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Case Report

Pericardiac angiosarcoma mistaken as constrictive pericarditis, with active treatment of surgery and chemotherapy, but poor prognosis

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Abstract: The incidence of pericardiac angiosarcoma is rare. Some cases have been reported of cardiac sarcomas in heart cavities but few are pericardiac angiosarcoma. Pericardiac angiosarcoma, as a kind of widespread malignancy, is difficult to diagnose and may be easily mistaken as constrictive pericarditis. Here we describe a case of pericardiac angiosarcoma where the patient underwent active treatment by surgery and chemotherapy but received poor prognosis. This is a clinical case of a 49-year-old male who suffered from a mass arising from the pericardium. The mass, regarded as constrictive pericarditis on the earlier days, had angiosarcoma features of positive immunohistochemical markers, such as CD31, CD34, Vimentin, and high Ki-67 labeling. After operation, the patient received two cycles of chemotherapy with Doxorubicin, Ifosfamide, and Mesna. Unfortunately, the patient died of multiple pulmonary metastases less than three months after the operation. In some way, cardiosurgery, radiation therapy, and chemotherapy might prolong survival but pericardiac angiosarcoma always presents rapid progression and death. Here our case confirms highly aggressive behavior and at least it is typical of both clinical and pathological features, which can be used for clinical reference.

Keywords: Pericardiac angiosarcoma, case report, serous carcinoma, immunohistochemistry

Introduction

Cardiac angiosarcomas are malignant tumors of mesenchymal origin with unclear etiology and are present in 0.0017%-0.033% of autopsy cases [1]. These tumors mostly occur in the third to fifth decade of life with male predominance [2]. Sometimes cardiac angiosarcomas can involve the pericardium. Primary pericardial angiosarcoma is extremely rare and few cases have been reported. The prognosis of patients with pericardial angiosarcoma is poor. It is an invasive malignancy showing early metastasis, rapid progression, and high relapse rate [3, 4]. Survival depends strictly on the stage of the disease at the time of diagnosis and the possibility of complete surgical excision [12]. Because of the inconspicuous symptoms for a long period at early stage, diagnosis of this kind of angiosarcoma is often delayed until the indicative symptoms of potential cardiac disease such as chest pain, fever, exertional dyspnea, syncope, arrhythmias and cardiac tamponade prompt the patients to seek medical treatment [13, 14]. So it's easily be mistaken as constrictive pericarditis. Sometimes it will present with recurrent pericardial effusion, hemorrhagic pleuropericarditis, cardiac tamponade, and thromboembolic phenomena [4-6]. The mean survival of pericardial angiosarcoma is 6-14 months, and few patients survive beyond 14 months. Early complete resection is recommended as the treatment choice [7, 8]. In our case, although active treatment of surgery and chemotherapy were undertaken, a poor outcome occurred.

Transthoracic or transesophageal echocardiography, CT scan, or PET-CT can be taken for preoperative detection [9, 10]. This kind of carcinoma is with cellular and nuclear features which include spindle or oval-sized cells, large and hyperchromatic nuclei. On immunohistochemical analysis, the tumor is often positive for CD31, CD34, and Vimentin. Although the cytologic abnormality can aid, the pathologic

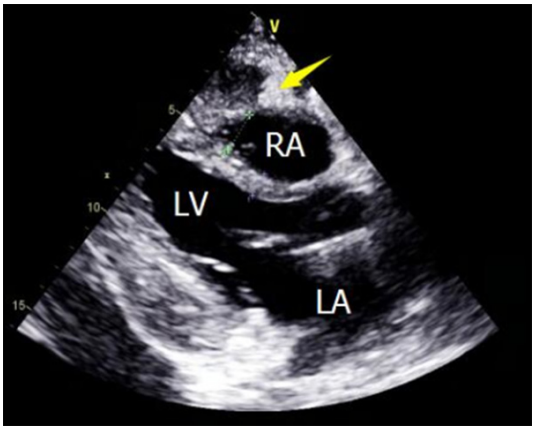

Figure 1. Transthoracic echocardiography showed bicuspid aortic valve with normal left ventricular (LV) dimensions and normal systolic function, cardiac and parietal pericardium were irregular thickening with the echo enhanced.

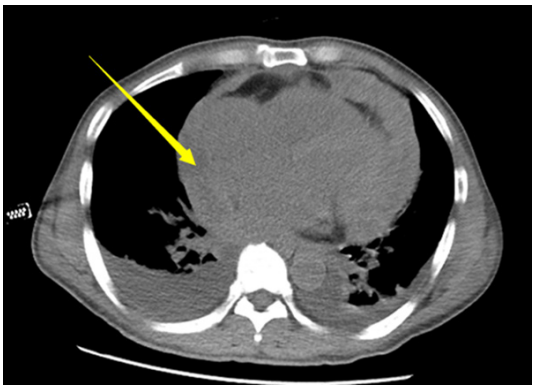

Figure 2. CT scan confirmed an uneven incrassate pericardium with encapsulated pleural effusion and enlarged mediastinal lymph nodes.

examination combined with immunohistochemical study is the main method to the diagnosis.

Clinical history

A 49-year-old male was admitted to our department with gradually increasing activity-related chest tightness and short breath for nearly 4 months on December 22, 2017. The patient's past medical history was remarkable and his family history was negative for malignancy and any other diseases. On chest physical examination, there was a Kussmaul's sign detectable on inspiration suggestive of an increased jugular venous pressure. The patient had tachycardia of 115 times per minute and normal blood pressure. Weakened cardiechema without murmurs or extra heart sounds was heard using a stethoscope. The pulse was feeble and weak.

Other physical examinations were essentially normal. Hematologic work-up revealed red blood count 3.45 × 1012/L; leukocyte count, 12.6 × 109/L; platelet count, 285 × 109/L. Normal urine routine test and stool routine test. Normal even the levels of the majority of the tumor markers: Carcinoembryonic antigen (CEA), cancer antigen (CA) 125 and CA199. Cardiac biomarkers: CTNT, 29.67 ng/L; myohemoglogin, 86.56 ng/mL; pro-bnp, 2020.0 pg/mL. The Eastern Cooperative Oncology Group (ECOG) performance status was 1.

He had initially been admitted to a primary care center, where constrictive pericarditis had been diagnosed. Because of persistent fever and gradually aggravated dyspnea, he was referred to our department. Transthoracic echocardiography showed bicuspid aortic valve with normal left ventricular (LV) dimensions and normal systolic function. LV end-diastolic and end-systolic diameters were 43 mm and 28 mm, respectively. Left ventricular ejection fraction was normal (65%). Cardiac and parietal pericardium were irregular, with thickening with the echo enhanced. The thickness of the left and right ventricular wall was about 8 mm. The inner diameter of each chamber was in the normal range (**Figure 1**). The interventricular septum and left ventricular posterior wall moved in the same direction with mitral inadequacy and tricuspid incompetence. No opaque dark area of fluid was seen in the pericardial cavity. Constrictive pericarditis was more likely to be the diagnosis according to the cardiac ultrasound.

CT scan confirmed an uneven incrassate pericardium with encapsulated pleural effusion and enlarged mediastinal lymph nodes (**Figure 2**). Bone and chest metastases were not confirmed according to the CT scan. The head CT was unremarkable. Superficial lymph node, urologic, and digestive system ultrasound were taken pre-operation and denied distant metastasis.

Partial pericardial stripping was optimally performed on December 30th, 2017. When the pericardium was opened, no hydropericardium was found. There was no unclear boundary between the thicken pericardium and the myo-

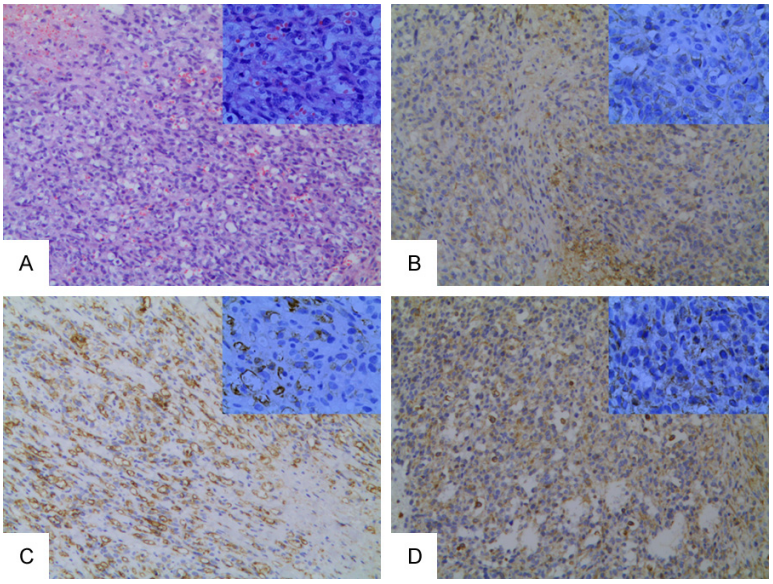

Figure 3. A. Microscopic examination showed the cells were short spindle, round to oval and polyhedral cells with irregular, well-formed, slit-like, or branched blood vessels. (original magnifications × 10 and × 40). B. On immunohistochemical analysis, the tumor had strong staining for CD31. (immunoperoxidase stain, original magnifications × 10 and × 40). C. Immunohistochemical analysis show strong staining for CD34 (immunoperoxidase stain, original magnifications × 10 and × 40). D. On immunohistochemical analysis, the tumor is positive for Vimentin. (immunoperoxidase stain, original magnifications × 10 and × 40).

cardium. Taking into further account that dissection of the tumor might cause massive bleeding or cardiac rupture which had no benefit for the patient, partial tumor resection was carried out and some sample of the pericardial tumor was sent to pathology.

Microscopic examination showed abundant necrosis. The cells were short spindle, round to oval, and with polyhedral cells irregular, well-formed, slit-like or with branched blood vessels. Irregular and expansive vascular cavities with nuclear fission were observed. The nuclei were hyperchromatic and pleomorphism with brisk mitotic activity (**Figure 3A**). Immunohistochemistry was diffusely positive with markers CD31 (**Figure 3B**), CD34 (**Figure 3C**) and Vimentin (**Figure 3D**), Negative for CK, EMA, Bcl-2, MC, calretinin, WT-1, SMA, CD10, CD68, CD163, TTF-1, PSA, Myoglobin, D2-40, Desmin, and P504S. Ki-67 proliferative index was 60%.

After the operation, the patient received two cycles of chemotherapy with Doxorubicin, Ifosfamide and Mesna on January 19th, 2018 and February 23th 2018. II-III degree of granulocytopenia was observed and improvement was seen after repeated treatment of resisting bone marrow suppression. Unfortunately, he finally died of multiple pulmonary metastases less than three months after the operation.

Discussion

Pericardiac angiosarcoma is an aggressive and rare entity and generally has a rapidly progressive course [1, 11]. Its biological behavior depends on the histological grade, site of origin and the possibility of complete surgical excision [12]. The prognosis is generally very poor even diagnosis is made at an early stage.

Diagnosis of this kind of angiosarcoma can be a challenge because it often remains clinically silent until the disease is advanced [13, 14]. Most cases are diagnosed incidentally and leading to cardiac tamponade which can be easily mistaken with constrictive pericarditis. Histologically, they can be admixed with liposarcoma or fibrosarcoma. Deep myometrial invasion, metastasis to distant organs, and decreased survival appear to be the features of angiosarcoma while spindle, round to oval, polyhedral cells, and irregular, well-formed, slit-like or branched blood vessels are microscopic characteristic [15-17]. The diagnosis is confirmed by immunohistochemical staining of diffuse positivity for neuroendocrine markers CD31, CD34 and vimentin and high Ki-67 labeling.

The survival time is short compared with that of other cardiac sarcomas. Surgical resection with or without adjuvant radiation or chemotherapy is the main treatment modality. But the effects can vary. The most common chemotherapeutic drugs are adriamycin, ifosfamide, cyclophosphamide, vincristine, and dacarbazine. Furthermore, weekly paclitaxel is also typically administered. Although there is no unified therapy for pericardiac angiosarcoma even for early stage disease, conventional treatment includes pericardial stripping, radical hysterec-

tomy, and adjuvant chemotherapy. These are still highly recommended due to the aggressive nature of angiosarcoma tumors. In our case, we gave the patient two cycle chemotherapy with Doxorubicin, Ifosfamide and Mesna after operation. Unfortunately, he finally died of multiple pulmonary metastases less than three months after the operation confirming the highly aggressive behavior, rapid progression, and death of pericardiac angiosarcoma.

In summary, a typical case of pericardiac angiosarcoma with both clinical and pathological features is reported here and serves as a clinical reference.

Disclosure of conflict of interest

None.

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