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Clinicopathological and genetic features of primary cardiac angiosarcoma

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Abstract: This article mainly discusses the clinicopathological and laboratory characteristics of cardiac angiosarcoma, makes a differential diagnosis of the basic condition of primary cardiac angiosarcoma, and improves the understanding of primary cardiac angiosarcoma, this article studies the clinical data, pathology and immunoassay results of three patients with cardiac angiosarcoma, discusses the clinicopathological features and differential diagnosis of cardiac primary angiosarcoma, and improves the understanding of the tumor. Methods The clinical data, pathomorphology and immunohistochemical results of 3 cases of angiosarcoma in the heart were analyzed retrospectively. Most of the patients had clinical symptoms such as chest pain and dyspnea at the initial stage of the disease. Through the examination of the tumor tissue, it was observed that the cell structure was fusiform and oval, and there was necrosis in the vascular lumen.

1. Introduction

Primary angiosarcoma in the heart is relatively rare, generally originating from vascular endothelial cells, head and neck, etc., followed by often appear in soft tissues, breast, liver, spleen and bone, angiosarcoma primary in the heart is a rare disease, and the degree of malignancy is very high. Primary cardiac angiosarcoma has no specific symptoms, is difficult for diagnosis, has a poor prognosis, and is prone to metastasis. This article studies the clinical data of three cases of angiosarcoma in our hospital, and explores the clinicopathological and genetic features of primary cardiac angiosarcoma.

2. Case studies

Case 1, patient gender, 35 years old, one month before the onset, symptoms of chest tightness and shortness of breath after exertion, cold one week before the onset, aggravation of dyspnea, edema of both lower limbs, difficulty sleeping flat, cough, sputum, physical examination: blood pressure

115/89mmHg, heart rate 93 beats / minute, rhythm, no bulge in the precordial area, no palpable tremor. Echocardiography: hypoechoic mass in the right atrium is visible, about 6.80 cm × 7. 10 cm in size, suspected peduncle, about 1 cm wide 1.59 cm, attached to the oval fossa of the atrial septum. Small-medium fluid dark areas can be detected in the pericardial cavity, with a maximum width of about 1 posterior to the posterior wall of the systolic left ventricle 1.13 cm, the width is about 0 in front of the anterior wall of the right ventricle 0.75 cm. Ultrasound findings: Right atrial myxoma considered, pericardial effusion. CT with contrast to the chest shows a right atrial mass. Seen during surgery: moderate pericardial effusion, full right atrium, accessible to the roof with tumor invasion, no pericardial involvement, broad pedicle of the mass, located on the roof, hard, 7 cm in diameter, intact capsule, thickened right atrial wall. Complete resection of the tumor and atrial tissue in the pedicle of the tumor. The pathological diagnosis showed angiosarcoma, and he was discharged from the hospital on the 10th day after the operation, and died in the hospital 5 months after the operation, the cause is unknown.

Case 2, the patient is a female, 53 years old, the first presentation is epigastric abdominal pain symptoms, the cause of abdominal pain is unknown, there is persistent dull pain, lasting three days, no other reflex pain, the patient has abdominal pain accompanied by nausea and vomiting, the number of vomiting is 2 times, and the vomit is gastric contents. The patient had no dizziness, headache, chest tightness, shortness of breath, no hematemesis, no diarrhea, no cessation of exhaust and defecation, and no symptoms of edema of both lower extremities. Physical examination: blood pressure 117/61mmHg, heart rate 86 beats per minute, rhythm, no pathological murmur heard in the auscultation area of each valve. Echocardiography: Moderately echogenic mass with a well-defined boundary in the right atrium close to the lateral wall of the right atrium, approximately 8.90 cm × 7.30 cm × 5.70 cm, ultrasound indicates: Parenchymal right atrium mass with a small effusion in the pericardium. MR images show that the shape of the heart is enlarged, the degree of enlargement is not high, and there is a clump-like abnormal signal foci at the right atrium of the heart, showing an irregular shape, large and small about 9.30cm × 4.50cm × 4.20 cm, the lesion is close to the right side of the right atrium, the demarcation is not clear, and the free edge of the heart chamber is not smooth. MR diagnosis: right atrial mass closely related to the right and anterior walls of the atrium, neoplastic lesions considered, small pericardial effusion. Pericardiocentesis aspirates 80 ml of bloody fluid, which routinely shows nucleated cell count 1 × 10E9/L, neutrophil 46%, and lymphocyte count 54%. Seen during surgery: The mass is located in the right atrium, occupies most of the free wall of the right atrium, grows into the cavity, is accompanied by intra-mass hemorrhage, intermyocardial hematoma, invasion of the right ventricular wall, invasion of the epicardium, and bloody effusion in the pericardial space. Most of the mass is removed during surgery, the hematoma is removed, and the right atrial wall is autologous pericardial reconstruction. The patient was discharged 12 days after undergoing angiosarcoma surgery and died at home three months after surgery for unknown causes [1].

Case 3, the patient is a female, 45 years old, recurrent cough 1 month ago, cough is irritating dry cough, no obvious trigger, no sputum, no chest tightness shortness of breath, no fever, no chest pain, history of pulmonary tuberculosis, treatment and no recurrence. Physical examination: clear breath sounds in both lungs, no case murmur on cardiac auscultation, echocardiogram: 2.80cm × 2.90cm hypoechoic mass in the right atrium, free dark area in the pericardial cavity, good sound penetration in the dark area. Ultrasound: right atrial mass, left ventricular diastolic dysfunction, mild tricuspid regurgitation, small pericardial effusion. Chest x-ray: clear texture in both lungs, multiple nodules and lumps of different sizes can be seen in both lungs, the lesions are located in the two middle and lower lungs, chest x-ray diagnosis: multiple clumps in both lungs, metastasis is considered first. Pulmonary nodule biopsy was performed and angiosarcoma was diagnosed pathologically.

3. The clinical pathology of primary cardiac angiosarcoma

The naked eye can see gray mass, soft, microscopic examination can show tumor cells, tumor cells are pleomorphic, composed of well-structured vascular lumen and papillary structures, the size and shape of the vascular lumen are irregular, and the anastomosis is sinus gap. The lining cells have pleomorphism and atypia, and the tumor cells can be seen in the spindle-shaped, arranged in sheets or bundles in lung tissue, and the lumen is common with nuclear division image, and hemorrhage, necrosis, and extensive hemorrhagic necrosis can be observed in the tumor tissue [2].

Primary cardiac angiosarcoma often occurs in the right atrial near the atrioventricular sulcus, tumor cells invade the pericardial cavity, and can grow to the ventricular muscle wall and cardiac cavity, the age distribution of patients is wide, 36 months to 81 years old can be present, the peak of the disease is 40 to 50 years old, the proportion of men and women is similar. There are no specific symptoms in the early stage of cardiac angiosarcoma, and patients often have symptoms such as dyspnea and irritating dry cough at the first visit, including chest pain symptoms and dyspnea symptoms. Primary cardiac hemangiomas have symptoms such as chest pain and dyspnea in the early stage, mid-stage angiosarcoma invades the pericardium, and right heart function fails, and patients often have clinical symptoms such as chest tightness, fever, anemia, syncope, and arrhythmia. The size and extent of invasion of angiosarcoma can be observed by CT and magnetic resonance imaging, and the pathology and immunohistochemistry of the diagnosis and postoperative diagnosis can be confirmed [3].

4. The genetic characteristics of primary cardiac angiosarcoma

Primary angiosarcoma is a malignant tumor originating from vascular endothelial cells or mesenchymal cells that differentiate towards vascular endothelial cells, primary angiosarcoma often occurs in the right atrium near the atrioventricular sulcus, chest pain and dyspnea symptoms are common in the early stage, and arrhythmic symptoms may occur when the tumor invades the conduction system and myocardium.

Immunohistochemistry and gene mutation detection results: sediment and paraffin section tumor cells were positive expression of CD31, CD34, ERG, Fli1, D2-40, p53, INI1, bcl-2 and CD99 were expressed to varying degrees, and the rest of the markers were negatively expressed, Ki-67 positive index 50%~70%, located in the 17th chromosome 17 TP53 gene exon base missense mutation, mutation frequency is low, the first visit is chest tightness, a large pleural effusion, Multiple metastatic small nodules in both lungs, postoperative for unknown reasons, lung infection and death in the short term. Primary angiosarcoma is treated with mass resection, routine chemotherapy, routine radiation therapy, and most deaths within one year [4].

Primary angiosarcoma accounts for a large proportion of cardiac sarcoma, can occur at any age, generally has the right side of the heart for the original onset, more onset and right atrium, after the onset of adjacent to the heart wall, atrioventricular valve, pericardium, superior and inferior vena cava local infiltration, new pericardial effusion, cardiac tamponade and other clinical manifestations, tumor invasion and wall necrosis can lead to myocardial rupture. Primary angiosarcoma is prone to metastasis, metastasis to lung nodules, liver, kidneys and spleen and other organs, according to pathology, the tumor is generally located in the right atrium, with pericardium, ventricle, superior vena cava opening and other infiltrates, commonly combined with pericardial effusion, pleural effusion. Pathological examination of cardiac hemangiomas shows that the tumor morphology presents a black-brown or black hemorrhagic area with unclear boundaries, and the section surface may be microcystic or spongeous. Histological examination of tumors can observe that tumor cells present well-differentiated or medium-differentiated tumors, the shape of the vascular lumen is

irregularly distributed, the size is not specific, and the vascular lumen communicates with each other and is sinus-shaped; Patients with primary cardiac angiosarcoma have insignificant cardiac vascular formation, large and deep stained nuclei, and obvious nucleoli; Extensive bleeding and necrosis are common in the tumor tissue of primary cardiac angiosarcoma. Primary cardiac angiosarcoma is often accompanied by serous cavity effusion, tumor cells are mostly spindle-shaped, polygonal and epithelial, branched papillary, adenoid, pseudochrysanthemum-like, nest-like or scattered distribution, in the diagnostic process, intracellular vacuoles have a suggestive effect on the diagnosis of primary cardiac angiosarcoma, but the papillary structure and epithelioid morphology of tumor cells are very easy to lead to primary cardiac angiosarcoma being misdiagnosed as adenocarcinoma, especially when the patient's medical history is unknown or there is a mass in the lung, misdiagnosis is more likely to occur.

Puncture or biopsy of tumor cells of primary cardiac angiosarcoma can detect that the tumor cell tissue is mainly spindle cell morphology, and the diagnosis is easy to be confused with other benign and malignant mesenchymal tumors, and tumor cell intracellular vacuoles and large hemorrhages have certain diagnostic value for primary cardiac angiosarcoma. In the process of identifying primary cardiac angiosarcoma, special attention needs to be paid to distinguishing cardiac sarcoma cells from sarcoma cells such as lung adenocarcinoma, malignant mesothelioma, fibrosarcoma, synovial sarcoma, and leiomyosarcoma. Tumor cells of primary cardiac angiosarcoma express a series of vascular endothelial cell markers, including CD31, CD34, ERG, factor 8-related antigen and Fli1. Molecular genetics PCAS often involves homozygous deletion mutations in KDR, PLCG1, KMT2D, and CDKN2A genes, while MYC and MDM4 amplification and RAS mutations are rare. TP53 mutations are common in sarcomas, lower mutation rates in soft-tissue angiosarcoma, and more rare in primary cardiac angiosarcomas [5]. TP53 mutations may be strongly associated with poor sarcoma prognosis, and p53 protein may also be sed as a molecular marker for predicting sarcoma prognosis. In the study of this group of cases, it was found that case 2 gene detection showed TP53 mutation, which is located in the LSH2 region of the p53 protein DNA-binding domain, which is a common gain-of-function mutation of p53 protein, and promotes the proliferation, invasion and drug resistance of tumor cells by affecting the transcriptional activation activity of p53 protein. In this study, patients with primary cardiac angiosarcoma were characterized by bloody pleural effusion, pericardial effusion, and multiple metastases in both lungs, high expression of p53 protein, rapid disease progression, and short-term death, suggesting that TP53 mutations may be related to aggressive biological behavior; In this study, the overall prognosis of primary cardiac hemangiomas with pleural effusion is worse than that of those confined to the heart, which may be due to tumor invasion and liver and lung metastasis, but whether there is a molecular genetic difference in primary cardiac hemangiomas with or without pleural effusion remains to be further studied and discussed.

5. Conclusions

In general, primary cardiac hemangiomas are relatively rare diseases, which are often difficult to show specificity clinically, and early diagnosis is more difficult, and the diagnostic method needs to rely on histopathology and immunohistochemistry.

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