan and bronchoscopy	No details	CD34, CD100, CD99	Surgical resection
4	Huang et al. [7]	2015	46y	Female	Cough and sputum	CT scan and bronchoscopy	Mixture of bland spindle cells and dense collagen bands	CD34, bcl-2 and vimentin	Surgical resection
5	Oliveira et al. [5]	2016	47y	Female	Pain and dyspnoea	X- ray, CT scan and bronchoscopy	Low-grade mesenchymal spindle cell neoplasm, with alternating cellularity, myxoid areas, mature adipose tissue outbreaks, blood vessels with irregular walls	CD34, CD99, Bcl2	Endoscopically removed
6	Zakri et al. [9]	2021	70y	Male	Cough	X-ray, CT scan, PET scan, bronchoscopy and EBUS	Spindle cells formed interlacing fascicles, with plump nuclei and mild cytologic atypia. No mitotic activity.	CD-34, BCL–2, vimentin, desmin, STAT6.	Endoscopically removed by hot snare

used markers and is typically diffusely positive in SFTs, although it may not be specific as it can also be positive in other mesenchymal tumors [1, 17]. However, the detection of nuclear STAT6 expression, which results from the *NAB2::STAT6* fusion gene, is highly specific for SFTs. Immunostaining for STAT6 shows strong and diffuse nuclear positivity in the majority of SFT cases, making it a valuable diagnostic marker [1,17]. In addition to CD34 and STAT6, SFTs often express other markers, including Bcl-2 and CD99, further supporting the diagnosis [1,17]. Conversely, SFTs typically lack expression of markers such as cytokeratins, desmin, S-100 protein, and smooth muscle actin, which helps to differentiate them from other mesenchymal and epithelial tumors [1, 17].

While SFTs are generally categorized as fibroblastic neoplasms with intermediate behavior, the latest classification system offers a more nuanced approach to risk assessment based on age, tumor size, mitotic activity, presence of necrosis [1].

SFTs exhibit a range of genetic alterations, although they are mostly associated with the *NAB2::STAT6* fusion gene, which is considered a hallmark genetic abnormality in these tumors. The fusion of the *NAB2* gene with the *STAT6* gene results in aberrant activation of the STAT6 transcription factor pathway, contributing to tumorigenesis [18]. Other genetic alterations reported in SFTs include mutations in the *TP53* tumor suppressor gene, as well as alterations in genes involved in chromatin remodeling, such as *ARID1A* and *SMARCB1* [19]. Additionally, SFTs may harbor mutations in genes related to growth factor signaling pathways, including PDGFRβ and CD34 [19].

The identification of these genetic alterations has not only improved our understanding of the molecular mechanisms underlying SFT development but also holds potential implications for targeted therapies and prognosis prediction. Further research into the genetic landscape of SFTs is ongoing and may lead to the discovery of additional genetic aberrations and therapeutic targets.

Typically, endobronchial polypoid lesions correspond to neuroendocrine tumors (carcinoid tumors) and, less frequently, to salivary gland-type tumors (mucoepidermoid carcinoma and pleomorphic adenoma) or soft tissue tumors (hamartoma or leiomyoma) [1]. In the case of endobronchial SFT, a complete surgical resection with margin negativity is the mainstay of treatment [8]. The location of the tumor needs to be exactly defined by preoperative investigations, because the principal aim of the surgeon is to achieve the greatest possible parenchyma preservation by means of bronchoplastic procedures such as sleeve or wedge bronchial resections. After surgery, adjuvant therapy is generally not recommended given the benign features of SFT [9,10]. Nevertheless, because these lesions are associated with high recurrence rates, regular follow-up with imaging and/or bronchoscopy is advised [20].

4. Conclusions

In conclusion, the rarity of endobronchial SFTs adds a layer of complexity to their diagnosis, which is accentuated by a wide spectrum of potential differential diagnoses due to the nonspecific clinical and radiological characteristics of SFTs. Notably, the expression of somatostatin receptors in SFTs introduces an additional challenge, often leading to misinterpretation and potential mimicry of neuroendocrine lesions during 68 Ga-DOTATOC PET/CT imaging. To address these challenges, our findings underscore that it is important to employ interventional bronchoscopy and biopsy as integral components in the diagnostic process, particularly when faced with endobronchial lesions. Furthermore, the results of our study advocate for the implementation of complete surgical resection in managing these tumors, given their propensity for recurrence and the potential presence of malignant features. This holistic approach not only facilitates accurate diagnosis but also lays the foundation for a comprehensive therapeutic strategy, reinforcing the significance of a multidisciplinary approach in the management of endobronchial SFTs.

CRediT authorship contribution statement

Fátima Ramalhosa: Writing – original draft, Investigation, Formal analysis. **Federica Pezzuto:** Writing – original draft, Investigation, Formal analysis, Data curation. **Davide Biondini:** Methodology, Investigation, Data curation. **Eleonora Faccioli:** Methodology, Investigation, Formal analysis, Data curation. **Francesco Fortarezza:** Visualization, Validation, Investigation. **Gianluca Canu:** Resources, Methodology, Data curation. **Fiorella Calabrese:** Writing – review & editing, Project administration, Conceptualization. **Roberta Polverosi:** Methodology, Investigation, Formal analysis, Data curation. **Chiara Giraudo:** Methodology, Investigation, Formal analysis, Data curation.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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