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Mediastinal Cavernous Hemangioma Presenting as a Cardiophrenic Angle Mass: A Case Report and Literature Review

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Abstract

Introduction: Mediastinal hemangiomas are uncommon benign vascular tumors. They are histologically classified into capillary, cavernous, and venous types, according to the size of their vascular spaces. Phleboliths, multiple enhanced vessels, and peripheral puddling of contrast enhancement are the typical diagnostic features on computed tomography (CT). The cardiophrenic angle (CPA) area is a particular area of mediastinum and diseases in this region are rare but various. This paper describes a case of cavernous hemangioma located in the right CPA, lacking the typical CT imaging findings, that was definitively diagnosed after surgery.

Case Presentation: On March 20, 2017, a 38-year-old woman referred to Da-Ping hospital, which is a level III military hospital affiliated to the Army Medical University, Chongqing, China. She had a three-week history of intermittent cough, dull aching chest pain, and occasional palpitation. Her general physical examination and other routine lab tests and tumor markers were reported within the normal ranges. One day later, the chest plain CT showed a well-defined and non-invasive mass with soft-tissue density interspersed with a fatty ingredient in the right CPA with contrast agent. The tumor demonstrated non-enhancement neither in the arterial phase nor in the venous phase, and no apparent feeding vessels to the tumor were identified. It was initially suspected to be a benign ectopic thymoma. On March 27, 2017, the tumor was completely resected by video-assisted thoracoscopic surgery (VATS). Post-operative histological findings confirmed the diagnosis of cavernous hemangioma. The patient was in good condition at a five-month follow-up.

Conclusions: Mediastinal cavernous hemangioma should be considered as an important differential diagnosis of mediastinal masses even though it is rare. Chest CT is useful in providing valuable information on the origin and invasiveness of the tumor, evaluating the relationship between tumors and intrathoracic vessels, and mapping the blood supply of tumors to select more suitable operative intervention.

Keywords: Cavernous, Cough, Hemangioma, Mediastinum, Thymoma, Thoracic Surgery, Tomography, Tumor, Video-Assisted, X-Ray Computed

1. Introduction

Although cavernous hemangioma is one of the most common benign soft tissue tumors of the liver, cerebral parenchyma, and subcutaneous tissue, it rarely occurs in the mediastinum, with the incidence rate of less than 0.5% among all mediastinal masses (1). Owing to its rarity, the preoperative diagnosis is difficult, and it is sometimes misdiagnosed as a malignant soft tissue tumor. The cardiophrenic angle (CPA) is a special region of the mediastinum that is easily overlooked. The common differential diagnosis of CPA masses includes Morgagni hernia, pericardial cyst, and mediastinal lung cancer. However, rare cases of cavernous hemangioma in the CPA have been reported. Although the CT imaging features of mediastinal cavernous hemangioma are often described as an enhancing mass or associated with calcified phleboliths (2), there are rare cases with non-enhancement after the enhanced CT was reported. Surgical intervention is often performed for the purpose of diagnosis and treatment of mediastinal cavernous hemangioma. Thoracotomy or median sternotomy could be suitable for cases with a giant size mass (3); however, with the development of minimally invasive technology, most small tumors are accessible and can be safely excised via the video-assisted thoracic surgery (VATS) (4). Here we describe a case of cavernous hemangioma in the right CPA of the anterior mediastinum, with atypical CT imaging findings, which was successfully resected using a VATS procedure.

2. Case Presentation

A 38-year-old female was referred to and hospitalized at the thoracic surgery department of our hospital (Da-Ping hospital, a level III military hospital affiliated to the Army Medical University, Chongqing, China), on March 20, 2017. She presented a three-week history of intermittent cough and dull aching chest pain, accompanied by sporadic palpitation. There were no other respiratory symptoms such as expectoration, hemoptysis, and dyspnea. The physical examination results included normal chest and cardiac examination results and no tenderness or organomegaly in the abdomen. The vital signs were as follows: BP = 100/64, PR = 84 beats/min, RR= 20/min, and T = 36.1°C axillary. The lab results were as follows: negative HIV and TB, HB = 130 g/L, WBC = 5.1×10^9/L, LYM = 5.1×10^9/L, PLT = 171×10^9/L, GLU = 4.8 mmol/L, and normal PT, PTT, and INR. Tumor markers, such as CA199, CA242, CA125, AFP, and NSE were all normal (Table 1). There was nothing of significance in the patient's medical history, drug history, allergy history, and social history.

On March 21, 2017, the patient underwent plain and dual-phase enhanced (arterial and venous phases) CT scanning by a 64-slice CT scanner (Lightspeed, GE Healthcare, Milwaukee, WI, USA), which was calibrated before use. The CT imaging data were directly interfaced with the picture archiving and communication system (PACS). The images were reviewed, and a consensus was reached by two senior thoracic radiologists (HY.K. and R.C., with 15 and 18 years of experience in thoracic imaging, respectively). The chest CT showed a heterogeneous mass with soft-tissue density interspersed with a fatty ingredient in the right CPA, with well-defined and circumscribed margin. The interface between the lesion and heart was clear, and the latter was slightly compressed and displaced to the left hemithorax (Figure 1). The CT value (attenuation) of the tumor was measured as follows. First, axial plain and contrast-enhanced CT images showing the tumor margin with the maximal area on the same section was selected. Second, three ROIs were manually drawn to cover the margin of the lesion (plain scan, arterial phase, and venous phase, in sequence) using the polygonal region of the ROI tool from PACS, carefully excluding adjacent mediastinal fat and pulmonary lobe; then, the attenuation of the lesion was obtained automatically. Each phase was measured three times. A sample of ROIs is shown in Figure 1A. Third, the average CT values of each section of the lesion were taken by using SPSS statistical software (version 19.0, Chicago, IL, USA). On the plain CT images (Figure 1B), the tumor had an attenuation of 47.66 $\pm$ 0.56 Hounsfield units (Hu). While on enhanced CT images, the tumor had an attenuation of 48.15 $\pm$ 0.57 Hu in the arterial phase (Figure 1C) and 48.70 $\pm$ 0.65 Hu in the venous phase (Figure 1D). No definite feeding vessel to the tumor was identified. Then, the two experts reached a consensus that the tumor showed non-enhancement after the enhanced CT scan since the absolute attenuation between the plain and enhanced CT was less than 10 Kim (5).On March 27, 2017, the patient underwent a VATS through the right fourth intercostal space. The intraoperative exploration revealed an anterior mediastinal pericardial mass, measuring 4.5 $\times$ 5.2 $\times$ 4.6 cm^3, closely adhered to the pericardium, and the phrenic nerve was completely wrapped. The total excision of the mass was performed. Post-operative histological findings showed an abundant vascular proliferative lesion within the tumor, with many thick-walled vessels with prominent muscular wall and cavernous spaces, and no thrombosis or hemorrhage (Figure 2). The final diagnosis was a cavernous hemangioma.

3. Discussion

Cavernous hemangiomas in the mediastinum are rare benign vascular tumors, and they are considered a type of developmental vascular malformation, derived from isolated embryonal hemangioblasts or normal vascular endothelium. Histologically, the tumors are composed of different sizes of dilated vascular spaces lined by a layer of cuboidal endothelial cells, filled with blood and phleboliths (calcified thrombus). The stromal elements contain varying amounts of fat, myxoid fibroblastic proliferation, and fibrous tissues. Cavernous hemangiomas may occur anywhere in the mediastinum, of which 70% are located in the anterior mediastinum (2, 3, 6, 7) and 20% in the posterior mediastinum (8-10). Middle mediastinal location is extremely rare, with only two cases reported in the literature, to the best of our knowledge (4, 11). Moreover, one case concurrently involving the mediastinum and the lung parenchyma has been reported (5). Although mediastinal hemangiomas usually manifest as nonspecific soft tissue masses, they have also been reported with cystic changes. To date, they have been reported in only six cases (5). Clinically, approximately 75% of the patients are diagnosed before the age of 35 years, with no gender preponderance; moreover, rare cases of mediastinal cavernous hemangiomas have been reported in fetuses and children (6, 7). Mediastinal cavernous hemangiomas are usually well defined and capsuled, and the tumor size can range from 2 to 18 cm (3).

The present case was a soft tissue mass with a regular margin arising from the right CPA of the anterior mediastinum, measuring 5.2 cm at the largest size. The clinical symptoms of mediastinal hemangiomas are usually nonspecific, including a cough, dyspnea, chest pain, hoarse-

Table 1. Variables of the Case

Variables	Results
Vital signs	BP: 100/64, PR: 84 beats/min, RR: 20/min, T: 36.1°C axillary
Chief complaints	Three weeks of intermittent cough, dull aching chest pain, and sporadic palpitation
Physical examination	Chest: no tenderness/dyspnea, normal bilateral lung auscultation; neck and axilla: no enlarged lymph nodes; heart: normal S1 and S2, no murmurs or gallops; abdomen: soft, no tenderness, no distention, normoactive bowel sounds
Laboratory findings	HIV and TB negative, HB 130 g/L, WBC 5.1 $\times$ 10^9/L, LYM, 5.1 $\times$ 10^9/L, PLT 171 $\times$ 10^9/L, GLU: 4.8 mmol/L, PT, PTT and INR: normal, CA199, CA242, CA125, AFP, and NSE: normal
Radiologic findings	A heterogeneous soft-tissue mass located in the right CPA, with well-defined and circumscribed margin; non-enhancement in enhanced CT scan, presence of fatty ingredient, and the absence of phlebolith

Abbreviation: CPA, cardiophrenic angle.

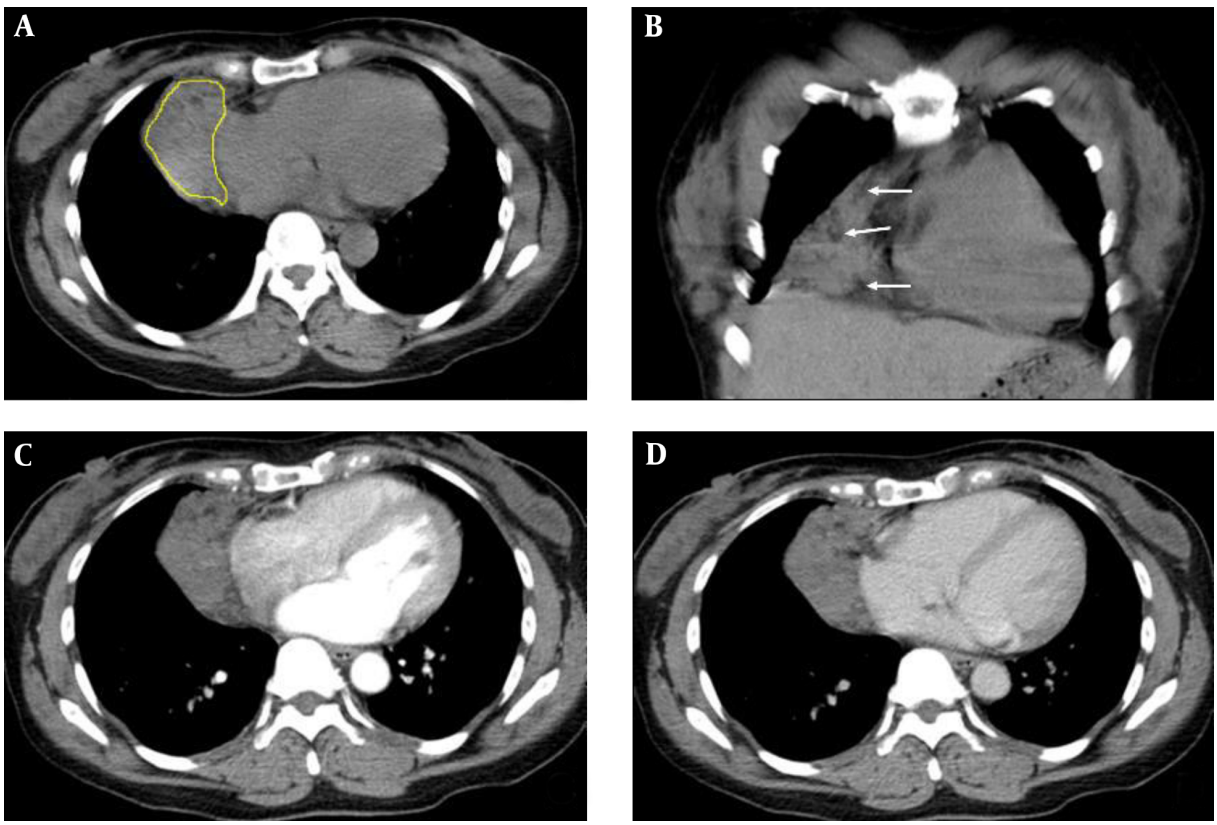

Figure 1. Transverse plain CT scan; A, an anterior mediastinal mass is shown with soft-tissue attenuation arising from the right CPA; no phleboliths or calcifications were observed; the outlined yellow area is a sample of ROI measured CT values. On coronal sections, B, the tumor had no capsule and appeared as an embedded growth pattern; the mass was closely related to the pericardium, with no evidence of invasion; there were discrete low-density areas representing fat in the tumor (white arrows). Transverse contrast-enhanced CT image (C and D for arterial and venous phases, respectively) showed non-enhancement within the tumor and no obvious feeding vessels to the tumor were identified.

ness, difficulty in swallowing, etc., mainly due to the pressure exerted by the tumor on adjacent organs; however, about 50% of patients are asymptomatic (4, 5, 11). Our patient presented intermittent cough, dull aching chest pain, and sporadic palpitation for three weeks. When the tumor grows rapidly, it can easily result in the compression or infiltration of the superior vena cava, thoracic duct, vagus nerve, phrenic nerve, and recurrent laryngeal nerve, thereby causing superior vena cava syndrome or Horner's syndrome (10), which can even lead to acute death (6). Mediastinal hemangiomas may be simultaneously associated with hemangiomas of other organs such as the skin, liver,

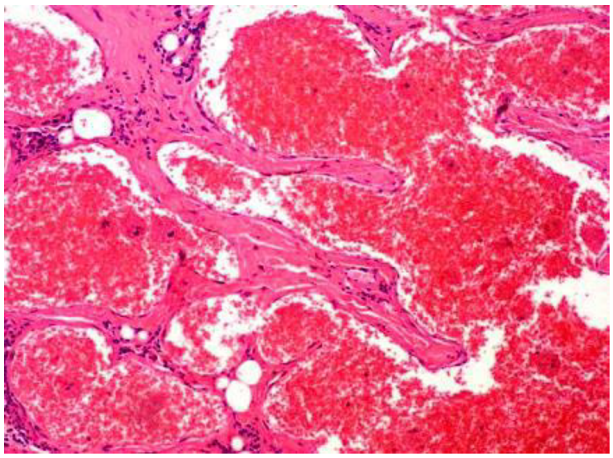

Figure 2. Microscopic examination showing dilated vascular spaces covered by a layer of endothelial cells, filled with blood; the surrounding stroma was interspersed with fat and fibrous tissue (H&E staining, ×400)

spleen, and kidneys, or rarely Klippel-Trenaunay syndrome (KTS) (10, 12). In Table 2, the characteristics of our case are compared with the features of previously published case series and reports.

On chest radiograph, mediastinal cavernous hemangiomas are usually rounded and lobulated with smooth margins. However, these signs are not significant for diagnosis. While chest plain CT scan usually shows a heterogeneous mass with well-defined smooth or lobulated margin, the mass with a diffuse growth can be characterized by the unilateral or bilateral widened mediastinum, which looks wavy. Although the margin is usually well-defined, only have a few tumors complete capsules, and the tumor has less probability of growth beyond the chest (1). There are rare cases of tumors with aggressive growth, the disordered boundary with the surrounding structure, and invasion of the adjacent organs (8). In this case, the mass had no capsule, and the chest wall and the pleural cavity were intact. On reconstructed coronal images, because of the slow growth under the influence of gravity, the mass appeared to be embedded in the right CPA; the base of the mass was located in the diaphragm and the right atrium and ventricle were both slightly compressed, indicating that the lesion had a soft-tissue structure with relatively high compressibility, which partly conforms to the histology of hemangiomas with benign biological properties. Ring-like calcification with central lucency (phleboliths) is reported as the characteristic imaging finding, which is derived from organized thrombi within vascular spaces, but phleboliths are present in up to 10% of cases. In this case, phleboliths or calcifications were not observed, similar to cases described by Lim et al. (2).

On contrast-enhanced CT scans, the patterns of enhancement are nonspecific, closely related to the blood flow and the degree of thrombosed vascular channels. The tumors are known to enhance heterogeneously and centrally (2). Classical peripheral enhancement and puddling of contrast (commonly in hepatic hemangioma) have also been reported (13). However, the type of homogenous enhancement and non-enhancement, as depicted in this case, is rarely reported. Moran et al. (14) reported that various stromal elements, such as inflammatory fibrosis and smooth muscle proliferation, may explain the heterogeneous enhancement or non-enhancement. Dynamic CT scans can provide valuable information for precise diagnosis, which can reveal "gradually increasing and persistent enhancement". Additionally, delayed images, although rare, may reveal aberrant draining vessels into the tumor, which are highly suggestive of the vascular nature of the tumor (15). In this case, a potentially confusing aspect, which may introduce difficulties in diagnosis, was the fat content representing low-density areas within the lesion on CT imaging (Figure 1B) and the author did not find a study with the same finding. This may be related to the varying amounts of fat in the stroma of the tumor. To the best of our knowledge, the differential diagnosis of a heterogeneous mass in the anterior mediastinum with soft tissue interspersed with fat includes Morgagni hernia, teratoma, and lymphoma. Morgagni hernia is a common fat-containing mass that occurs in the right CPA; however, it usually includes omentum accompanied by intestinal canal or small omental vessels. Most teratomas are benign, and cystic and the mass usually shows heterogeneous attenuation due to a mixture of soft tissue, fat, fluid, and laminar calcifications. Mediastinal lymphoma can appear as a heterogeneous mass derived from the thymus or lymph nodes in the mediastinal fat; tracheal/bronchial vessels are always embraced, and contrast enhancement is homogenous and moderate.

Reviewing the previously reported cases in the literature, complete surgical resection as performed in this case is the primary treatment of choice for mediastinal cavernous hemangiomas in which, we should consider the protection of nearby large vessels, major airways, and other vital structures to prevent serious complications, primarily bleeding (2, 3, 8, 12). However, partial resection is proposed as the best treatment protocol if extensive mediastinal resection may be associated with high morbidity and mortality, and the residual tumors generally do not grow (1, 5). Selection of a correct surgical approach is essential to achieve radicality and safety of the procedure. In the case of large, especially bilateral tumors, or tumors closely adhered to surrounding large vessels, phrenic nerve, thoracic duct, pericardium, etc., the correct surgi-

Table 2. Comparison of the Patient's Characteristics with Previously Published Case Series and Reports

First Author	Year	Study Description	Demography (Age, y/Gender)	Clinical Presentation	Location/Size	Treatment	Prognosis
Kuo (12)	2003	Cavernous hemangioma in a patient with Klippel-Trenaunay syndrome	30/M	Intermittent cough with scanty sputum	Between the SVC and azygous vein/none	Thoracotomy, complete excision	Alive
Chan (11)	2009	Cavernous hemangioma in the middle mediastinum	62/F	Asymptomatic	Middle mediastinal/6.8 × 4.5 × 5.9 cm	VATS, Complete excision	Alive
Lim (2)	2014	Cavernous hemangioma in the anterior mediastinum	26/M	Chest pain and mild dyspnea	Anterior mediastinum/ 8.5 × 6.0 × 5.0 cm	Median sternotomy, complete excision	Alive and well after five months
Das (10)	2014	Hemangioma in the posterior mediastinu	56/F	Right-sided dull aching chest pain	Posterior mediastinum/6.5 × 5.3 cm (on chest CT)	Right posterolateral thoracotomy	Alive
Yozgat (7)	2015	Foetal mediastinal cavernous hemangioma	None	None	Anterior mediastinal/4 × 5 ×7 cm	Left posterolateral thoracotomy (when the patient was three-week-old)	Alive, with no recurrence after one year
Kaya (3)	2015	Giant cavernous hemangioma in the mediastinum	56/M	Back pain	Anterior mediastinum/18 cm in diameter	Posterolateral thoracotomy, complete excision	Alive
Shikada (4)	2015	Cavernous hemangioma in the middle mediastinum	51/F	Asymptomatic	Middle mediastinal/3.8 × 2.2 cm (on chest CT)	VATS, complete excision	Alive and well after 10 months
Yun (8)	2016	Cavernous hemangioma with bony invasion	58/F	Intermittent back pain	Posterior mediastinum/6.0 × 5.0 cm (on chest CT)	Hemilaminectomy with costotrans-versectomy, complete excision	Alive, with no recurrence after one year and five months
Kim (5)	2017	Cavernous hemangioma concurrently involving the mediastinum, lung, and parenchyma	61/M	Asymptomatic	Anterior, middle mediastina and parenchyma/ approximately 1.5 cm to 8 cm (on chest CT)	Thoracotomy, partial excision	Alive, with a decreased number of masses
Igari (6)	2017	Sudden death caused by a giant cavernous hemangioma	4/Girl	Severe coughing	Anterior mediastinum/ 13 × 13 × 7 cm	None	Dead
The current study		Cavernous hemangioma in the right CPA	38/F	Intermittent cough, dull aching chest pain and sporadic palpitation	Anterior mediastinum /4.5 × 5.2 × 4.6 cm	VATS, Complete excision	Alive, with no recurrence after five months

Abbreviations: CPA, cardiophrenic angle; SVC, superior vena cava; VATS, video-assisted thoracoscopic surgery.

cal approach should be obtained by thoracotomy or sternotomy (2, 3, 7, 10, 12). However, the VATS is justified in the case of small, limited vascular lesions in the mediastinum as found in the present case. The VATS has also been used for the excision of hemangiomas located in the middle mediastinum (4, 11) or posterior mediastinum (9), thus avoiding late functional complications and/or morbidity associated with large thoracotomy incisions. The prognosis of cavernous hemangioma after resection is usually favorable. At a five-month follow-up, the present patient had no clinical symptoms or recurrence.

3.1. Conclusions

We reported a rare case of cavernous hemangioma located in the right CPA that was definitively diagnosed after surgery. We also reviewed the previously reported cases in the literature. Our case had four atypical features, including atypical location, non-enhancement in enhanced CT scan, the presence of fatty ingredients, and the absence of phlebolith. This study presents three important findings. First, cavernous hemangioma must be considered in the differential diagnosis of anterior mediastinal tumors, although the preoperative diagnosis of these tumors is often difficult. Second, it is important to keep in mind that a small number of tumors can present with atypical CT findings, that is, non-enhancement and absence of phlebolith. Third, anterior mediastinal cavernous hemangioma resection using VATS would be a better option for small non-infiltrative lesions. There are also some defects in this report. First, no three-dimensional reconstruction of CT images was performed, which would well display the relationship between lesions and surrounding tissues, vessels, and organs. Second, the figures for the operation are not provided for personal privacy reasons.

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Footnotes

Conflict of Interests: The authors declare that they have no competing interests.

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