Epithelioid hemangioendothelioma of the right atrium invaded the superior vena cava: case report and review of literature

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Abstract
Epithelioid hemangioendothelioma (EHE) is a rare hemangioma that can occur anywhere in the body. It occurs most commonly in the liver and lungs, rarely from the heart, and the etiology or risk factors are unclear. So far, timely detection and radical resection is a more acceptable treatment. Reviewing the literature, few cases of cardiac EHE have been reported. We present a rare case of EHE of the right atrium invaded the superior vena cava.

Keywords Heart neoplasms · Epithelioid hemangioendothelioma · Tomography, X-ray computed · Magnetic resonance imaging

Abbreviations
EHE Epithelioid hemangioendothelioma
CT Computed tomography
MRI Magnetic resonance imaging
FLI-1 Friend leukemia integration 1

Introduction
Epithelioid hemangioendothelioma (EHE) is a rare low-grade malignant angiogenic tumor with local invasiveness and metastatic potential. EHE is a rare low-grade malignant angiogenic tumor with local invasiveness and metastatic potential. Clinically, EHE can occur simultaneously or sequentially in many parts, such as lung, liver, bone, soft tissue and other organs, and there is no obvious specificity in clinical symptoms. There are few case reports of EHE in the literature. We report a unique case of EHE of the right atrium invaded the superior vena cava and review of the literature.

Case report
A 54-year-old man had intermittent chest tightness for 49 years. There was no obvious inducement of facial and eyelid edema 2 months ago, and it was aggravated when he got up in the morning. However, physical examination found that the patient did not have dyspnea, hemoptysis, cyanosis, limb edema, sensory abnormalities and other symptoms. There is no previous history of surgery or other diseases. Laboratory examination showed that hemoglobin 115.0 g/L, erythrocyte 3.63 × 1012, 24-h urine protein and tumor markers were not abnormal.

After admission, the cardiac function of the patient was examined. First, echocardiography showed that the right atrium near the entrance of the superior vena cava could be hypoechoically attached to the heart wall, with an area of about 22 mm × 16 mm (Fig. 1a). The fluid dark area was detected in the pericardium. Ultrasound doctors considered the formation of emboli extending from the right atrium to the entrance of the inferior vena cava. Subsequently, the patient underwent cardiac magnetic resonance imaging, showing a massive low-signal shadow in the right atrium on the trufu sequence (Fig. 1b). The right atrium was small and the right ventricle was large, so delayed contrast-enhanced scan was performed 2 h later. After intravenous injection of contrast medium, the lesions in the superior vena cava near the heart and adjacent right atrium showed mild enhancement (Fig. 1c), multiple nodular mild to moderate enhancement foci could be seen in the mediastinum, and a small or moderate amount of effusion could be seen in the pericardial...
cavity. Dr. MRI considered the mass in the proximal end of the superior vena cava and adjacent right atrium. Further CT examination showed patchy low density shadow in right atrium and superior vena cava (Fig. 1d), inhomogeneous and moderate enhancement of the low-density shadow in the right atrium (white arrow). e The delayed contrast-enhanced sequence of cardiac magnetic resonance imaging showed that the lesions were slightly enhanced in mass (white arrow). f The re-formatted multiple planar reformation image showing invasive lesions of the superior vena cava (white arrow). g The size of the tumor was about 6.5 cm × 3.0 cm × 2.5 cm and the capsule was intact. h The tumor cells in the tissue were epithelioid, the atypia was not obvious, and mitosis was rare. Vacuoles of different sizes were seen in the eosinophilic cytoplasm, forming a vascular cavity-like structure.

Discussion

Primary cardiac tumors are very rare, about 20–30% are malignant tumors [1]. Epithelioid hemangioendothelioma (EHE) is a rare hemangioma originating from vascular endothelial cells or pre-endothelial cells, first described by Weiss and Enzinger in 1982 [2]. Its biological behavior is between benign hemangiomia and malignant angiosarcoma, and it has local invasiveness and metastatic potential. Metastases (lung, lymph nodes, liver, bones, retroperitoneum, soft tissues) and death can occur in about 25 and 15% of EHE, respectively [3]. In the new WHO classification in 2002, this tumor was classified as a malignant vascular tumor in soft tissue tumors and classified as a low-grade malignant angiogenic tumor [4]. It is reported that EHE originates from almost every organ system, including lung, liver, bone, soft tissue, limbs, spleen and other organs, but rarely occurs in the heart. The cause is not clear and may be related to trauma, radiotherapy and hormone levels [5].

An extensive literature search was performed on PubMed databases using the keyword Epithelioid hemangioendothelioma and heart. The reference lists of all retrieved studies were scrutinized for additional articles to supplement the search result. All the duplicates articles were excluded. To our knowledge there have been 22 cases of Epithelioid hemangioendothelioma of the heart in the English literature. These are summarized in Table 1. Most of the studies are case reports, and the clinical symptoms of this kind of tumor with unknown etiology have no obvious specificity, which mainly depends on the location and size of the tumor. If it occurs in the heart, it may show respiratory distress, hemoptysis, palpitations, chest pain, or no obvious manifestation. It can occur in any part of the heart, of which the right atrium is the most common site of. The mean age in the reported case reports was 45 years (range 2 months–77 years), there is no significant gender difference.

EHE has unique histological, immunohistochemical and molecular characteristics. Histologically, round or polygonal endothelial cells were arranged in nests and cords. The cytoplasm of tumor cells is usually rich in eosinophilic hyaline and the presence of cytoplasmic vacuoles and vesicular nuclei. Immunohistochemistry is also useful in contributing to the diagnosis. The vascular nature of EHE is identified by Friend leukemia integration 1 transcription factor (FLI-1), which is a transcription factor, expressed in endothelial cells [6]. CD34 is expressed in more than 90% of vascular tumors, so although it is relatively sensitive, it is not very specific to EHE. In contrast, CD31 is a more specific vascular tumor marker, so some scholars recommend immunohistochemical staining combined with CD31, ERG, FLI-1 as an important index for the diagnosis of EHE. CD31[7], ERG and FLI-1 are all positive in our patient.
Table 1  Clinical and pathological characteristics and management of cardiac EHE

| Sr.no. | Author (year) | Age (year) | Sex | Camber | Size (cm) | Presenting symptoms | Recurrence | Final therapy | Follow up |
|--------|---------------|------------|-----|--------|-----------|---------------------|------------|---------------|-----------|
| 1      | Rosai et al. [9] (1979) | 25 | M | Left atrium | None | Rheumatic heart disease with mitral valve stenosis | None | Resection | Survived |
| 2      | Hayward et al. [10] (1979) | 49 | F | Mitral valve, PML chorda | NA | Diastolic murmur | NA | Resection | Survived |
| 3      | Kuo et al. [11] (1985) | 65 | M | Left atrium | None | Recalcitrant pruritus | None | Resection | Survived |
| 4      | Singal et al. [12] (1987) | 19 | F | Left atrium | $4 \times 4 \times 5$ | Heart murmur | None | Resection | Liver metastasis |
| 5      | Montes et al. [13] (1991) | 56 | F | Right ventricle | $8 \times 5 \times 4$ | Pulmonary stenosis | None | Resection | Pulmonary metastasis (4 months) |
| 6      | Marchiano et al. [14] (1993) | 71 | F | Left atrium | $5.5 \times 4.5 \times 3.5$ | Palpitations, dizziness | None | Resection | Buttock metastasis (4 months) |
| 7      | Bille et al. [10] (1993) | 59 | M | Aortic valve | 0.5 | Cerebral infarction | NA | Resection | NA |
| 8      | Biasi et al. [15] (1995) | 35 | M | Right ventricular | $2 \times 3.5$ | Moderate mitral regurgitation | None | Resection | Survived |
| 9      | Bisesi et al. [16] (1996) | 12 | F | Right atrium | None | Hemothysis | None | Conservative | NA |
| 10     | Agaimy et al. [17] (2002) | 68 | M | Right ventricle | 0.8 | Incidentally discovered on autopsy | NA | Resection | NA |
| 11     | Tansel et al. [18] (2005) | 2 months | F | Left atrium | None | Respiratory distress | None | Resection | Survived |
| 12     | Kitamura et al. [10] (2005) | 36 | F | Right atrium | $12 \times 11$ | Cough, lung edema | None | Resection | Survived |
| 13     | Val-Bernal et al. [19] (2005) | 69 | F | Left ventricle | 0.4 | Incidentally discovered on echocardiogram | None | Resection | Survived |
| 14     | Moulai et al. [10] (2006) | 53 | M | Cardiac mass invading | NA | Incidentally discovered on echocardiogram | None | Chemotherapy | Survived |
| 15     | Safirstein et al. [5] (2007) | 51 | F | Right atrium | $5 \times 4 \times 4$ | Incidentally discovered on echocardiogram | None | Resection | Survived |
| 16     | Lisy et al. [20] (2007) | 61 | M | Left atrium | 4.2 | Incidentally discovered on computed tomography | None | Resection | Survived |
| 17     | Messias et al. [10] (2008) | 21 | F | Left atrium | $3.9 \times 2.7$ | Chest pain | None | Resection | Survived |
| 18     | Sugimoto et al. [10] (2013) | 77 | F | Right atrium | 2.5 | Incidentally discovered on echocardiogram | None | Resection | Survived |
| 19     | Allain et al. [21] (2014) | 35 | M | Right atrium | $6 \times 7 \times 11$ | Rapidly progressive dyspnea | None | Resection | Survived |
The imaging findings of cardiac EHE were not specific. Our patient’s EHE was located in the right atrium, part of the tumor grew upward to the vena cava, CT plain scan showed patchy low density, and enhanced scan showed inhomogeneous and moderate enhancement. Multiple lymph nodes and spotted calcification could be seen in the mediastinum; MRI showed mass iso-T1 and slightly short T2 signal intensity, delayed enhancement showed mild enhancement, and multiple nodular mild to moderate enhancement lesions in the mediastinum. Before operation, the imaging diagnosis was misdiagnosed as thrombus formation in the right atrium and superior vena cava, but in this case, the density of the filling defect was uneven and there was enhancement, and there were no blood vessels in the thrombus, so the possibility of the tumor should be considered. and multiple spots of calcification can be seen in the mediastinum, indicating that the mass invades the mediastinum, but the thrombus will not invade the mediastinum.

At present, surgical treatment is the main treatment of cardiac EHE. Some chemotherapeutic drugs and radiotherapy regimens have been reported in affected patients, but there are no significant therapeutic benefits. Because the sensitivity of the heart to radiation injury, resulting in cardiomyopathy or chronic pericarditis at therapeutic dosages, limits the benefits of radiotherapy.

The prognosis of cardiac epithelioid hemangioendothelioma is unpredictable. the tumor may stop growing, or it may recur and metastasize. Clinical symptoms, tumor lymphatic vessel spread, distant organ metastasis and peripheral lymph node lesions have all been shown to be associated with poor prognosis [8]. After discharge, patients still need long-term follow-up to monitor for distant metastasis or recurrence. In the review of the literature, postoperative metastasis was reported in 4 cases. Our patients survived disease-free for a long time and were followed up for 15 months without recurrence or metastasis. We cannot rule out the possibility of recurrence of this kind of tumor in the future, because delayed recurrence may occur in EHE after many years.

Conclusion

In summary, Cardiac EHE is rare and the prognosis and clinical behavior are uncertain. Long-term follow-up of patients after discharge is necessary in order to more accurately evaluation the prognosis of cardiac EHE. We present the case report of the right atrium invaded the superior vena cava. In our patient, was effectively treated with surgery management and in concordance with the available literature.

Author contributions Conceived and designed the experiments: WH; analyzed the data: WH, LL, and JG; wrote the paper: WH. All authors read and approved the final manuscript.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration, and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from the patient before enrollment in the study.

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Table 1 (continued)

| Sr.no. | Author (year)   | Age (year) | Sex | Camber         | Size (cm) | Presenting symptoms                  | Recurrence | Final therapy | Follow up                  |
|--------|----------------|------------|-----|----------------|-----------|--------------------------------------|------------|---------------|---------------------------|
| 20     | Ellouze et al. [10] (2015) | 53         | M   | Right atrium   | 2.7 × 2.8 | Chest pain and palpitation            | None       | Resection     | Pulmonary metastasis (10 months) |
| 21     | Patel et al. [22] (2018)    | 49         | M   | Right atrium   | 4 × 4     | Syncope                              | None       | Resection     | NA                         |
| 22     | Wu et al. [23] (2019)       | 32         | M   | Right atrium   | 4.1 × 5.9 | Palpitations, chest tightness and chest pain | None       | Resection     | Survived                  |
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