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The First Case of Composite Hemangioendothelioma in The Heart

Xiao-Jie Zhang, MD,[1] Shi-Qiang Wang, MD,[1] Mei Jin, MD[2]

[1]Department of Cardiovascular Surgery, Sir Run Run Shaw Hospital Affiliated to Medical College of Zhejiang University, Zhejiang, China;
[2]Department of Pathology, Sir Run Run Shaw Hospital Affiliated to Medical College of Zhejiang University, Zhejiang, China

ABSTRACT

Composite hemangioendothelioma (CHE) is an extremely rare vascular neoplasm that is characterized by an admixture of benign, low-grade malignant, and malignant vascular components. It is usually located superficially in the dermis and subcutis of the extremities, and other sites involved include the head and neck region, oral mucosa, and viscera of the kidney and spleen. CHE has a low-grade malignant potential because it is locally aggressive. Here, we report a case of CHE in the heart in a 46-year-old man, who presented with a palpable mass arising from his right ventricle. Echocardiogram imaging revealed a 13.3 × 14.2 mm mass with high-signal intensity. Excision was performed, and microscopic examination revealed a heterogeneous mixture of vascular components, consisting of spindle-cell hemangioma, retiform hemangioendothelioma, and epithelioid-like hemangioendothelioma areas. To our knowledge, this is the first report on the behavior of this distinctive vascular neoplasm occurring in the right ventricle. Due to the unclear biological behavior of CHE in the heart and the paucity of cases, no further therapy was undertaken despite the risk of local recurrence and distant metastasis. The result of a six-month follow-up after surgery was disease-free.

INTRODUCTION

Composite hemangioendothelioma (CHE) is a rare vascular tumor morphologically comprising several distinct components, and it exhibits borderline malignant potential. It most commonly occurs in the distal extremities. CHE in the heart has not been reported before. We report CHE of the right ventricle in a patient who was identified incidentally. This report was approved by the local research ethics board. Written informed consent was obtained from this patient.

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Correspondence: Xiao-Jie Zhang, MD, No.3 Qingchun Rd. Hangzhou, Zhejiang Province, China, 310013 (e-mail: drzhangxiaojie@zju.edu.cn).

CASE REPORT

A 46-year-old male was admitted for excision of a right ventricular mass. He had gone to a local hospital, due to prior pain from kidney stones. As part of his preoperative screening, he had undergone a transthoracic echocardiogram, which showed evidence of a right ventricular mass. He had no history of congenital or valve heart disease, primary cardiac tumor, alcohol or drug abuse, hypertension, myocardial infarction, or atherosclerotic heart disease. He denied fever, chills, weight loss, nausea or vomiting, dyspnea, chest pain, or palpitations. Physical examination yielded unremarkable results. An electrocardiogram showed normal sinus rhythm without ST–T wave changes. An echocardiogram revealed normal left and right ventricular systolic functions, normal chamber sizes, and normal wall thickness, as well as the presence of a right ventricular mass interpreted as myxoma versus papillary elastic fibroma. A computed tomography scan confirmed that a primary tumor that might result in cardiac metastasis yielded negative results and revealed no cardiac abnormalities. Intraoperative transesophageal echocardiogram showed a mobile mass (13.3 × 14.2 mm) adjacent to the tricuspid valve orifice that did not originate from and also did not interfere with the tricuspid valve.

The patient underwent surgery. A median sternotomy was performed, and cardiopulmonary bypass was instituted via aortic and bicaval cannulation. Myocardial protection was achieved by anterograde administration of the Del Nido cardioplegic solution. After aortic cross-clamping, the right atrium was opened. The mass was found under the tricuspid valve orifice in the right ventricle. It was an oval lesion measuring 2×1.2×0.5 cm and was in the free wall of the right ventricle. There were no obvious ischemic changes in the myocardium. The entire tumor was resected, and the pericardium patch was used to repair the endocardium. Aortic cross-clamping time was 74 min, and cardiopulmonary bypass was 95 min. The postoperative course was uneventful, and the patient was discharged on the seventh postoperative day. The final pathology report revealed a CHE. Histologically, on gross examination, the polypoid cystic mass with a smooth bosselated external surface attached to a 1.0×1.0×0.5cm stalk. The cut surface of the tumor showed thin-walled blood-filled spaces 0.5 cm in diameter, separated by areas of firm, white, focally edematous, solid tissues. Microscopically, it is typical of spongy angiogenesis with short cords and nested epithelioid endothelial cells. Endothelial cells frequently have an epithelioid appearance with abundant eosinophilic cytoplasm and intracytoplasmic vacuoles, some of which contain broken

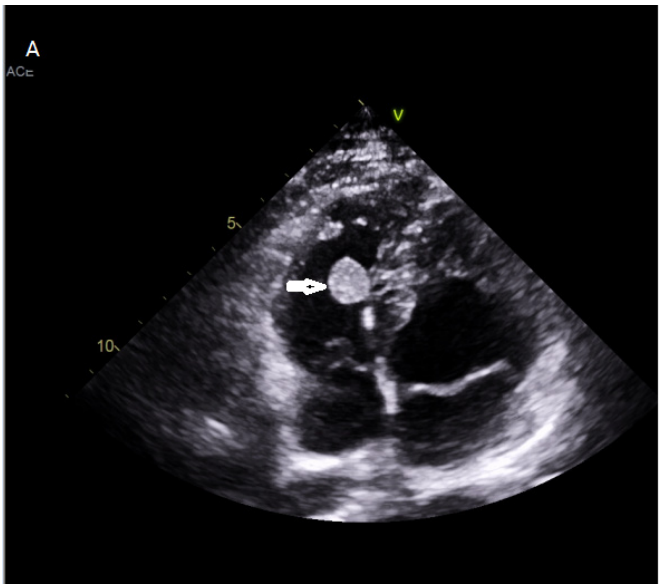

Figure 1. A) Echo showed the mass in the right ventricle.

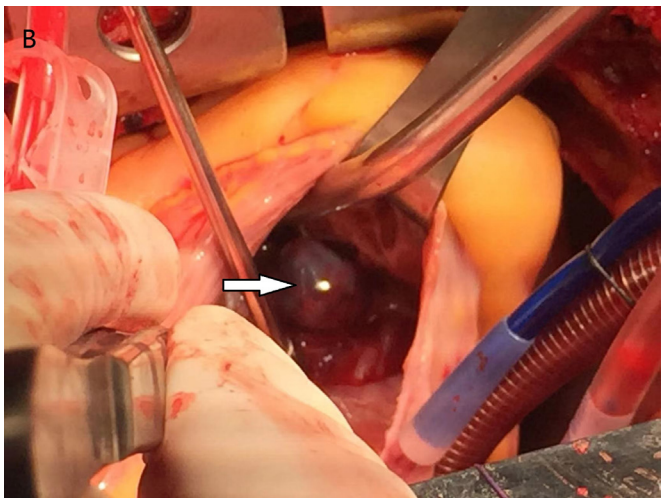

Figure 1. B) The tumor was in the right ventricle

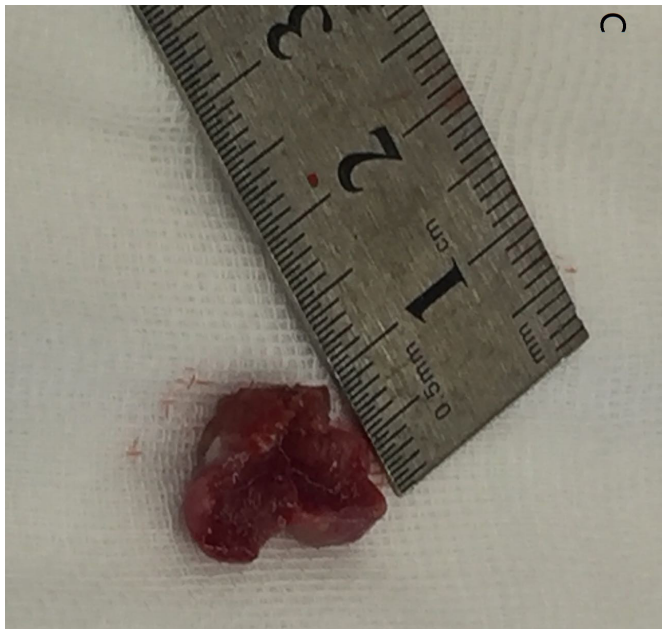

Figure 1. C) Gross appearance of the cut surface of the tumor of the right ventricle

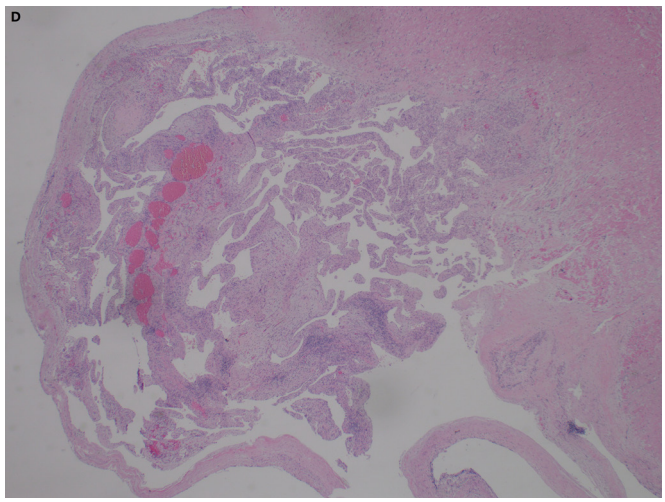

Figure 1. D) Microscopically, the tumor was typical of spongy angiogenesis

red blood cells. Nuclear atypia and mitotic activity were absent, and there was no evidence of necrosis. An inflammatory infiltration, composed of lymphocytes, surrounded the tumor. Immunohistochemically, CD34 and ERG were positive in the tumor cells. Ki-67 was slightly expressed in the tumor lesion. No local recurrence or metastasis was found during 6 months of follow-up after the operation.

DISCUSSION

CHE is a very rare vascular tumor classified as a moderately differentiated borderline vascular tumor, according to the World Health Organization (WHO) classification, which was first described by Nayler et al. [Nayler 2000]. Its poorly defined lesions usually are solitary and less frequently multiple [Bhat 2016]. Benign, neutral, and malignant components are histologically mixed with each other, as in our case, making it difficult to identify those components. So far, fewer than 60 clinical cases have been reported [Li 2021]. It commonly has occurred as long-standing lesions in the dermis and subcutis of the extremities but also increasingly has been reported at other sites, including the oral cavity, mediastinum, manubrium sterni, and in viscera such as the kidney and spleen [Chen 2012]. In the present case, it was a primary tumor in the right ventricle, which was rare and never reported before, suggesting that CHE may affect a wider range of body locations than previously reported. The age of patients diagnosed

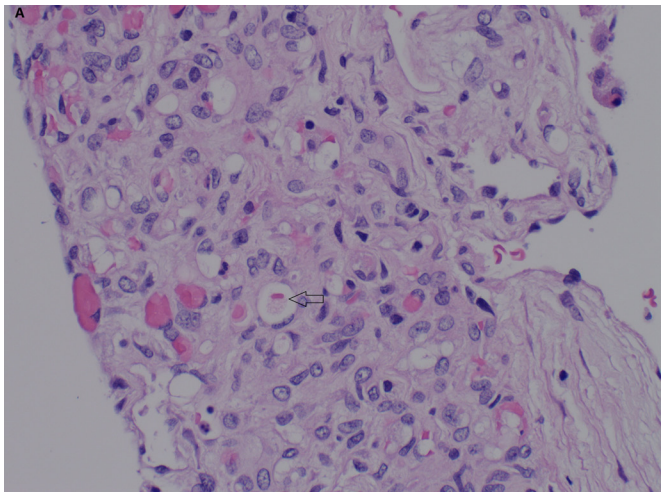

Figure 2. A) Hematoxylin and eosin staining demonstrated epithelioid endothelial cell of the tumor (original magnification, ×400)

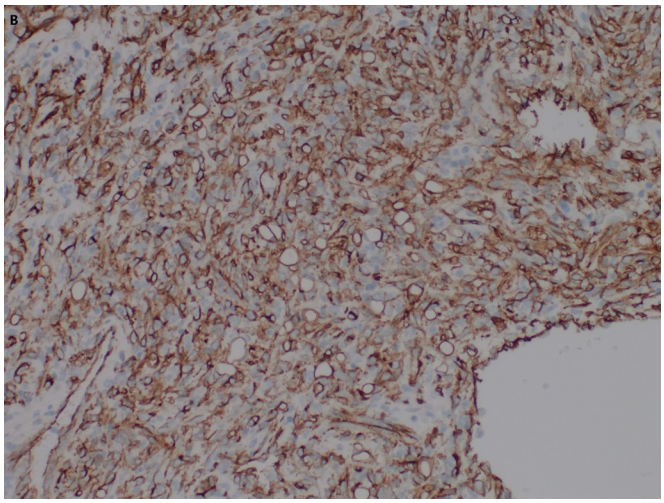

Figure 2. B) Immunohistochemical analysis demonstrated that the endothelial cells and epithelioid endothelial cells of the tumor were positively stained for CD34 (original magnification, x 400)

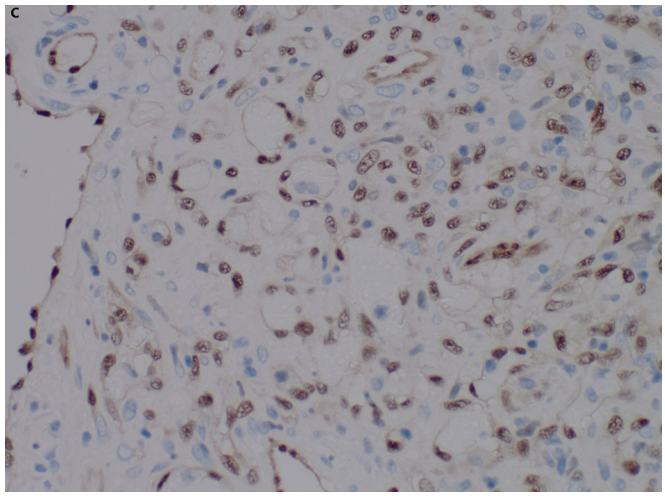

Figure 2. C) Immunohistochemical analysis demonstrated that the endothelial cells and epithelioid endothelial cells of the tumor were positively stained for ERG protein (x 400)

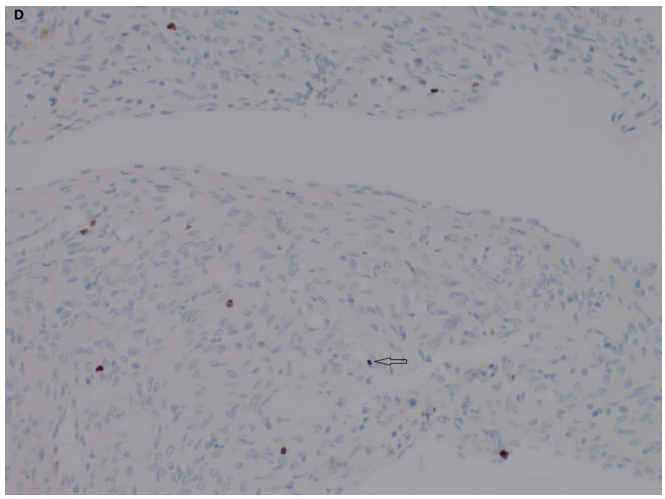

Figure 2. D) Immunohistochemical analysis demonstrated that the endothelial cells and epithelioid endothelial cells of the tumor were positively stained for Ki-67 (D) (original magnification, x 200)

with CHE varies widely from newborns to the elderly; it more commonly is seen in adults and is slightly more common in females [Bhat 2016].

Histologically, reticular HE is the most common intermediate component while the malignant component epithelioid HE is not uncommon [Tsai 2011]. Highly differentiated hemangiosarcomatoid or epithelioid hemangiosarcomatoid areas are also expressed in more than half of CHE cases [Rokni 2017]. In terms of immunohistochemistry, although vascular endothelial marker CD34 is occasionally negative or slightly expressed on tumor vascular endothelial cells, other markers such as CD31, ERG, and von Willebrand factor are highly expressed with specificity [Zhang 2013]. Recent literature suggests that some CHE rich in neuroendocrine markers may be more aggressive [Miyamoto 2021]. Hisaoka et al. found that the proliferative index based on staining with Ki-67 range is 0.1-14.9% by studying 12 spindle cell tumors [Hisaoka 1995]. In the present case, the proliferative index showed a low proliferative rate, while the tumor tissue was widely and strongly stained with ERG and membranous staining with CD34 which support an endothelial origin tumor.

In fact, CHE is very difficult to diagnose and often requires differentiation from other unique vascular tumors with different aggressions. Parts of these tumors can include spindle cell hemangioma, reticular HE, epithelioid HE, highly differentiated hemangiosarcoma, and epithelioid hemangiosarcoma. Therefore, a pathological examination is a key to CHE diagnosis and differential diagnosis. Due to the morphologic heterogeneity and complexity of CHE components, it often is necessary to take samples from multiple sites for pathological

examination. In our case, the pathological examination was misdiagnosed and later corrected. At present, in addition to an electron beam, interferon and radiotherapy, and chemotherapy, extensive surgical resection is the most common and effective treatment for CHE [Fasolis 2008]. So far, there have been no reports of CHE-related death [Leen 2015]. Relevant literature reports showed the local recurrence rate after surgery could be as high as over 50%, including those with local recurrence following extensive total resection and lymph node dissection, while the incidence of local lymph node or soft tissue metastasis or even distant metastasis was very rare [Zhang 2013; Aydingoz 2009]. The interval for local recurrence and metastasis ranges from a few months to more than 10 years [Aydingoz 2009]. Biagioli believed that the high risk of local recurrence of CHE was related to the multicentric origin of the tumor and incomplete surgical resection [Biagioli 2005]. Although it has been reported that adjuvant chemo- or radiotherapy has a role in preventing local recurrence and lymphatic metastasis of CHE, further verification is needed due to the unclear biological behavior of CHE and the paucity of cases [Mahmoudizad 2014]. CHE is the skin has a better prognosis than in other sites. In our case, CHE was in the right ventricle, which has not been reported before and the prognosis is unknown. Only marginal resection was performed instead of extensive total resection. Therefore, long-term strict follow-up observation is necessary even though the result of follow-up six months after surgery was disease-free.

CONCLUSION

In summary, CHE of the heart is an extremely rare vascular neoplasm that is moderately differentiated and carries low malignancy. Local surgical radical resection is effective in reducing local recurrence. Postoperative long-term follow-up observation is necessary, due to local recurrence and the aggressive nature of this tumor. Postoperative adjuvant radiotherapy or chemotherapy treatment remains to be further discussed.

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