



Right Sided Reconstruction of the Heart for Invasive Angiosarcoma of the Right Atrium

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Abstract

A 35-year old male presented with new diagnosis of cardiac angiosarcoma. We describe the case, diagnosis, treatment modalities and first observations concerning survival.

Overall, cardiac sarcomas are a rare entity. There are several subtypes of sarcomas and the angiosarcoma is the most common type of heart sarcomas in adults, especially in male population. The symptoms of cardiac sarcomas are non-specific and depend on the size of the tumor, the anatomical localization, the myocardial involvement and the presence of metastatic disease. Dyspnea is the most common symptom by diagnosis.

The number of angiosarcomas diagnosed, has increased since non-invasive imaging (echocardiography, MRI, CT) has improved in quality. Final diagnosis can only be made by cytological and immunohistochemical examination. Once the diagnosis has been established, the therapy has to be started as soon as possible.

Most important in the treatment of sarcomas is a complete surgical resection, as this gives the most successful disease-free survival. Until now, the role of chemotherapy is unclear.

Unfortunately, the prognosis of cardiac sarcomas is poor. The median time to relapse is longer in patients with angiosarcoma than other sarcomas.

Keywords: Angiosarcoma; Cardiac malignancy; Cardiac tumor; Diagnosis; Treatment

Abbreviations

RA: Right Atrium; LA: Left Atrium; LV: Left Ventricle; RV: Right Ventricle; MRI: Magnetic Resonance Imaging; CT: Computed Tomography; FDG- PET: Fluorodeoxyglucose - Positron Emission Tomography; TTE: Transthoracic Echocardiography; TEE: Transesophageal Echocardiography; RCA: Right Coronary Artery; CABG: Coronary Artery Bypass Grafting

Introduction

Primary cardiac tumors are a rare entity (0.0017 to 0.033%, based on autopsies)[1-6]. Most cardiac tumors are metastatic locations of other primary tumors. About 75% of the primary cardiac tumors are benign, and 75% of these benign tumors are myxomas [4,5,7]. The remaining 25% of the primary tumors of the heart are malignant, with a majority of sarcomas (75%) [2,3,5,7]. Median survival for cardiac sarcomas is only six months [4,5].

Cardiac sarcomas can be divided into three categories, based on localization: right heart sarcoma (as in our case), left heart sarcoma or pulmonary artery sarcoma [8]. There are several subtypes of sarcomas; the angiosarcoma is the most common type of heart sarcoma in adults, especially in male population [6,8]. One third of the heart sarcomas (37%) is estimated to be angiosarcomas and male-female ratio is 2-3/1 [4,5,10]. Other types of cardiac sarcomas are rhabdomyosarcoma, osteosarcoma, leiomyosarcoma, undifferentiated sarcoma and primary cardiac lymphoma [3]. Mean age at diagnosis of angiosarcoma is forty and 90% is right-sided [3,5,7]. The most common type of heart sarcoma in children is rhabdomyosarcoma[6].

Angiosarcomas are endothelial cell tumors and have a poor prognosis due to their aggressive nature (early metastatic disease and infiltration) and delay in onset and diagnosis [2,7-9].

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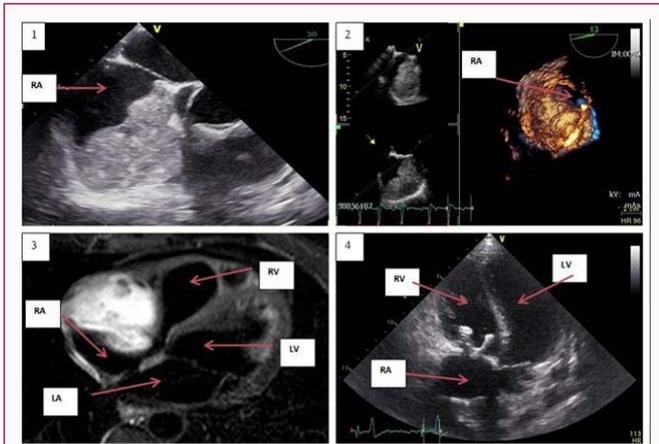


Figure 1: Pre- and postoperative imaging.
 1 + 2. Pre-operative echocardiography (TEE): large right atrium mass.
 3. Pre-operative MRI: large right atrium mass.
 4. Post-operative echocardiography (TTE).

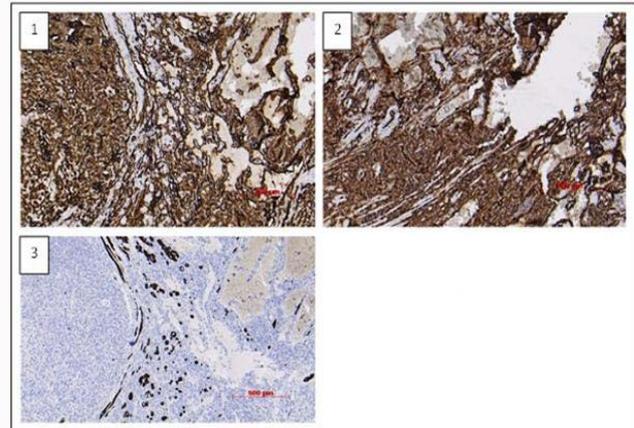


Figure 3: Histological evaluation
 1. CD 31 positive (vessel marker).
 2. CD 34 positive (vessel marker).
 3. Desmine positive cells (myocard fibers), which proves it is a heart tumor.

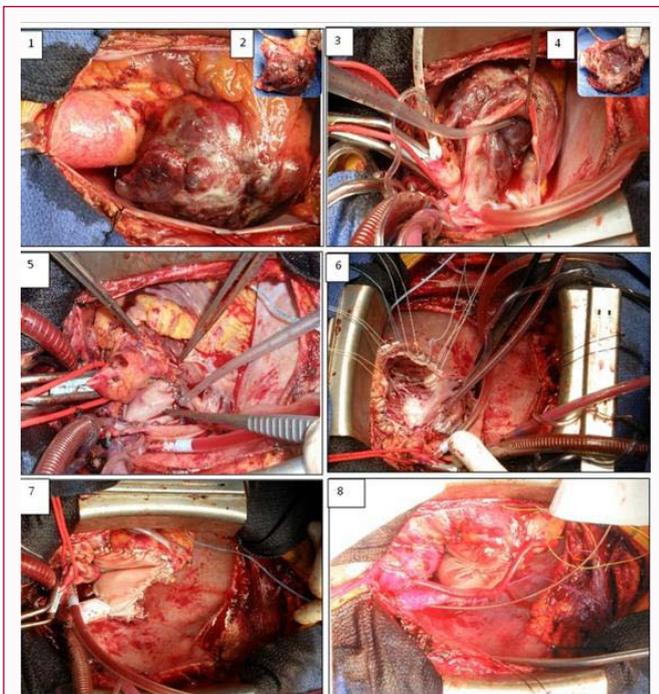


Figure 2: Overview of surgical procedure and reconstruction.
 1. Pre-operative situation.
 2. Macroscopic removal of the tumor; outside wall.
 3. After removal of the tumor.
 4. Macroscopic removal of the tumor; inside wall.
 5. Closure of RC ostium and of closure LA.
 6. Reconstruction base tricuspid by patch and placement of prosthetic valve, followed by reconstruction VCS.
 7. Patch reconstruction RA with venous CABG to branches RCA.
 8. End result in reperfusion phase.

Case Presentation

A 35-year old male presented with palpitations and progressive dyspnea since five weeks. ECG showed atrial fibrillation and transthoracic echocardiography (TTE) demonstrated a large right intra-atrial mass (7.8 x 5.2 cm), infiltrating the interatrial septum and the tricuspid valve. There were no signs of right ventricular inflow obstruction. Initial medical treatment consisted of systemic anticoagulation and rhythm control using amiodarone.

He was immediately referred to our hospital for further investigation. ECG showed sinus rhythm. TEE and cardiac MRI confirmed a large intra-atrial mass (59x 49x 68 mm) and because of the density, the irregular shape and the localization, an angiosarcoma was suspected (Figure 1).

In addition infiltration of the pericardium and pericardial effusion were found. A FDG-PET/CT scan did not show signs of metastatic disease. Coronary angiography showed normal coronary arteries. The right filling pressures were normal.

After fourteen days, a resection was performed under general anesthesia and full extracorporeal circulation (Figure 2).

Opening of the pericardium confirmed the effusion and there were spot lesions on the aorta and pulmonary artery. These were evaluated by frozen sections, ruling out malignancy before the resection was performed. Bicaval cannulation high in the vena cava superior and from the femoral vein allowed a macroscopic complete resection including the right atrium, the roof of the left atrium, the membranous atrioventricular and interventricular septum, the tricuspid valve and the basis of the free wall of the right ventricle. A reconstruction of the fibrous part of the septum and tricuspid annulus allowed implantation of a tricuspid bioprosthesis (Mosaic 33). Right and left atrium and the basal part of the right ventricle were reconstructed using pericardial patches. The vena cava superior was reconstructed using a PTFE graft. CABG was performed on branches of the right coronary artery using a saphenous vein graft.

Patient was weaned uneventfully from extracorporeal circulation. The ECG showed an ectopic atrial rhythm. He was extubated twenty hours after the operation. A permanent pacemaker was implanted after ten days because of persistent total AV-block. After surgery pleural punctions (temporary pigtail) were performed for relapsing right sided pleural effusion, with a total hospitalization time of four weeks.

Pathologic examination showed a classic angiosarcoma, with resection margins free of tumor. CD31 and CD34 immunohistochemical staining was positive, confirming vascular differentiation and the diagnosis of an angiosarcoma (Figure 3).

After multidisciplinary consultation between oncologists, pathologists, radiologists and cardiac surgeons, three possible

treatment options were proposed to the patient (watchful waiting, intensive adjuvant chemotherapy (doxorubicin/ ifosphamide) or paclitaxel monotherapy). In agreement with the patient an intensive adjuvant chemotherapy treatment was initiated.

Preliminary evaluation using computed tomography (CT) after three cycles of chemotherapy showed several subcentimetric liver lesions. PET-CT showed normal metabolism in the liver, no arguments for metastatic liver disease. Up until the moment of evaluation there is a survival of six months, with a NYHA classification I.

Discussion

Symptoms

The symptoms of cardiac sarcomas are non-specific. They depend on the size of the tumor, the anatomical localization, the myocardial involvement and the presence of metastatic disease [3,4,7]. Dyspnea is the most common symptom by diagnosis[3,9].

Symptoms may be systemic (e.g. anorexia, fatigue, fever, weight loss) but also signs of obstructive cardiac invasion (e.g. pulmonary edema, syncope, sudden cardiac death), arrhythmias (e.g. atrial fibrillation, ventricular arrhythmias) or signs of right-sided heart failure, pericardial effusion and cardiac tamponade may occur. Sometimes, systemic embolization causes the first sign (e.g. stroke, transient ischemic attack, myocardial infarction)[3,4,5,7].

Diagnosis

The number of angiosarcomas diagnosed, has increased since non-invasive imaging (echocardiography, MRI, CT) has improved in quality [4]. The rarity and variation and specificity in presenting symptoms explain the delay in diagnosis [9]. Other tumors that can mimic angiosarcomas are benign entities such as myxomas or pseudotumors (like thrombus, vegetation, and abscess).[4]. Also metastasis of other tumors as well as other sarcomas, mesotheliomas or lymphomas has to be considered [9].

Diagnosis is made using echocardiography, computed tomography (CT), magnetic resonance imaging (MRI), positron emission tomography (PET), and catheterization. Cardiac ultrasound is an important diagnostic method [3,5,7]. It is routinely used, noninvasive, cheap and can give information about the size and the localization of the tumor. Computed tomography and magnetic resonance imaging give clues to the subtype of tumor, as angiosarcomas are known for their irregular shape and invasion of the pericardium [3]. Positron emission tomography is used for detection of metastatic disease. They show the localization and relationship with other structures. A coronary angiography evaluates the coronary arteries before surgery, also to evaluate the possibility of resection and reconstruction.

Criteria suggesting malignancy are size >50 mm, involvement of more than one chamber of the heart, hemorrhagic pericardial effusion and infiltration into the vessels or mediastinum [4].

Like in our case, there was a large intra-atrial mass of 59 mm with infiltration of the pericardium and the presence of a pericardial effusion. Macroscopically, the tumors are usually hemorrhagic and necrotic, with a dark red or brown appearance [9].

Final diagnosis can only be made by cytological and immunohistochemical examination[4]. An angiosarcoma is a malignant tumor that contains cells with endothelial differentiation [3]. Diagnosis is confirmed by presence of endothelial markers, such

as CD31 and CD34 [3,9]. CD 31 is positive in 90% of angiosarcomas and is highly sensitive and specific for vascular neoplasma[9]. CD 34 is less sensitive and is positive in 50-74% of all angiosarcomas [9].

Once the diagnosis has been established, the therapy has to be started as soon as possible. Multidisciplinary collaboration of the cardiologist, cardiac surgeon, radiologist and oncologist is essential[4,6]. Due to the small number of angiosarcomas, there are currently no evidence-based treatment guidelines yet [3,5]. Most important in the treatment of sarcomas is total surgical resection; it gives the most successful disease-free survival [4]. Surgery can be challenging given the localization of the tumor and infiltration in nearby tissue, and therefore isn't always possible. It is restricted to a small number of patients because of the large number of metastatic disease by diagnosis [3]. When there are extracardiac manifestations, surgical resection has no survival benefit [7]. In many cases, an anatomic and functional reconstruction is only possible with an atrial patch, as in our patient.

The role of chemotherapy is unclear, given the limited experience in these types of tumors. Sometimes neo-adjuvant chemotherapy is given to reduce the size of the tumor [4]. Adjuvant therapy mostly includes anthracyclines (e.g. doxorubicine) and nitrogen mustard alkylating agents (e.g. cyclophosphamide, ifosphamide) [4,6]. Given lack of hard evidence for chemotherapy in angiosarcomas, chemotherapy protocols from extracardiac soft tissue studies are used [10]. Most oncologists prescribe an adriamycine based therapy [6]. The most common regimen is doxorubicin and ifosphamide [7,10]. When surgery isn't possible, palliative chemotherapy can be given to reduce symptoms [4]. Radiation therapy is sometimes used in people with pulmonary artery sarcomas, but is usually not an option in cardiac sarcomas due to complications (e.g. chronic pericarditis, cardiomyopathy) [7,10]. The heart in itself is more sensitive to radiation than the tumor [7].

There are no universal guidelines for treatment but complete resection of the tumor followed by adjuvant chemotherapy is estimated as the most optimal strategy [4,7]. Further investigation in (neo-)adjuvant chemotherapy is necessary.

Prognosis

Prognosis of cardiac sarcomas is poor. Most people (>80%) die within one year after diagnosis [4,5,7]. In 66-89% of cases with cardiac angiosarcoma, there is metastatic disease at the time of diagnosis [3,8]. Pulmonary metastases are most common. Occasionally there can also be metastases in the lymph nodes, bone, liver, brain, bowel, spleen, adrenal glands, diaphragm, kidneys, thyroid and skin [3]. Angiosarcomas have an aggressive biological nature and given their rarity aren't suspected initially[3,4,6,9]. However, early detection can improve disease free survival [3]. The size and the localization of the sarcoma are more important for prognosis than histological subtype [4]. Localization in the left heart might have a better prognosis [4,5]. Right heart sarcomas are more likely to induce late symptoms, are more infiltrative and produce earlier metastatic disease than left heart sarcomas [4]. Left heart sarcomas would have a lower mitotic index [5]. The median time to relapse is greater in patients with angiosarcoma than other sarcomas [6]. Surgical resection for cardiac sarcomas give a median survival of twelve months [4,6]. Without treatment the survival is less than a month [4].

Learning Objectives

With this case we describe a complete surgical resection with

complex reconstruction of right side of the heart after an invasive angiosarcoma of the right atrium. This case description could be a stepping stone for other surgeons and future treatments of right sided angiosarcomas. It addition, it includes an overview of the current available literature and possible additional chemotherapeutic that could be used.

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