Case Report | Oncology: Other

Angiofibrolipoma of the anterior mediastinum: a case report

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Background: The anterior mediastinum is the cavity between sternum and pericardium below the level of clavicles. Tumors of the anterior mediastinum can be caused by malignant or benign pathologies. This case report describes an angiofibrolipoma in the anterior mediastinum, and there is only one other reported case of mediastinal angiofibrolipoma found in the posterior mediastinum. However, angiofibrolipoma is a rare benign tumor that has not been previously reported in the anterior mediastinum.

Case Description: In this report, a case of angiofibrolipoma in the anterior mediastinum of an 84-year-old woman is presented. The patient has no relevant medical history or family history of lung diseases, malignancies, or mediastinal abnormalities. She presented with long-standing exertional dyspnea as the main symptom. The tumor was discovered incidentally. On computed tomography scan a suspected malignant tumor with 5.7 cm diameter was located in the left anterior mediastinum. Transthoracic punctures as well as endoscopic catheter biopsy yielded unspecific histologic findings. The tumor was completely removed by video-assisted thoracoscopic surgery (VATS). Histological examination showed adipose tissue and hyalinized connective tissue between numerous blood vessels. Therefore, the tumor was diagnosed as angiofibrolipoma. The patient had a smooth postoperative recovery and was discharged on the third day in stable condition. Follow-up 2 months after discharge showed the patient was symptom-free and in good health.

Conclusions: Based on the presented case of an anterior mediastinal angiofibrolipoma, our case report emphasizes the importance of considering this rare entity as a possible differential diagnosis when evaluating anterior mediastinal masses. The diagnostic challenges encountered in this case underscore the need for further documentation and awareness of angiofibrolipoma in this location. VATS was proved to be a safe and effective approach for complete tumor resection. Overall, these findings contribute valuable information to the limited literature on mediastinal angiofibrolipoma.

Keywords: Angiofibrolipoma; mediastinal masses; anterior mediastinum; case report

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Introduction

Background

The anterior mediastinum [according to International Thymic Malignancies Interest Group (ITMIG) the current anatomical term for anterior mediastinum is prevascular mediastinum] extends from the body of the sternum to the surface of the pericardium. The histopathologic findings of mediastinal masses cover a wide spectrum. Fifty percent of mediastinal tumors occur in the anterior compartment, the most common being thymomas, teratomas, thyroid goiter and lymphomas (1). The precise identification of the tumor type in the mediastinum holds significant importance for patient management and treatment outcomes. The differential diagnoses and treatment approaches differ dramatically. Treatment options range from radiotherapy, chemotherapy to resection or extended resection or a combination of that. An accurate diagnosis allows physicians to select the most suitable treatment approach, ultimately improving the patient's prognosis and survival.

We detected an extremely rare benign tumor in the anterior mediastinum, an angiofibrolipoma.

It is a benign soft-tissue tumor composed of mature adipocytes, vascular tissue, and collagenous connective tissue. Angiofibrolipoma is a histological variant of lipoma that usually presents as a solitary, subcutaneous, circumscribed lesion in the back, neck, or shoulders (2,3).

This entity has not been described in this localization in literature so far. Therefore, angiofibrolipoma should be considered amongst the differential diagnostic possibilities of tumors of the anterior mediastinum.

Attia *et al.* published the first documented case of mediastinal angiofibrolipoma in 2017, although in this case it was in the posterior mediastinum (3).

Highlight box

Key findings

- The case report presents a rare case of a benign tumor, an angiofibrolipoma, located in the anterior mediastinum.

What is known and what is new?

- Anterior mediastinum can be a site of various malignant and benign alterations. Examples of malignancies that may develop here include thymoma, thymic carcinoma, lymphoma, and germ cell tumors; benign changes, teratoma and thyroid goiters.
- This manuscript describes a rare case of angiofibrolipoma in the anterior mediastinum, providing new insight into both clinical and radiological characteristics of this tumor.

What is the implication, and what should change now?

- This paper emphasizes the significance of accurate diagnosis and management when dealing with anterior mediastinal masses, especially rare entities like angiofibrolipoma. Clinicians should be aware of this entity and include it in their differential diagnosis when diagnosing anterior mediastinal masses.

Rationale and knowledge gap

The rationale of this paper is to document a rare case and emphasize the need for considering this entity when making an anterior mediastinal mass diagnosis, which currently lacks sufficient documentation in the literature due to its rarity.

Objective

We report a rare case of benign tumor in the anterior mediastinum and discuss relevant studies related to this condition. We present this article in accordance with the CARE reporting checklist (available at https://amj.amegroups.com/article/view/10.21037/amj-23-141/rc).

Case presentation

We report the case of an 84-year-old Caucasian woman. She presented herself for the first time at our hospital in October 2022. The patient reported experiencing exertional dyspnea for several years, along with a weight loss of 10 kg over the past year, attributed to dietary changes. Little dry cough, no sputum and no hemoptysis were reported. She described heat waves, but no night sweats. She has been a lifelong non-smoker.

Her past medical history includes a history of lung tuberculosis in 1946, Sjögren's syndrome diagnosed two years ago which has been managed without medication, arterial hypertension, and a history of gynecological total hysterectomy for myoma. Additionally, she had a history of hepatitis in the 1960s and is currently being treated for subclinical hypothyroidism with L-thyroxine. Furthermore, the patient is also being treated for Gout with Allopurinol, along with medications for arterial hypertension (ramipril, lercanidipine).

Upon admission, the patient was found to be in stable general condition. There were mild bilateral lower leg edema, and physical examination revealed diminished breath sounds and dullness to percussion on the left basal lung field.

Pulmonary function tests demonstrated no restriction

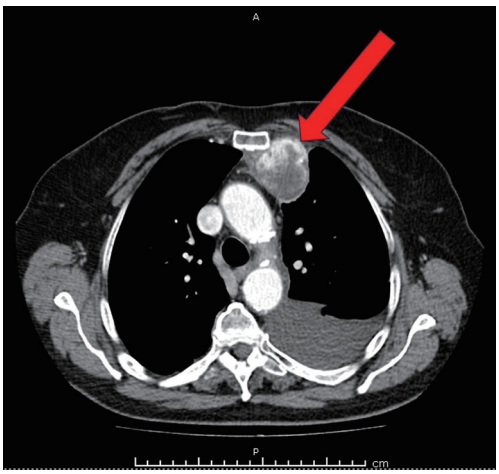

Figure 1 Chest CE-CT scan in mediastinal window showing an inhomogeneous structured tumor (red arrow) with dense and necrotic components. The tumor is in extensive contact with the pleura of the anterior mediastinum. It protrudes into the left lung, causing adjacent compression dystelectasis, and extends into the mediastinal fat without contacting the aortic arch. There is contact with the sternum, but no definite bone destruction. Additionally, left pleural effusion is evident, leading to compression-related reduced ventilation in the basal left lower lobe. CE-CT, contrast enhanced computed tomography.

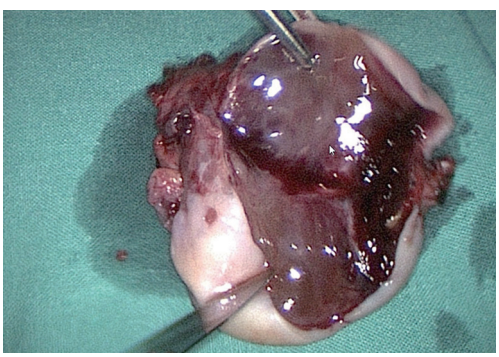

Figure 2 Resected tumor specimen—highly elastic, blue-grey to brownish tissue with a cystic part. Pale gray plaque-like layer covering large portions of the tumor.

or obstruction. In the context of her known gout, routine laboratory monitoring showed a slight elevation in uric acid levels, and C-reactive protein (CRP) was mildly increased at 27.6 mg/L, while all other parameters were within normal limits. The assessment of tumor markers, including carcinoembryonic antigen (CEA), neuron-specific enolase (NSE), and cytokeratin 19 fragment antigen 21-1 (CYFRA 21-1), revealed all values within the normal range.

Since the patient was female, we did not determine alpha fetoprotein (AFP) or beta-human chorionic gonadotropin (β-hCG). Furthermore, there was nether an evidence in the computed tomography (CT) scan nor a clinical sign for sarcoidosis, so we did not determine IL2-R.

Chest CT scan showed an inhomogeneous structured tumor up to 5.7 cm in diameter with dense as well as necrotic parts and extensive contact with pleura of the anterior mediastinum. The tumor protruded into the left lung with adjacent compression dystelectasis and extended into the mediastinal fat without contact to the aortic arch. There was contact with the sternum, but no certain bone destruction. Furthermore, we saw left pleural effusion with compression-related reduced ventilation in the basal left lower lobe (*Figure 1*).

A previous thoracocentesis revealed a exudative clear, serous fluid. Cytologically, no malignant cells were detected, but some lymphocytes, granulocytes, and individual eosinophils were observed.

A CT-guided transthoracic fine-needle aspiration biopsy did not yield any significant histopathological findings, nor were there any significant results after endoscopic catheter biopsy. Finally, a CT-guided core needle biopsy was performed. Histological findings were unspecific as well: connective tissue and adipose tissue surrounded by blood components. Since these results appeared to be insufficient for diagnosis given a malignant process was suspected, the patient was readmitted for tumor resection to the Department of Thoracic Surgery.

The surgical procedure was performed 14 days after her first presentation, and it involved a triportal video-assisted thoracoscopic resection of the mediastinal tumor. The procedure began with an incision in the 5th intercostal space along the mid-axillary line. This access was used for camera inspection, aspiration of the effusion, and dissection of adhesions between the lung and parietal pleura. Additionally, two additional incisions were made in the 7th intercostal space along the anterior and posterior axillary lines to access the anterior mediastinum and perform the tumor resection. After fine preparation of the tumor, extensive adhesions to the chest wall had to be loosened. The tumor was in direct relation to the left internal thoracic artery; therefore, it had to be ligated initially before the tumor could be completely removed. After resection, the tumor was retrieved from the thoracic cavity using a specimen retrieval bag through the incision made in the 5th intercostal space.

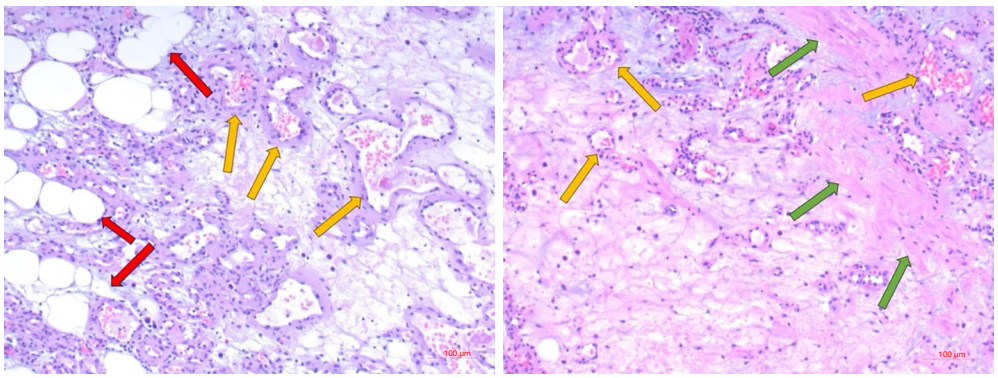

Figure 3 Pathological images of the tumor (hematoxylin and eosin, 10× objective magnification): demonstrating the characteristic angiomatous growth pattern (yellow arrows), fibrous component (green arrows), and adipose tissue (red arrows) component; no evidence of mitosis or cellular pleomorphism. These findings are characteristic of angiofibrolipomas.

Macroscopically, the resected tissue consisted of highly elastic, blue-grey to brownish tissue with a cystic part (approx. 30%). A plaque-like indurated pale gray layer of tissue covered large parts of the tumor (*Figure 2*).

Histological findings showed numerous, varyingly dense, predominantly small-caliber and occasionally also medium-caliber vessels, which mostly had thin wall layers; the proportion of moderately wide wall layers was relatively small. The lining of the vessels consisted of very flat endothelium. Between these numerous vessels very cell-poor, partially hyalinized connective tissue structures with regressive changes as well as adipose tissue were found. Small cystic areas with intraluminal deposits of blood components were found in focal forms. Large parts of this lesion were covered by a band-like cell-poor hyalinized layer (see *Figure 3*).

Immunohistochemical analysis

The adipose component of the tumor shows strong positivity for S100, which is consistent with its origin from mature adipocytes. S100 is a sensitive marker for lipomatous differentiation, helping to confirm the lipomatous nature of the tumor.

CD34 shows strong positivity in the lining of the vascular structures, indicating a well-developed vascular component within the tumor. Similarly, factor VIII staining corroborates the presence of endothelial cells, reinforcing the diagnosis of an angio-component.

Low Ki-67 proliferation index (>1%) indicates the tumor's benign nature with slow-growing potential and a reduced likelihood of active inflammation or aggressive malignancy (see *Figure 4*).

Pathological thought process: the diagnostic approach began with a detailed histological examination, where the mixture of adipose, fibrous, and vascular components suggested a lipomatous tumor with significant vascular involvement. The decision to use S100, CD34, and factor VIII immunostains was driven by the need to confirm the nature of both the adipose and vascular components. The low Ki-67 index was crucial in affirming the benign nature of the tumor.

Differentiating angiofibrolipoma from other entities with overlapping features is crucial, especially considering the presence of mature adipose and vascular components. The key differentials include liposarcoma, angiomyolipoma, other fibrous tumors, and notably thymolipoma.

Thymolipoma is a rare, benign tumor typically involving the anterior mediastinum and is characterized by a mixture of mature adipose tissue and thymic tissue. The absence of thymic tissue in the current specimen is a critical factor that argues against thymolipoma. Thymolipomas generally show areas resembling normal thymic parenchyma interspersed within the adipose tissue, which was not observed in this case.

Liposarcoma: the lack of atypical features and a low Ki-67 index helps to exclude liposarcoma, which typically shows more cellular atypia and a higher proliferation rate.

Angiomyolipoma: while this tumor also contains fat and vascular elements, the absence of smooth muscle, which is a key component of angiomyolipomas, and the specific immunoprofile (S100+, CD34+, factor VIII+), support the diagnosis of angiofibrolipoma.

The postoperative recovery was unremarkable. The patient was discharged from inpatient treatment in stable

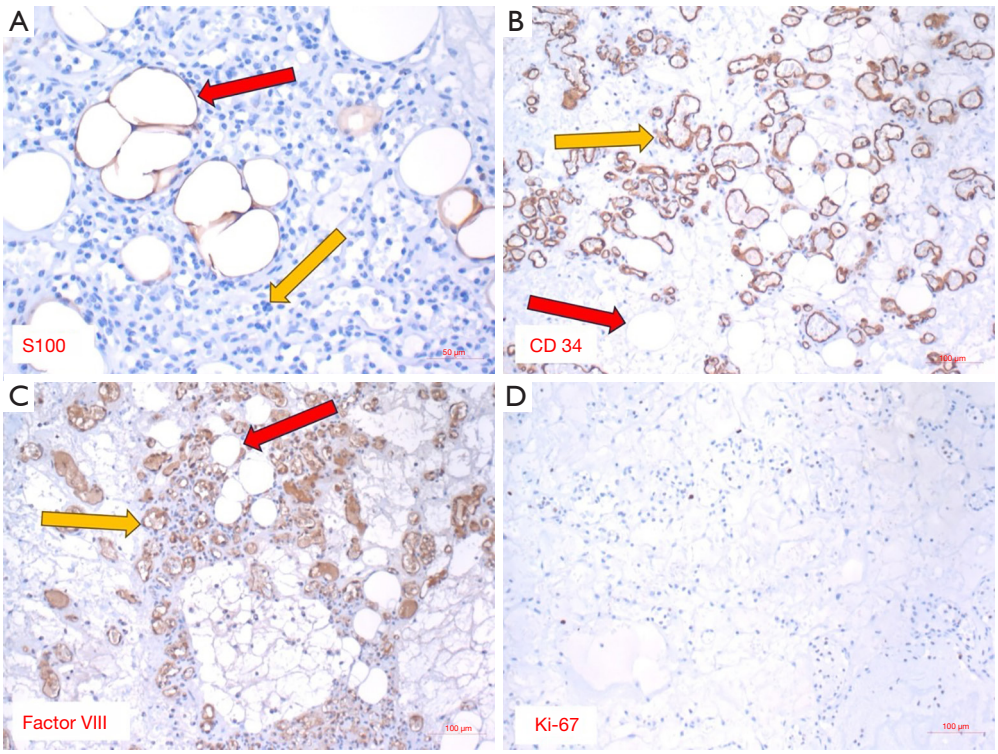

Figure 4 Immunohistochemical images of the tumor: yellow arrows highlight the angiomatous growth pattern, while red arrows indicate the adipose tissue component, integral to the diagnosis of angiofibrolipomas. (A) S100 staining, 20× objective magnification: exhibiting strong S100 positivity in the adipose tissue components, characteristic of angiofibrolipomas. (B) CD 34 staining, 10× objective magnification: demonstrating pronounced CD 34 expression in the vascular structures, indicative of a well-developed vascular component. (C) Factor VIII staining, 10× objective magnification: showing factor VIII positivity in the blood vessels, confirming the vascular nature of the tumor. (D) Ki-67 staining, 10× objective magnification: revealing low Ki-67 expression, suggesting a low proliferation rate, aligning with the benign nature of angiofibrolipomas.

condition on the third postoperative day. There were no adverse or unanticipated events after the surgery.

The patient was presented for a follow-up about 2 months after discharge and presented herself free of symptoms and in good general condition. No significant pleural effusion was observed. The patient did not report relevant dyspnea or signs of infection. Mild lower limb edema persisted, and there was no information provided regarding further weight loss.

We conducted a systematic search in PubMed and Google Scholar using the keywords "Angiofibrolipoma" AND "Mediastinum". The search resulted in one relevant article, including the case report by Attia *et al.* on angiofibrolipoma in the posterior mediastinum (3).

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

Discussion

Key findings

This case report describes a rare instance of angiofibrolipoma in the anterior mediastinum. The patient, an elderly woman in her 80s, presented with exertional dyspnea, lower leg edema and weight loss due to this tumor which was initially suspected to be malignant due to its size and location but ultimately diagnosed as angiofibrolipoma after surgical removal. After video-assisted thoracoscopic surgery (VATS) the tumor was completely removed; her postoperative

recovery was uneventful.

Histological examination revealed adipose tissue and hyalinized connective tissue between numerous blood vessels, indicative of angiofibrolipoma in the anterior mediastinum - first case reported in medical literature.

Strengths and limitations

This study's strengths may include its unique case presentation, as well as the use of multiple diagnostic modalities to accurately diagnose angiofibrolipoma. One limitation of our study is that we did not fully utilize modern imaging techniques such as magnetic resonance imaging (MRI) or positron emission tomography (PET)-CT, which could have facilitated preoperative diagnosis. Nonetheless, the combination of individual symptoms allowed for the conclusion that a malignant condition existed, necessitating resection. However, limitations include only one case sample size and lack of generalizability to larger populations.

Comparison with similar researches

Comparing our research with existing work was particularly difficult due to the unique circumstances of our case. Attia *et al.* presented a case of an 75-year-old man presented with chest pain and was diagnosed with angiofibrolipoma located in the posterior mediastinum. An incomplete removal was achieved through right postero-lateral thoracotomy; however, preoperative MRI provided valuable clues as it suggested a benign mixed mesenchymal tumor which contained fatty tissue (3).

Uwale *et al.* reported the case of a 9-year-old boy with angiofibrolipoma in his calf, which had been slowly growing and becoming painful about one year before presentation. The mass extended from the popliteal fossa to the gastrosoleus junction with no systemic symptoms present and no history of trauma or fall. Preoperative plain radiographs, incisional biopsy, and other ancillary investigations were done and histopathology results after excisional biopsy confirmed angiofibrolipoma (2).

Explanations of findings

The anterior mediastinum usually includes the following anatomical structures: thymus, lymph nodes, adipose tissue, nerves, blood vessels and rarely in the case of thyroid goiter, displaced thyroid tissue from the neck. Anterior mediastinal masses generally arise from these structures.

Clinically, a mediastinal mass can be asymptomatic or present unspecific symptoms and is diagnosed incidentally. Mediastinal tumors become symptomatic due to compression or invasion of adjacent structures. Compression or invasion of nerves can lead to pain, elevation of the diaphragm, paralysis of the vocal folds or cardiac arrhythmia. Furthermore, compression or invasion of blood vessels may lead to e.g., superior vena cava syndrome; compression or invasion of airways leads to cough, dyspnea or hemoptysis and compression or invasion of esophagus could lead to dysphagia. In addition, some tumors lead to systemic symptoms related to extreme release of hormones, cytokines or antibodies (4).

Lipomas are benign tumors consisting of adipose tissue, they are the most common soft tissue tumors in adults (5). Lipomas are usually present subcutaneously and are extremely rare to find in the thoracic cavity (6). Histological variants of lipomas include fibrolipomas, angiolipomas, angiofibrolipomas, angiomyolipomas and infiltrating angiolipomas (2). The origination of lipomas, angiolipomas and especially angiofibrolipomas is unclear. Angiolipomas may develop from pluripotential mesenchymal cells. Abnormal adipose tissue and endothelium develops from these mesenchymal cells (7). Other theories of pathogenesis of angiolipomas assume a secondary vascular proliferation of a congenital lipoma or fatty metaplasia of a hemangioma (8). An important differential diagnosis that should also be discussed is thymolipoma. Thymolipoma and angiofibrolipoma are both rare mediastinal tumors, but they differ significantly in their histopathological features. Thymolipoma is composed of mature adipose and thymic tissue and may present with nonspecific symptoms. On the other hand, angiofibrolipoma is a benign soft-tissue tumor composed of mature adipocytes and vascular tissue. It is essential to differentiate between these tumors due to their distinct characteristics and potential variations in clinical management. Thymolipomas can be differentiated from angiofibrolipomas based on the presence of thymic tissue components, which is absent in angiofibrolipomas (9,10).

In this particular case, a malignant process was suspected. In retrospect, the presence of an ipsilateral pleural effusion does not appear to be directly related to the existence of an angiofibrolipoma in the anterior mediastinum. The calculated protein quotient was >0.5, indicating an exudative pleural effusion.

The presence of lymphocytes, granulocytes, and individual eosinophils in the pleural effusion cytology

indicates an inflammatory reaction in the pleural effusion. This may suggest an infection, inflammatory disease, or immune-mediated response. In some cases, malignant tumors can induce an inflammatory reaction, leading to an increased number of lymphocytes in the pleural effusion. The presence of Sjögren's syndrome in the patient can provide further explanations for the pleural effusion and the cytological findings. Sjögren's syndrome is an autoimmune disease that primarily affects the salivary and lacrimal glands but can also impact other tissues in the body, including the pleura (11).

The preoperative attempts at histological confirmation by means of biopsies had to fail, since the findings had to yield only non-specific results (fatty tissue, connective tissue, blood components). Nevertheless, in absence of typical symptoms and imaging features, histological diagnosis is necessary. A biopsy should be carried out in accessible lesions before surgery (12).

In retrospect, an MRI examination probably would have provided the necessary clues to determine the dignity. Complete surgical excision and histopathological confirmation of margins are adequate for diagnosis and treatment.

The patient suffered from tuberculosis in her early youth. However, we consider a post-tuberculosis lesion to be unlikely. A pulmonary tuberculosis usually leads to the formation of cavities and granulomas. Through the course of disease abnormal repair may resulting in focal or extensive fibrosis of lung parenchyma (13). There is no evidence for the formation of lipomas as a consequence of a cured tuberculosis.

The findings of this case report are significant in that angiofibrolipomas are typically found as solitary, subcutaneous, circumscribed lesions in the back, neck, or shoulders. This case demonstrates that angiofibrolipomas can occur in the anterior mediastinum, although it is a very rare occurrence. The case also highlights the difficulty in diagnosing anterior mediastinal tumors, as demonstrated by the non-specific histologic findings on various biopsy techniques.

Finally, the successful complete resection of the tumor through VATS shows that this minimally invasive technique can be a viable option for treating anterior mediastinal tumors. VATS was chosen as the method for tumor resection due to its numerous advantages, including less postoperative pain, reduced hospital stay, and faster recovery compared to open surgery. Additionally, VATS allows for better visualization and manipulation of tissues through small incisions, leading to improved cosmetic outcomes (14). Also robotic-assisted thoracoscopic surgery (RATS) could have been an alternative operative method.

Complications during the surgical removal pose a low risk, including bleeding, injury to surrounding tissues or major blood vessels, and infection (15). The risk of tumor spread to surrounding tissues or organs is generally low, given that Angiofibrolipomas are typically well-defined tumors with limited aggressive behavior.

In discussing the necessity of further follow-up, we acknowledge that, although our patient benefited from short-term follow-up, the decision to skip long-term follow-up was multifactorial. The tumor's benign nature, coupled with a complete and uncomplicated resection, suggested a favorable prognosis. This, combined with the lack of infiltrative growth, led us to conclude that routine long-term follow-up might not be necessary. However, we recommend that clinicians consider the individual circumstances of each case, including the surgical complexity and tumor behavior, when determining the follow-up protocol (8,16-18).

Implications and actions needed

This study suggests that angiofibrolipoma should be considered as a possible differential diagnosis when dealing with anterior mediastinal masses. Due to its rarity in this location, more documentation in the medical literature is necessary.

Conclusions

We document an extremely rare case of anterior mediastinal angiofibrolipoma being the only case published at the level of the anterior mediastinum. The diagnostic difficulty in this case highlights the challenges in identifying the nature of anterior mediastinal tumors. Biopsy techniques can yield non-specific results, as it was seen in this report.

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Footnote

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Peer Review File: Available at https://amj.amegroups.com/article/view/10.21037/amj-23-141/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://amj.amegroups.com/article/view/10.21037/amj-23-141/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

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