Multidisciplinary Treatment In Cardiac Angiosarcoma: Lessons From A Case

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Citation

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Abstract

A 32 years-old patient with a right atrium angiosarcoma presented with congestive heart failure and chest pain.
Primary malignant tumours of the heart are uncommon diseases, typically sarcomas presenting aggressive behaviour and unfavourable prognosis. Due to their rarity, evidence-based recommendations for management are lacking and as a consequence, treatment must be individualised. A multidisciplinary approach is preferred in most cases. Our patient was successfully treated with a sequence of surgery, chemotherapy, and radiotherapy followed by further chemotherapy. A review of the available literature is also provided.

INTRODUCTION

Malignant tumours of the heart and pericardium are rare. The diagnosis may be challenging, due to unspecific symptoms and unpredictable presentation. The prognosis is typically poor and since randomised studies are lacking, therapeutic decisions must be individualised. Treatment is often multidisciplinary, such that the greatest challenge is how to ensure optimal integration of surgery, chemotherapy and radiotherapy. Complete resection is the ultimate goal, although rarely feasible due to anatomic reasons and loco-regional spread. Pre-operatory chemotherapy or chemo-radiation may have a role in the management of unresectable tumours.

CASE REPORT

A 32 years-old, previously healthy man presented to the emergency room with fever, atypical chest pain and signs of cardio-respiratory collapse. Unspecific symptoms had started two months before but dramatically worsened a few days prior to presentation. ECG findings were also unspecific. The echocardiography suggested the presence of a cardiac mass, confirmed by transoesophageal echocardiography. A computed tomography (CT scan) showed a large mass extending to the right mediastinum and pericardium, with a moderate pericardial effusion. The superior vena cava was partially compressed (figure 1a). An arteriography was performed and showed signs of neovascularization without evidence of myocardial infarction.

Clinical deterioration prompted thoracotomy, and a tumour mass of 12 cm was found in the right atrium. Resection was incomplete, and the tissue reconstituted with bovine pericardium. Postoperatively, the patient had a cardiac arrest which was successfully reverted. The histological diagnosis was that of a moderately differentiated angiosarcoma, staged IIB according to TNM staging system (G2T2N0M0). The postoperative CT scan showed a significant reduction in the tumour mass such that the patient had no assessable disease prior to the chemo-radiation (figure 1b).

Early post-operatory chemotherapy was administered. The regimen consisted in a combination of doxorubicin 20 mg/m2/day, dacarbazine 300 mg/m2/day, and ifosfamide 2500 mg/m2/day with mesna (MAID regimen), given as a continuous infusion for 3 days. Twenty days later the patient received radiotherapy, 54 Gy over 27 days. Chemotherapy was subsequently resumed. A total of 4 cycles were given. At the time of this report, the patient was being followed with regular visits and chest CT scans (every 3-months) and after a follow-up of 12 months, there was no evidence of recurrence.

Figure 1

Figure 1a: preoperative chest CT scan showing a tumour mass in the right atrium

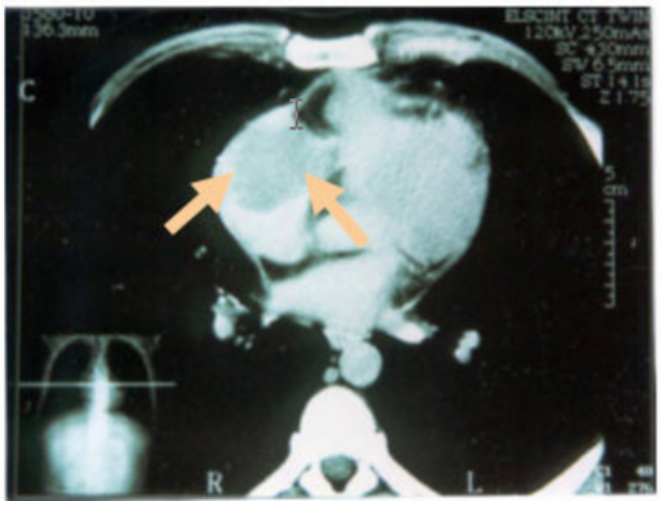
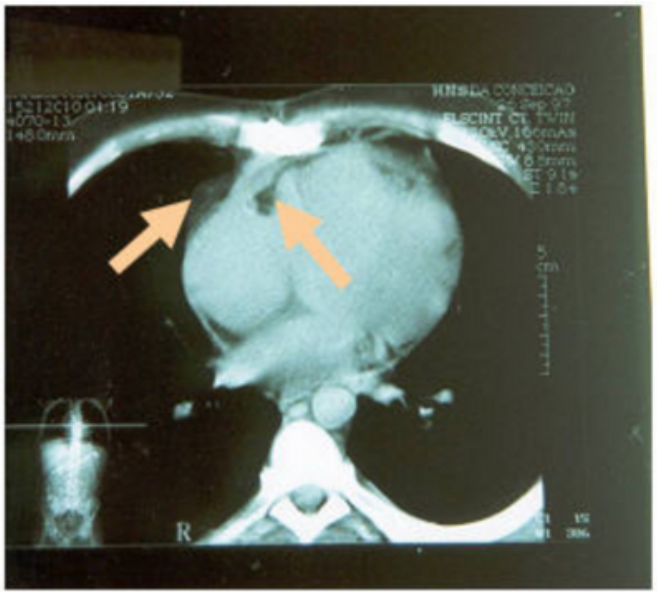


Figure 2

Figure 1b: postoperative chest CT scan: most of the mass was resected



DISCUSSION

Primary tumours of the heart are uncommon diseases, most benign sarcomas, of which 75% are atrial myxomas[1]. Among the malignant tumours, angiosarcomas are the most common, followed by non-classifiable sarcomas, malignant fibrous histiocytoma, osteogenic sarcoma, leiomyosarcoma, fibrosarcoma, mixed mesenchymal sarcoma, rhabdomyosarcoma and liposarcoma. The largest series of cardiac angiosarcomas is that of Rettman et al in which they report on 108 cases, confirming their rarity and unfavourable prognosis[2]. Men are twice as commonly affected as women, typically between the 3rd and 5th decades[1]. Their occurrence has also been linked to prolonged immunosupression in one report[3].

Survival in cardiac angiosarcomas is typically of less than 1 year, although it may be much longer in selected cases.[4,5,6] Aggressive behaviour, as well as delayed diagnosis due to unspecific symptoms, may result in early loco-regional spread. Involvement of mediastinal lymph nodes is frequent. Systemic spread is not uncommon at the time of diagnosis, the lung being the most common site, but metastases have been reported virtually in any organ.

The diagnosis may be a challenging semiotic exercise as patients can present with a multitude of clinical syndromes such as left or right-sided CHF (due either to direct myocardial involvement or to obstruction of venous return as seen with intracavitary tumours), compression of great vessels (sometimes resulting in classical clinical syndromes such as superior vena cava obstruction), ischemic syndromes due to coronary involvement, thromboembolic phenomena[2,7], valvular disfunction[7], arrhythmia[1] and pericarditis[7].

Staging should include chest imaging, and magnetic resonance imaging (MRI) appears to produce better vascular imaging, when compared to CT scan[8]. Similarly, transoesophageal echocardiography is superior to transthoracic echocardiography and can also safely guide transvenous biopsy, allowing for pre-operative histological diagnosis[9]. Arteriography (with coronary catheterization) allows for optimal evaluation of peri-tumoral neovascularization as well as the extent of great vessel's involvement and therefore is a crucial step in the surgical planning.

Surgery remains the mainstay of treatment although it is often challenging due to the presence of huge areas of necrosis and extensive loco-regional spread. Pre-operative histological diagnosis and careful evaluation of resectability are recommended. Neo-adjuvant chemotherapy or chemo-radiation may be proposed in patients with unresectable disease. Contrary to earlier reports, encouraging results have been seen with cardiac transplantation in selected patients with localised disease[1]. In a series of 15 cardiac sarcomas receiving adjuvant doxorubicin-based chemotherapy regimens, Llombart-Cussac et al reported that 13 eventually presented loco-regional failure, reinforcing the importance of optimal loco-regional therapy[5]. Of interest, one report showed an improved loco-regional control as well as the

feasibility of low doses of radiation with razoxane as a radiosensitizer[6]. Although anthracycline-based chemotherapy and cardiac irradiation have both been associated with an increased risk of cardiomyopathy and coronary heart disease, such complications typically occur in the long term such that, considering the poor survival observed in this disease, the potential benefit is likely to overweigh the risk.

Our decision to administer early post-operative chemotherapy in this case was based on young age and incompleteness of surgical resection in the setting of a very aggressive disease. The MAID regimen is known as one of the most active regimens in soft tissue sarcomas[10] and has been shown to prolong the time to relapse, although it failed to improve survival and seems more toxic when compared to the combination of doxorubicin and dacarbazine[11]. In addition, it is unknown whether these results can be extrapolated to angiosarcomas. Liposomal doxorubicin also appears to be active[11]. One minor response was reported with gemcitabine[13], but the most encouraging data come from two phase 2 studies showing the activity of paclitaxel in angiosarcomas of the scalp and face[14,15]. Combinations of paclitaxel with anthracyclines could further improve response rates and deserve investigation. Responses to immunotherapy with interleukin-2 in angiosarcomas have been reported in sites other than the heart[16,17], but not to interferon alpha[18] . Some authors, however, have questioned the role of early chemotherapy in angiosarcomas based on retrospective, historical comparisons[19]. Nevertheless, due to their rarity, it is unlikely that this question will ever be answered by controlled trials.

CONCLUSION

The best regimen, duration and timing of chemotherapy remain unknown. The Integration of chemotherapy, radiotherapy and surgery is recommended but the best sequence remains unknown. For the time being, treatment should be individualised. Pre-operative diagnosis and careful surgical planning are crucial. Selected patients with unresectable disease may benefit from neoadjuvant chemotherapy or chemo-radiation.

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