

Mediastinal cavernous angioleiomyoma: A case report and review of literature

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Abstract. Angioleiomyoma is a type of pericyte tumor with a benign biological behavior. It typically features proliferation of mature perivascular smooth muscle cells around blood vessels. Angioleiomyoma may be categorized into solid, cavernous or venous subtypes. Usually, it occurs in the dermis or subcutaneous tissue, while the rare cavernous subtype is most common in the upper extremities. Only a small number of cases of angioleiomyoma located in the mediastinum have been reported to date. In addition, there are few reports of mediastinal angioleiomyoma described as a cavernous histopathological subtype. The present study reported a case of mediastinal angioleiomyoma presenting as an unusual cavernous histopathological subtype. The histopathological and immunohistochemical features, based on which a diagnosis of cavernous angioleiomyoma was confirmed, were desmin- and smooth muscle actin-positive expression in spindle tumor cells, as well as ETS-related gene (ERG)- and CD31-positive expression in vascular endothelial cells. Cavernous angioleiomyoma of the mediastinum rarely occurs in the clinical setting but should be considered as a differential diagnosis of mediastinal tumors.

Introduction

Angioleiomyoma (ALM) is a slow-growing, benign pericyte tumor, comprising mature smooth muscle cells arranged around blood vessels. It is divided into three common histopathological subtypes: Solid, venous and cavernous (1). ALM usually originates from the cutaneous area of the lower extremities and forms subcutaneous nodules (2). The cavernous subtype of ALM is rare and usually occurs in the upper extremities (3). ALM

may originate from undifferentiated mesenchymal tissue of ectopic embryos, smooth muscle cells in the vascular wall or both. Approximately 3% of ALM also has mature adipocytes, which are usually related to the venous histologic subtype and are located in the head and neck area; these are termed angioleiomyomas with adipocyte differentiation. Recently, novel pathological subtypes have been proposed: Myomatoid angioleiomyoma, lipomatoid angioleiomyoma, hemangiomatoid angioleiomyoma and mixed type according to the proportion of vascular structure, smooth muscle cells and adipose tissue (2,3). However, to the best of our knowledge, there is no previous report on the cavernous subtype of ALM originating from the mediastinum. The present study reported a rare case of mediastinal cavernous ALM.

Case report

A 49-year-old female presented with a mediastinal mass found during a routine annual medical examination at the First Hospital of Jiaxing (Jiaxing, China) in April 2021. On chest computed tomography examination, a patchy, low-density shadow was observed in the anterior mediastinum with internal calcification and no obvious enhancement (Fig. 1). The patient had no history of malignancy and the only relevant surgical history was of a previous mastectomy performed two decades earlier. Furthermore, the patient had a family history of lung cancer (first-degree relative). The preoperative differential diagnoses were thymoma and teratoma according to the computed tomography findings. Considering the size of the mass, the possibility of thymoma and the family history of lung cancer, surgical management was suggested. On thoracoscopy, the mass was indicated to have originated from the anterior mediastinum and was located near the pericardium. The mass was resected along the capsule with ultrasonic and electric knives. The intraoperative blood loss was 30 ml. The operative time was 1 h and the postoperative hospital stay was 8 days. There were no postoperative complications. The size of the resected tumor was 6.8x2.7x2.5 cm. Histopathologically, the tumor consisted of cavernous blood vessels and differentiated smooth muscle bundles that lacked cell atypia and mitosis (Fig. 2). Immunohistochemical (IHC) staining confirmed the presence of smooth muscle cells by indicating positive expression of smooth muscle actin (SMA) and desmin. In addition, positive expression

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of CD31 and ERG confirmed vascular endothelial cells (Fig. 3). Human melanoma black 45 (HMB45) expression was negative, ruling out angiomyolipoma. These observations led to the diagnosis of cavernous ALM. At the 3-month follow-up examination, no signs of recurrence were detected. However, magnetic resonance imaging (MRI) scans are not available, as the patient did not undergo any MRI examination throughout the entire clinical course and no macroscopic photographs of the tumor or sections thereof and its boundary were recorded at the time.

The histopathological analysis was performed as follows: The tumor samples were fixed with 10% neutral buffered formalin at room temperature for 24 h, embedded in paraffin and then cut into 4- μ m sections for hematoxylin-eosin staining (H&E) and IHC staining. H&E staining was performed with hematoxylin for 3 min and eosin for 3 min. A light microscope was used for observation. IHC staining of these sections was performed on a BenchMark XT (Roche Diagnostics), an automatic IHC staining device. All procedures were performed as per the manufacturer's protocols. The endogenous peroxides and protein were blocked using the Endogenous Biotin Blocking kit (cat. no. ab64212; Abcam) at 37°C for 4 min. The following primary antibodies were used: Anti-SMA (cat. no. ab5831; 1:200 dilution; Abcam), anti-Desmin (cat. no. ab227651; 1:100 dilution; Abcam), anti-ERG (cat. no. ab133264; 1:250 dilution; Abcam), anti-CD31 (cat. no. ab28364; 1:50 dilution; Abcam) and anti-HMB45 (cat. no. ab212829; 1:1,000 dilution; Abcam). Primary antibodies were added and incubated for 16 min at 37°C.

Discussion

Initially, ALM was considered a smooth muscle tumor. However, it was reclassified in the World Health Organization (WHO) classification of tumors as a pericyte (perivascular) tumor (4). ALM tends to occur in individuals aged 40-60 years and primarily in females (female/male ratio: 1.7:1) (5). Clinically, ALM usually presents in the lower limbs as an isolated, slow-growing, active, hard and occasionally painful skin mass. The pain is usually sudden and is caused by exposure to wind and coldness, which are thought to cause ischemia by the active contraction of the smooth muscles (6). ALM mainly occurring in females may support the hypothesis of hormone-dependent tumor growth (7). An increased size and pain of ALM during pregnancy and related to the menstrual cycle were previously reported (7). ALM rarely occurs in the mediastinum. The presence or absence of symptoms in patients with mediastinal ALM depends on the location and size of the ALM. When the tumor compresses nerves, patients may present with back pain (8).

Based on histopathology, ALM is a pericyte tumor associated with vascular smooth muscles without elastic fibers. On macroscopic examination, ALM is a solid nodule with a clear boundary. ALM does not usually exceed 2 cm in size. If located in the mucosal tissue, its surface is covered by the mucosa and it appears as a pink mass (9). ALM manifests as a solitary mass composed of mature smooth muscle bundles with abundant vascular channels and an unobstructed lumen (10). According to the WHO, ALM is histopathologically divided into three subtypes: Solid, venous and cavernous. Solid ALM is characterized by numerous compact smooth muscle bundles, which include slit-like blood vessels. Venous ALM features blood vessels with thick muscle walls and non-dense smooth

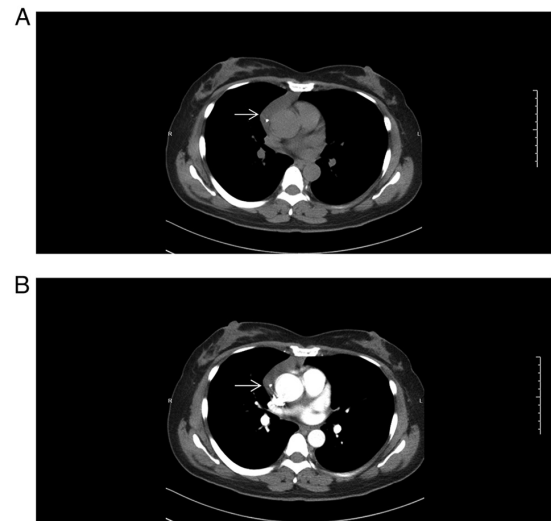


Figure 1. Radiological results of chest computed tomography. (A) A patchy low-density shadow with punctate calcification is present in the anterior mediastinum (white arrow indicates the tumor). (B) No enhancement on contrast enhancement is observed (white arrow indicates the tumor).

muscle bundles around the vascular channels. Cavernous ALM comprises only a small amount of smooth muscles and diffuse, dilated vascular channels (5). Upon IHC analyses, most ALMs were positive for SMA, desmin, calponin, h-caldesmon, vimentin and collagen type IV (7,11). The vascular endothelial cells were positive for CD31 and CD34 (12).

The cavernous subtype of ALM is rare and has unique clinicopathological features. Unlike the most common solid type, the cavernous type is common in males (11). Patients with the cavernous subtypes of ALM usually do not experience any pain (13). Edo *et al* (14) defined the low- or equal-intensity linear or branching structures on T2-weighted images as the 'dark reticular sign' by extracting the MRI features of ALM. The characteristic MRI manifestation is mainly observed in cases of cavernous ALM (14). Upon histopathological analyses, the frequency of concentric circles in the cavernous type and the proportion of desmin-negative expression were higher than those in the solid type (15).

To review the cases of mediastinal angioleiomyoma, the PubMed database (<https://pubmed.ncbi.nlm.nih.gov/>) was searched and available literature in the English language that met the set requirements was screened. The following search terms were used in all databases: {(mediastinal[Title/Abstract]) AND (angioleiomyoma[Title/Abstract])}. Studies published between 1965 and 2022 were considered. Mediastinal ALM has been rarely reported, according to the current literature. In certain studies, mediastinal ALM was observed to originate from the aorta or the superior intercostal vein (16,17). Mediastinal ALM may compress the intercostal nerves or involve the intervertebral foramen, resulting in thoracic radiculopathy. The patients reported in the literature underwent surgical resection, after which their neuropathic pain improved immediately (8,18). However, microscopic pleural involvement may lead to local recurrence, which may require resection in the future (19).

The limitation of the present study is that the MRI information of the patient is not available to demonstrate the characteristic manifestation of cavernous angioleiomyoma.

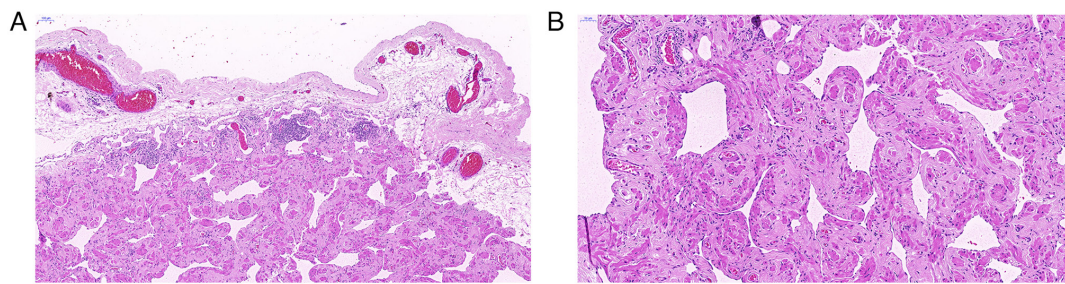


Figure 2. Histology of tumor samples. (A) The boundary of the tumor is clear and the tumor is wrapped by thin fibrous tissue (H&E; magnification, x100; scale bars, 100 μ m). (B) The tumor is composed of dilated cavernous vessels and smooth muscles (H&E; magnification, x200; scale bars, 50 μ m). H&E, hematoxylin and eosin.

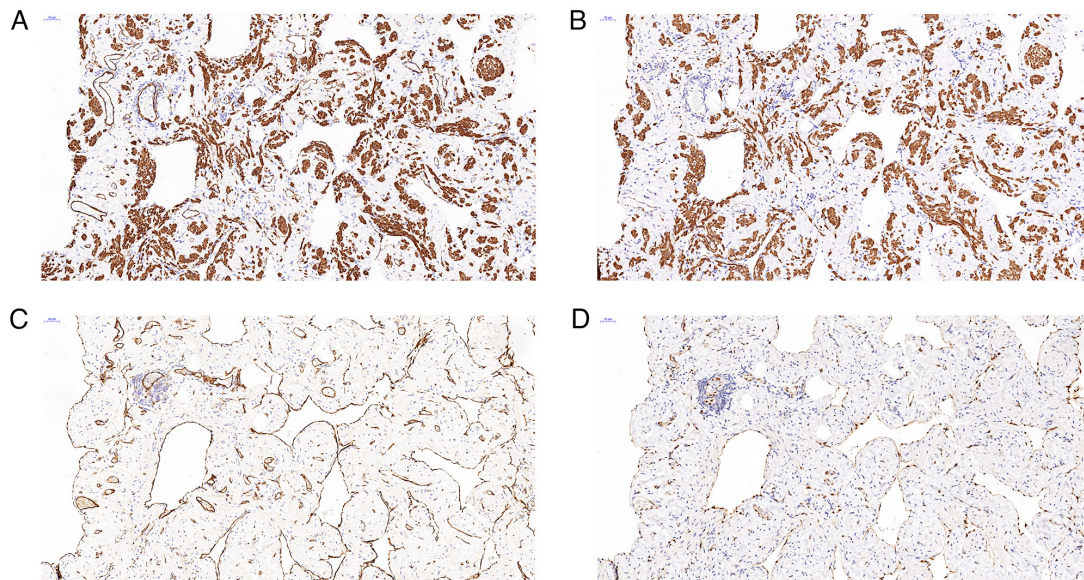


Figure 3. Microscopic images of immunohistochemical staining. The smooth muscle cells were (A) positive for smooth muscle actin and (B) positive for desmin. The vascular endothelial cells were (C) positive for CD31 and (D) positive for ERG (magnification, x200; scale bars, 50 μ m).

Furthermore, macroscopic photographs of the resected tumor were not recorded to show the color, boundary and section.

In conclusion, the present report emphasizes the requirement for clinicians to include ALM in the differential diagnosis of mediastinal tumors. Despite the insufficient evidence of radiological findings, histopathological analysis is essential for diagnosis. Due to the benign nature of mediastinal ALM with a low risk of recurrence, simple surgical resection is suitable for its treatment.

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Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Authors' contributions

ZZ and QZ obtained and analyzed the patient's information and wrote the manuscript. XL and LZ collected and analyzed the patient data. JW contributed to data extraction and quality assessment. ZG and SH analyzed and interpreted the imaging findings. ZG and SH confirm the authenticity of all the raw data. ZZ and WW designed the study and reviewed the manuscript. All authors contributed to the manuscript and read and approved its final version.

Ethics approval and consent to participate

The study was approved by the Medical Ethics Committee of the First Hospital of Jiaxing (Jiaxing, China).

Patient consent for publication

The patient provided written informed consent for the publication of this case report and all accompanying images.

Competing interests

The authors declare that they have no competing interests.

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