

## Case Report

# Epithelioid angiosarcoma of the mediastinum: a case report and literature review

Yuanzhou He, Ying Zhou, Min Xie, Xiansheng Liu

*Department of Respiratory Diseases, Tongji Hospital, Key Lab of Pulmonary Diseases of Health Ministry, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430000, China*

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**Abstract:** Epithelioid angiosarcoma (EA) is an infrequent malignant tumor that has been reported in multiple organs and tissues, including the spleen, kidney, skin, soft tissues, breast, and bones, and reports of mediastinal localization are extremely rare. Herein, a case study is presented of EA in the mediastinum that metastasized to the lungs in a 44-year-old male who presented with hemoptysis. A chest computed tomography scan revealed anterior mediastinal carcinoma with multiple bilateral pulmonary metastases. A needle biopsy of the mediastinum was performed, and histological examination of the specimens showed pleomorphic epithelioid cells with vesicular nuclei, prominent nucleoli, and eosinophilic cytoplasm that lined irregular vascular spaces. In addition, immunohistochemical staining revealed that the tumor cells were positive for CD31, CD34, and vimentin. Based on the histopathological and immunohistochemical findings, the patient was diagnosed with EA. The patient subsequently refused chemotherapy and radiotherapy and succumbed to the disease after one month of follow-up. This case indicates that an early, accurate diagnosis of this disease may improve EA treatment outcomes.

**Keywords:** Epithelioid angiosarcoma, mediastinal, pulmonary metastases

## Introduction

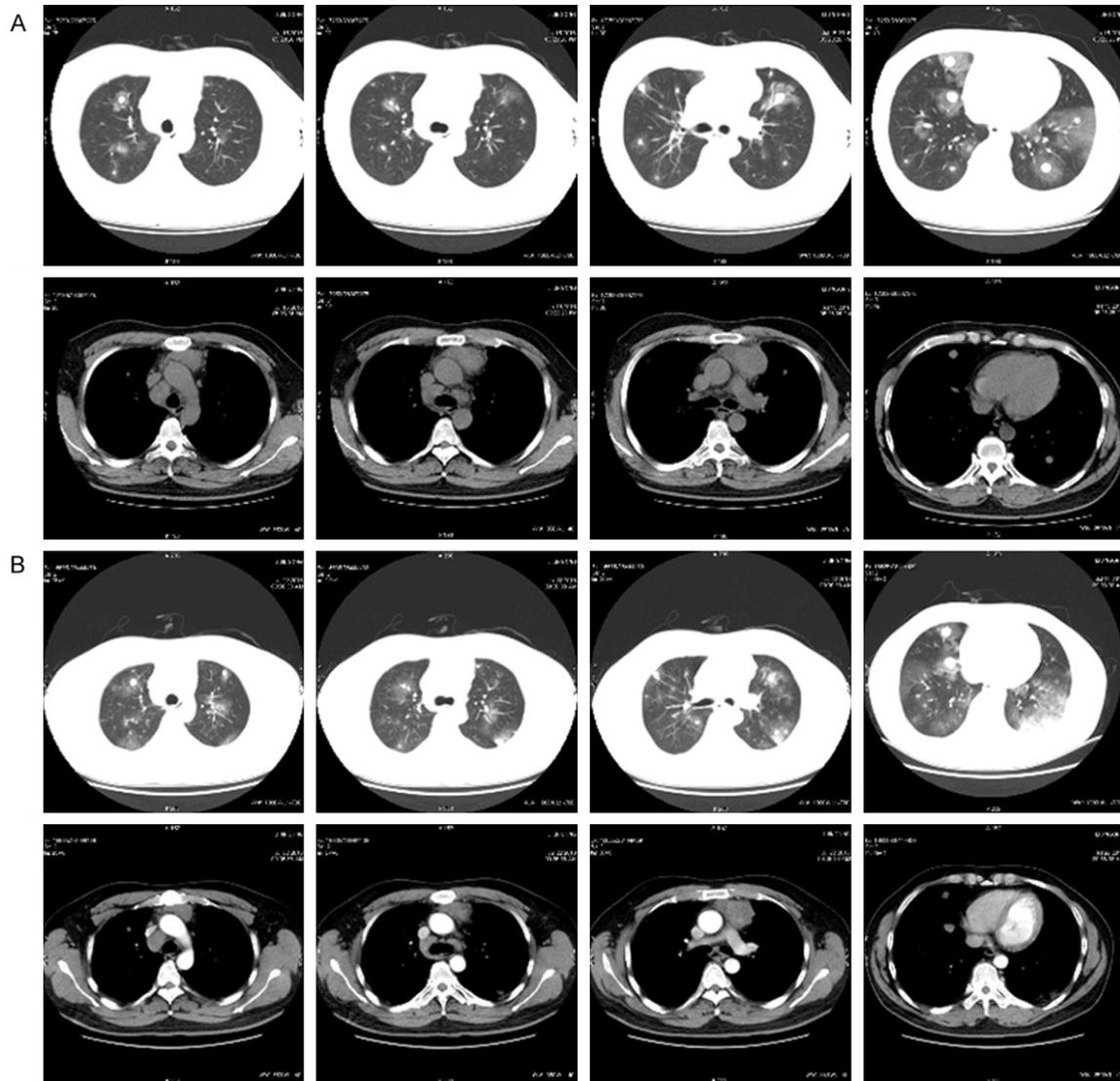
Epithelioid angiosarcoma (EA) is a rare sarcoma that arises from the endothelial cells of small blood vessels and may occur in various organs, including the spleen, kidney, skin, soft tissues, pleura, breast, and bones [1]. As a result, diagnosis of EA remains difficult due to the rarity of morbidity and diversity in clinical manifestations. In addition, EA has a male predilection and has the highest incidence in the seventh decade of life. Furthermore, an early diagnosis and treatment with chemo- and radiotherapy improves long-term survival [2]. Therefore, it is crucial to identify an early, accurate diagnosis of this disease. Although radiological studies may provide assistance in the diagnosis and assessment of the prognosis of the disease, pathological examination is the gold standard for diagnosis [3]. Primary EA of the mediastinum is an extremely rare malignancy. In addition to reviewing the relevant literature, the case of a 44-year-old Chinese male diagnosed with primary EA of the mediastinum is reported

here. Written informed consent was obtained from the patient's family.

## Case report

A 44-year-old male was referred to the Affiliated Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology in 2018 (Wuhan, China) for further evaluation of hemoptysis. The patient did not display any fever, night sweats, chest pain, or wheezing. Symptoms worsened one week before admission. The patient had a 10-year history of smoking with no cessation. The patient had no significant medical history and no familial history of genetic disorders or cancers. No other symptoms were noted during a physical examination. Chest computed tomography (CT) revealed a very large anterior mediastinal soft tissue mass and multiple lymph node enlargements, with multiple bilateral pulmonary metastases (multiple ground-glass foci in both lungs) (**Figure 1**). Initially, a percutaneous CT-guided needle biopsy was performed. Histopathological examina-

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**Figure 1.** Radiographs showing. A. Chest computed tomography (CT) revealed a very large anterior mediastinal soft tissue mass and multiple lymph node enlargement, with bilateral pulmonary multiple metastases. B. Contrast-enhanced computed tomography was confirmed.

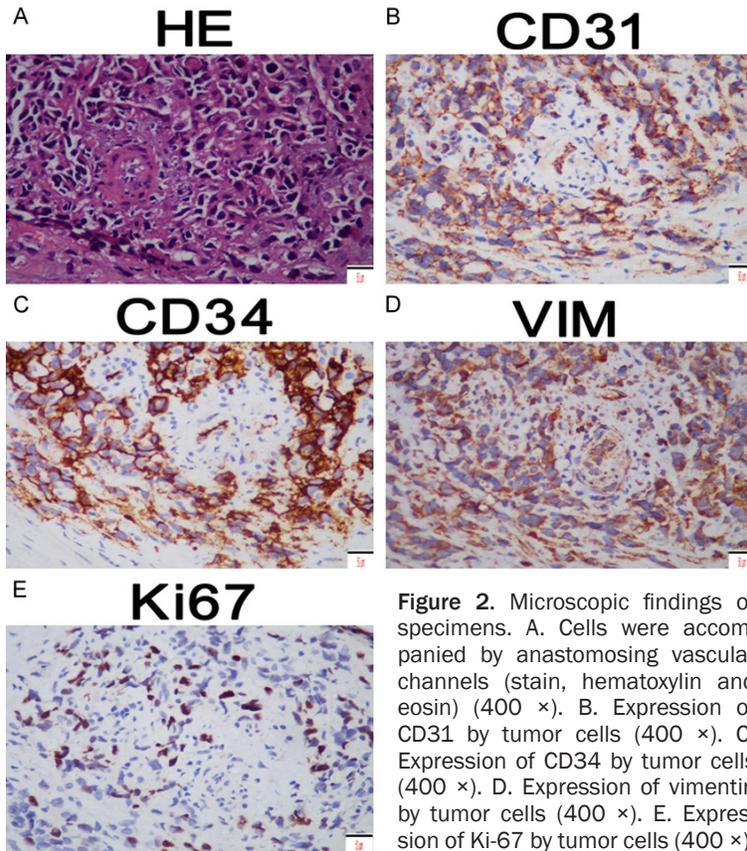
tion revealed pleomorphic epithelioid cells with vesicular nuclei, prominent nucleoli and eosinophilic cytoplasm that lined irregular vascular spaces. In addition, immunohistochemical staining revealed that the tumor cells were positive for vascular and stromal markers [cluster of differentiation (CD) 31, CD34 and vimentin] and negative for PCK, EMA, CK8/18, CK19, CK5/6, P40, CK7, TTF-1, napsin A, CDX-2, villin and CD117. Staining for Ki-67 was 60% (Figure 2), confirming the highly proliferative nature of these neoplasms. Thus, the overall immunohistochemical findings supported the diagnosis of EA. Therefore, the recommendation was that the patient undergo treatment with chemo- and

radiotherapy. However, the patient refused, and the patient's general condition worsened rapidly. Finally, the patient died 1 month after follow-up.

### Discussion

Angiosarcoma is an extremely rare and heterogeneous malignant tumor. The major presentations of this highly differentiated sarcoma were malignant proliferation of vascular cells and malignant transformation of epithelioid cells. However, the typical structure of the vascular lumen samples almost disappeared. Phenotypic diversity, papillary hyperplasia, and the ma-

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**Figure 2.** Microscopic findings of specimens. A. Cells were accompanied by anastomosing vascular channels (stain, hematoxylin and eosin) (400 ×). B. Expression of CD31 by tumor cells (400 ×). C. Expression of CD34 by tumor cells (400 ×). D. Expression of vimentin by tumor cells (400 ×). E. Expression of Ki-67 by tumor cells (400 ×).

lignant proliferation of epithelioid and plasma cells are relatively common in poorly differentiated sarcoma. EA normally presents with undifferentiated malignant epithelioid cells that infiltrate the main features of the structure of the vascular lumen, which produces many cytokeratin and epithelial membrane antigens [4]. It has been reported that the cytokeratin is expressed in more than 50% of EA cases, but tumors that undergo transformation can also activate the expression of cytokeratin, which greatly complicates the pathology for the diagnosis of the disease [5]. Additionally, atypical epithelial membrane antigens used in the diagnosis of the disease are not reliable [6].

EA is a special type of angiosarcoma that is characterized by epithelioid cells. The disease is rare, mostly affecting elderly male patients, with rapid progression, easy metastasis and a poor prognosis. The etiology is unknown and may be closely related to iodine metabolism abnormalities, use of glucocorticoids, radiotherapy and arsenic exposure [7, 8]. The disease mainly occurs in soft tissues, such as the deep peritoneum of the extremities [9]. It can also

occur in the thyroid and adrenal glands and the gallbladder, liver, spleen, lungs, and other organs. However, it is rare in the mediastinum.

The clinical manifestations of EA of the mediastinum are not specific. The symptoms include cough, shortness of breath, and early metastasis. Other nonspecific features, such as chest pain, fever, progressive wasting, and fatigue, are also less common. In this case, pulmonary metastasis occurred early, hemoptysis was a prominent clinical symptom, and other relatively specific clinical manifestations did not appear in the early stage. The imaging assessment of the tumor also varied, which was characterized by a solid and cystic or solid signal. There are no specific imaging characteristics and EA is very difficult to distinguish from other diseases in the mediastinum, contributing

to its diagnostic difficulties. Other studies have indicated that a change in the T2 signal weight in MRI is an indirect way to detect tumor origin in blood vessels, and it has a certain role in the diagnosis of the disease [10]. PETCT can provide an early indication of its malignancy, although it does not provide an accurate diagnosis of the disease.

Pathological changes and immunohistochemistry alterations are the primary indicators in the diagnosis of EA. The overall pathologic features are sponge-like soft tissue masses, hemorrhage, and an unclear tumor boundary. Microscopically, the morphological diversity of EA cells present as nest-like, flake-like or funicular. The cells are large with abundant cytoplasm; they have a clear nuclear center that contains mitotic figures and are porous and pleomorphic. The cytoplasm is mainly eosinophilic. However, some of the cytoplasm is hyperchromatic, and a small amount is basophilic, and the cell membrane boundary is not clear [11]. Additionally, necrosis of tumor cells, infiltration of inflammatory cells, and formation of fibroblasts can be observed. Typical angiosarcomas are

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composed of focal epithelioid cells. However, EA is almost entirely composed of epithelioid cells and vascular differentiation is rare, which also causes difficulty in the pathologic diagnosis. Immunohistochemistry is particularly important for the diagnosis of EA. Although the waveform protein is not specific, its sensitivity is high, which indicates that almost all angiosarcomas are positive with immunohistochemical analysis. Other common antibody markers are CD31 and CD34, which are thought to be markers of the origin of epithelioid cells. CD31 is not only specific but also highly sensitive, and the positive expression of CD31 is above 90% in all angiosarcomas [12]. The specificity of CD34 is slightly less than that of CD31, but the sensitivity in angiosarcoma is higher, and the positive expression rate is more than 90%, which is also found in other soft tissue tumors [13]. In this report, the vascular cavity in the tumor tissue was highly irregular, cell differentiation was extremely poor, and the nuclear fission was significant; waveform protein, CD31 and CD34 were all positive (**Figure 2**).

The morphology of EA is similar to that of clear cell sarcoma, epithelioid sarcoma and synovial sarcoma, which often causes misdiagnosis. Some forms are confused with metastatic carcinoma, Kaposi sarcoma and other sarcomas with epithelioid morphology [14]. Additionally, EA is easy to confuse with epithelioid hemangioendothelioma, melanoma and epithelioid sarcomatoid hemangioendothelioma. Compared with EA, epithelioid hemangioendothelioma is a low to moderate malignant tumor that often presents in younger patients and has higher vascular differentiation, a smaller nucleus, lighter nuclear fission and heterogeneity. Moreover, it easily forms lesions with clear boundaries, which may be accompanied by a large number of eosinophil infiltrations that rarely occur before transformation and immunohistochemical analyses of CD31, CD34, and FLI-1 are positive [15]. Malignant melanoma of the mediastinum is indistinguishable from EA. However, melanoma cell cytoplasm is more transparent and arranged in ground-glass opacity nodules, and it can be observed with acidophilus red dye. Visible cytoplasm outside or inside of the cytoplasmic melanin particles is a typical malformation in the lumen area, and the immunohistochemical staining of S-100 and HMB-45 are helpful in the diagnosis of mela-

noma [16, 17]. Epithelioid sarcomatoid hemangioendothelioma is also an angiogenic tumor but is less malignant than EA. It is full fusiform or circular and contains nucleoli, and nuclear fission is visible but relatively rare. The tumor often forms as nest-like, flake-like, or funicular. Furthermore, the original vascular structure of the epithelioid tumor cell lining is typical, and immunohistochemical CD34 is often negative for identification [18].

The malignancy degree of EA is extremely high. Systemic metastasis can occur in the early stage and the prognosis is extremely poor. Due to the atypical symptoms, there are often many other areas of metastasis at the time of diagnosis. Currently, there is no unified treatment plan for the disease, with the current treatment mainly including surgery, radiotherapy, chemotherapy, or comprehensive treatment. The targeted therapy of antiangiogenic genes is promising for the treatment of these patients. However, the overall effects are poor [19]. The prognosis depends on the size, the degree of differentiation, and the presence of metastasis of tumor cells. In this case study, it was found that a metastatic lesion with multiple lung metastases had formed with obvious cachexia, and the patient died after one month of follow-up.

### Conclusion

In summary, the present study reports a case of mediastinal EA and reviewed previous studies. Although these malignancies mostly occur elsewhere in the body, they may also occur in the mediastinum. Medical history collection, medical imaging and the identification of pathological features are conducive to an accurate diagnosis. Early, accurate diagnosis and active intervention is a reliable guarantee for improving the survival rate.

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### Disclosure of conflict of interest

None.

**Address correspondence to:** Xiansheng Liu, Department of Respiratory Diseases, Tongji Hospital, Key

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Lab of Pulmonary Diseases of Health Ministry, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430000, China. Tel: +862783663617; E-mail: doctorliu69@126.com

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