Cardiac angiosarcoma presenting with death due to cardiac perforation

AYYAZ SULTAN, AHMED AMOUR, SARFRAZ KHAN

Abstract

Cardiac angiosarcomas are malignant tumours that are rare, often with non-specific symptoms. They almost always have a rapid and fatal evolution, making diagnosis challenging. Therapeutic approaches include surgery, chemotherapy and radiotherapy alone, or in combination, but because the tumour is rare there are no randomised studies to guide treatment. Management is, therefore, usually individualised and often multidisciplinary.

Br J Cardiol 2006;**13**:213–15

Case report

We report here the case of a 59-year-old woman who was referred to the Accident & Emergency (A&E) department with sudden onset of central chest pain. The pain was griping in nature, it radiated to the chin, recurred every few minutes, lasted only a few seconds and was associated with mild shortness of breath. It had started when the patient was swimming the twelfth lap of the pool. She had had a deep vein thrombosis (DVT) 12 years before and there was a strong family history of ischaemic heart disease in relatives under the age of 50.

She was haemodynamically stable and systemic examination was unremarkable. Initial blood reports and electrocardiogram (ECG) were normal. Chest X-ray revealed a left basal wedge-shaped shadow. Elevated D-dimer levels and normal cardiac troponin levels led to pulmonary embolism as the primary diagnosis. However, the patient had a normal ventilation/perfusion (V/Q) scan followed by a normal CT pulmonary angiogram. These unexpected results changed the management. The patient was treated for probable unstable angina. She was discharged home after stabilisation, with plans for an early echocardiogram and exercise tolerance test (ETT).

Chorley & South Ribbles DGH, Lancashire Teaching Hospitals NHS Foundation Trust, Preston Road, Chorley, Lancashire, PR7 1PP.
Ayyaz Sultan, Registrar in Cardiology
Ahmed Amour, Consultant Cardiologist

Royal Preston Hospital, Lancashire Teaching Hospitals NHS Foundation Trust, Sharoe Green Lane North, Fulwood, Preston, PR2 9HT.
Sarfraz Khan, Consultant Cardiologist

Correspondence to: Dr A Sultan, 26 Dutch Barn Close, Chorley, Lancashire, PR7 1PR.
(email: drayyaz@gmail.com)

Figure 1. Transthoracic apical four-chamber echocardiography showing a distinct homogenous oval mass in the right atrium with a large pericardial effusion

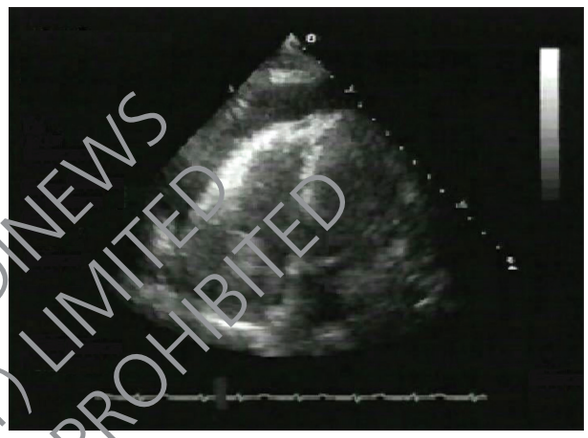
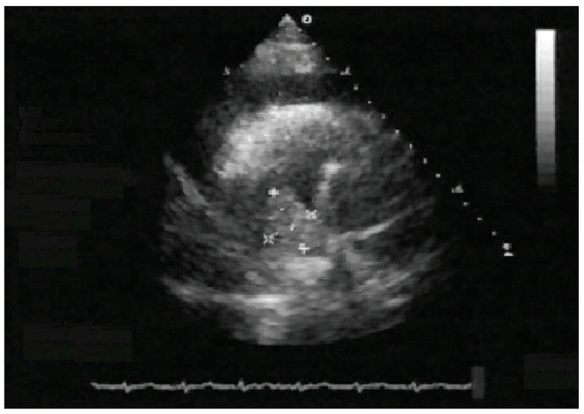
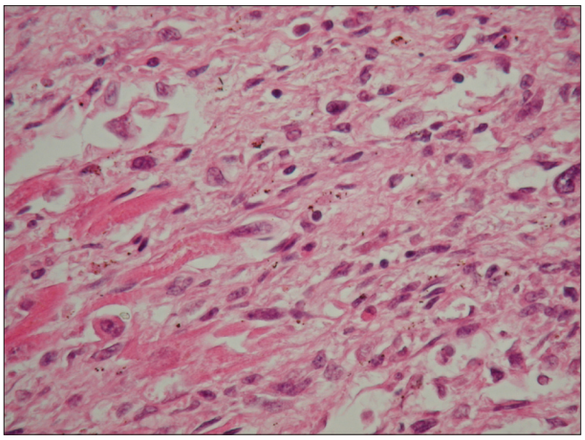


Figure 2. Parasternal short-axis view of the mass in the right atrium, showing possible attachment to the atrial wall



The ETT was normal except for shortness of breath: this was the main reason for termination of exercise during the fourth stage of the Bruce protocol. The patient presented again at A&E, about a week after the ETT, in a collapsed and hypotensive state. It was preceded by sudden central chest pain with nausea, that was not relieved by GTN spray. Despite aggressive resuscitation

Figure 3. Examination of the resected mass showed a mesenchymal, poorly differentiated tumour, consisting of polymorphic, predominantly spindle-shaped cells spreading within the myocardium, corresponding to an angiosarcoma



with intravenous fluids, the patient remained hypotensive. The patient was given inotropes without any satisfactory response. Initial ECG and chest X-ray were unremarkable but, later, a second review of the chest X-ray raised the suspicion of pericardial effusion. An urgent echocardiogram was performed (figures 1 and 2) which showed a mobile right atrial mass of 3.14 cm x 2.55 cm with a pericardial effusion of 1.64 cm and an ejection fraction of 40%. The possibility of angiosarcoma was raised. We contacted our regional tertiary cardiac centre with a view to possible thoracotomy and on their advice we thrombolysed the patient. Unfortunately, the patient sustained a cardiac arrest later, which she did not survive despite vigorous resuscitation.

At post-mortem the lungs were normal externally, and there was no evidence of infection or tumour. The heart weighed 330 g and was surrounded by a massive haemopericardium resulting in tamponade. This arose from a highly vascular 5 x 3 x 3 cm right atrial tumour which had perforated to the surface of the heart. Histology (figure 3) revealed high-grade angiosarcoma infiltrating deeply into the adjacent muscle wall, with atrial perforation and haemopericardium. Immunohistochemistry confirmed that the cells were positive for CD34 and CD31 vascular markers.

Discussion

Primary tumours of the heart are uncommon, with an incidence of 0.001% to 0.03% in autopsy reports.[1] Of these, 75% are benign tumours, mainly myxomas,[2] and the remaining 25% are malignant. Angiosarcoma constitutes 35% to 40% of the latter, being the most common primary cardiac malignant tumour.[3,4] Men are twice as commonly involved as women, typically between the third and fifth decade.[2-4]

Angiosarcoma arises in 80% of cases as a right atrial intracavitary lobulated mass, with necrotic foci ranging from 2 to 30 cm. It may extend beyond the pericardium to reach the pericardial sac.[5,6] Left atrial origin has been reported.[4] Prolonged exposure to immunosuppression has been reported as a factor in the aetiology.[7] The natural history of angiosarcoma is characterised by a short clinical course because of its aggressive behaviour and by delayed diagnosis due to the non-specific clinical picture and its rarity.[1,8] Ninety per cent of cases survive less than nine months (mean 6–11 months).[1] Metastasis is found in 66% to 89% of cases at the time of diagnosis.[9,10]

Clinical features are mainly dependent upon the location of the tumour in the heart, local myocardial infiltration and metastases.[11] Fatigue, lethargy, weight loss and fever can occur weeks or months before the onset of symptoms. Presentations may include chest pain, dyspnoea, orthopnoea and haemoptysis due to pulmonary metastases. Peripheral pedal oedema and right heart failure can be the consequences of pulmonary hypertension due to recurrent tumour embolisation and right ventricular outflow tract obstruction or due to superior vena caval obstruction.[4] Pericardium, lungs, mediastinal lymph nodes and vertebrae are the most frequent sites for metastases.[9,10]

Cardiac angiosarcomas grow rapidly, usually within the myocardial wall, and are characterised by friability and a tendency towards bleeding. They are, therefore, often associated with cardiac tamponade and recurrent pericardial effusion, multi-septate haemopericardium being the most frequent echocardiographic finding in the few cases reported. Myocardial rupture may occur due to tumoural infiltration and necrosis of the wall. Our decision to use thrombolysis, which was based on the echocardiographic finding of right atrial mass and discussion with the tertiary care centre, probably augmented the process, with tumoural bleeding and necrosis leading eventually to myocardial rupture.

The challenge is not only to differentiate between primary or secondary, and malignant or benign, tumours but also between neoplastic and non-neoplastic lesions.[12] Imaging modalities are required for rapid diagnosis and staging. Transthoracic echocardiography is the most frequently used tool but transoesophageal echocardiography is more sensitive.[13,14] Magnetic resonance imaging is the preferred choice to computerised tomography (CT) scans since it produces better vascular images.[15-17] Arteriography allows for optimal evaluation of involvement of the great vessels and coronary circulation plus peri-tumour neovascularisation, a crucial step pre-operatively.[18]

Treatment of angiosarcoma is controversial due to its poor prognosis: modalities include surgical resection, chemotherapy, radiotherapy and cardiac transplantation. Total tumour resection should be selected if tumour is confined to the interatrial septum, to the atrial free wall or to a small portion of the ventricle or a cardiac valve, in an attempt to reduce symptoms and increase post-operative survival.[4,19] Chemotherapy and radiotherapy are frequently used as adjuvants in non-resectable tumours or in cardiac transplant cases[20] but, alone, they neither increase the survival nor attenuate symptoms.[4,21] Cardiac transplant is one answer in a selected group of patients with non-resectable tumour and localised spread with no metastases;[2] otherwise survival rates are similar to those in patients not having transplanta-

Key messages

- Angiosarcoma, though rare, is the most common primary cardiac malignant tumour
- Presentation depends upon the location, local infiltration and metastases
- The best treatment regime remains to be discovered

tion.[1] Dissemination of undetected pre-existing metastases by post-transplant immunosuppressive treatment might explain this finding.[22]

Integration of these various modalities was reported in a study by Baay *et al.*[20] The patient had chemotherapy with doxorubicin, dacarbazine, ifosfamide and mesna initially. This was followed by radiation of 2600cGy and, after that, cardiac transplantation was performed. The patient received two additional courses of chemotherapy with the same drugs after two months and was maintained on cyclosporine and prednisone. The clinical outcome was favourable; up to 33 months after surgery, no metastases were detected.

Conclusion

Angiosarcoma continues to challenge because of its rarity, delay in diagnosis, variable clinical presentation and variable response to current therapeutic modalities. The best treatment regime is yet to be discovered.[18] The threshold for diagnosis should be low in patients with recurrent haemorrhagic pericardial effusions, evidence of right-sided heart failure, and pulmonary metastases with emboli and infarction. Treatment modalities should be individualised.

Acknowledgement

Our thanks to Maxine Lange, Cardiorespiratory Department, Lancashire Teaching Hospitals NHS Foundation Trust, for figures 1 and 2; and to Dr Jane Edward, Consultant Pathologist at Lancashire Teaching Hospitals NHS Trust, for figure 3.

Conflict of interest

None declared.

References

1. Kakizaki S, Takagi H, Hosaka Y. Cardiac angiosarcoma responding to multidisciplinary treatment. *Int J Cardiol* 1997;**62**:273-5.
2. Vander Salm TJ. Unusual primary tumors of the heart. *Semin Thorac Cardiovasc Surg* 2000;**12**:89-100.
3. Klima U, Wimmer-Greinecker G, Harringer W, Mair R, Grob CH, Brucke P. Cardiac angiosarcoma – a diagnostic dilemma. *Cardiovasc Surg* 1993; **1**:674-6.
4. Putnam JB, Sweeney MS, Colon R, Lanza LA, Frazier OH, Cooley DA. Primary cardiac sarcomas. *Ann Thorac Surg* 1991;**51**:906-10.
5. Herrmann MA, Shankerman RA, Edwards WD *et al*. Primary cardiac angiosarcoma: a clinicopathologic study of six cases. *J Thorac Cardiovasc Surg* 1992;**103**:655-64.
6. Satou Y, Nakagawa Y, Miki H *et al.* Cardiac angiosarcoma with ruptured right atrium diagnosed by echocardiography. *Chest* 1991;**100**:274-5.
7. Rigatelli G, Cotogni A, Rugolotto M *et al.* Extensive cardiac angiosarcoma in the course of immunosuppressive therapy after kidney transplant. *Ital Heart J* 2000:**1**(9 suppl):1199-202.
8. Rettmar K, Stierle U, Sheikhzadeh A, Diederich KW *et al.* Primary angiosarcoma of the heart. Report of a case and review of the literature. *Jpn Heart J* 1993;**34**:667-83.
9. Biniwale RM, Pathare HP, Aggrawal N, Tendolkar AG, Deshpande J, Sivaraman A. Cardiac sarcomas: is tumor debulking justifiable therapy? *Asian Cardiovasc Thorac Ann* 1999;**7**:52-5.
10. Shapiro S, Scott J, Kaufman K. Metastatic cardiac angiosarcoma of the cervical spine: case report. *Spine* 1999;**24**:1156-9.
11. Afzal MN, Alguacil-Garcia A. Primary cardiac angiosarcoma: clinical and pathological diagnostic problems. *Can J Cardiol* 1997;**13**:293-6.
12. Basso C, Valente M, Poletti A, Casarotto D, Thiene G. Surgical pathology of primary cardiac and pericardial tumors. *Eur J Cardiothorac Surg* 1997;**12**:730-8.
13. Hammoudeh AJ, Chaaban F, Watson RM *et al.* Transesophageal echocardiography-guided transvenous endomyocardial biopsy used to diagnose primary cardiac angiosarcoma. *Cathet Cardiovasc Diagn* 1996;**37**:347-9.
14. Frohwein SC, Karalis DG, McQuillan JM *et al.* Preoperative detection of pericardial angiosarcoma by transesophageal echocardiography. *Am Heart J* 1991;**122**:874-5.
15. Araoz PA, Eklund HE, Welch TJ, Breen JF. CT and MR imaging of primary cardiac malignancies. *Radiographics* 1999;**19**:1421-34.
16. Laissy JP, Bernier P, Patrux B *et al.* Primary left atrial angiosarcoma: follow-up by magnetic resonance imaging. *Magn Reson Imaging* 1990; **8**:651-5.
17. Link KM, Lesko NM. MR evaluation of cardiac/juxtacardiac masses. *Top Magn Reson Imaging* 1995;**7**:232-45.
18. Guimaraes JLM, Sutmoller SFMc, Mano MS *et al.* Multidisciplinary treatment in cardiac angiosarcoma: lessons from a case. *Internet J Oncol* 2004;**2**:1.
19. McFadden PM, Ochsner JL. Atrial replacement and tricuspid valve reconstruction after angiosarcoma resection. *Ann Thorac Surg* 1997;**64**:1164-6.
20. Baay P, Karwande SV, Kushner JP, Olsen S, Renlund DG. Successful treatment of a cardiac angiosarcoma with combined modality therapy. *J Heart Lung Transplant* 1994;**13**:923-5.
21. Vergnon JM, Vincent M, Perinetti M *et al.* Chemotherapy of metastatic primary cardiac sarcomas. *Am Heart J* 1985;**110**:682-4.
22. Crespo MG, Pulpón LA, Pradas G *et al.* Heart transplantation for cardiac angiosarcoma: should its indication be questioned? *J Heart Lung Transplant* 1993;**12**:527-30.