Rare tumours of the heart – angiosarcomas

Vit Martin Matejka[1], Lubos Holubec[1], Petr Mukensnabl[2], Ondrej Ondic[2], Jana Dreslerova[1], Ondrej Fiala[1], Petra Mrazkova[3], Jindrich Finek[1]

[1]Department of Oncology and Radiotherapy, Faculty Hospital in Pilsen, Pilsen, Czech Republic
[2]Department of Pathology, Faculty Hospital in Pilsen, Pilsen, Czech Republic
[3]Radiodiagnostic Clinic, Faculty Hospital in Pilsen, Pilsen, Czech Republic

Primary cardiac tumours are rare, with a reported prevalence of 0.001–0.3% of routine autopsies. More than three-quarters of them are benign, with myxoma as the most common histological type. The malignant primary tumours of the heart are angiosarcomas, rhabdomyosarcoma, osteosarcoma, leiomyosarcoma, undifferentiated sarcoma and primary cardiac lymphoma. The angiosarcoma is an extremely rare neoplasm has a very poor prognosis for recovery because of late diagnosis, aggressive biological behaviour and minimal response to chemotherapy. The mean survive is six to eleven months. We reported two cases treated in the Department of Oncology and Radiotherapy at the University Hospital in Pilsen.

Key words: angiosarcoma, heart, primary tumour, chemotherapy.

Contemp Oncol (Pozn) 2014; 18 special issue
DOI: 10.5114/wo.2014.40601

Introduction

Primary tumours of the heart are very rare. Reported prevalence is about 0.001–0.3% of routine autopsies [1, 2]. More than three-quarters of them are benign, with myxoma as the most often histological type. The malignant primary tumours of the heart are angiosarcomas, rhabdomyosarcoma, osteosarcoma, leiomyosarcoma, undifferentiated sarcoma and primary cardiac lymphoma [3]. Angiosarcoma is, with its prevalence 0.000075–0.00225%, the most common of them [4, 5]. The very poor prognosis of this disease is caused by its late diagnosis and treatment because of limited information on the clinical aspects for this type of tumour. The mean overall survive is from 6 to 13 months [5, 6]. Two cases, treated in the Department of Oncology and Radiotherapy at the University Hospital in Pilsen, are presented in this paper.

Case report I

A 65-year-old man was admitted to the internal ward with a suspicion of bronchitis and pericarditis. No fever, weight loss, syncope nor unconsciousness was reported. The patient's medical history was negative for any secondary malignant disease, hypertension, tuberculosis, diabetes mellitus or ischaemic disease of the heart or icterus. His family history also showed no cases of cancer. The physical examination was normal, blood pressure 140/80 mm Hg and heart rate of 90 beats per minute. Electrocardiogram showed normal sinus rhythm with no artefacts. Routine laboratory studies were normal. A chest X-ray showed bilateral fluidothorax. A transthoracic echocardiogram, targeted at pericardial effusion, was carried out. It confirmed fluid in the pericardium. The solid tumour growing from the posterior wall of the right atrium was found as the second finding. About 800 ml of fluid was drained, but because the solid tumour was confirmed by a CT scan, the patient was transferred to the department of cardiosurgery. The patient immediately underwent an open right atrial operation. The tumour of the right atrium was completely removed, sized 35 mm × 20 mm × 6 mm, and the implantation of a pericardial patch was made. Postoperative recovery was without any adverse event or effects and the patient was discharged without any complications. Histological and immunohistochemical examinations were performed. Histologically, the tumour sections showed a poorly differentiated, well vascularized malignant neoplasm with a high marker of nuclear pleomorphism and atypical mitosis. The immunohistochemical stain showed that the tumour cells were positive for CD34, CD31 and fVIII and negative for Aktin S, Myoglobin, S100 and AE 1–3 (Fig. 1). Because of localized disease without any signs of generalization, adjuvant chemotherapy was indicated. The patient underwent 6 cycles of adjuvant chemotherapy monotherapy of doxorubicin with cardio-protective dexrazoxane. At the

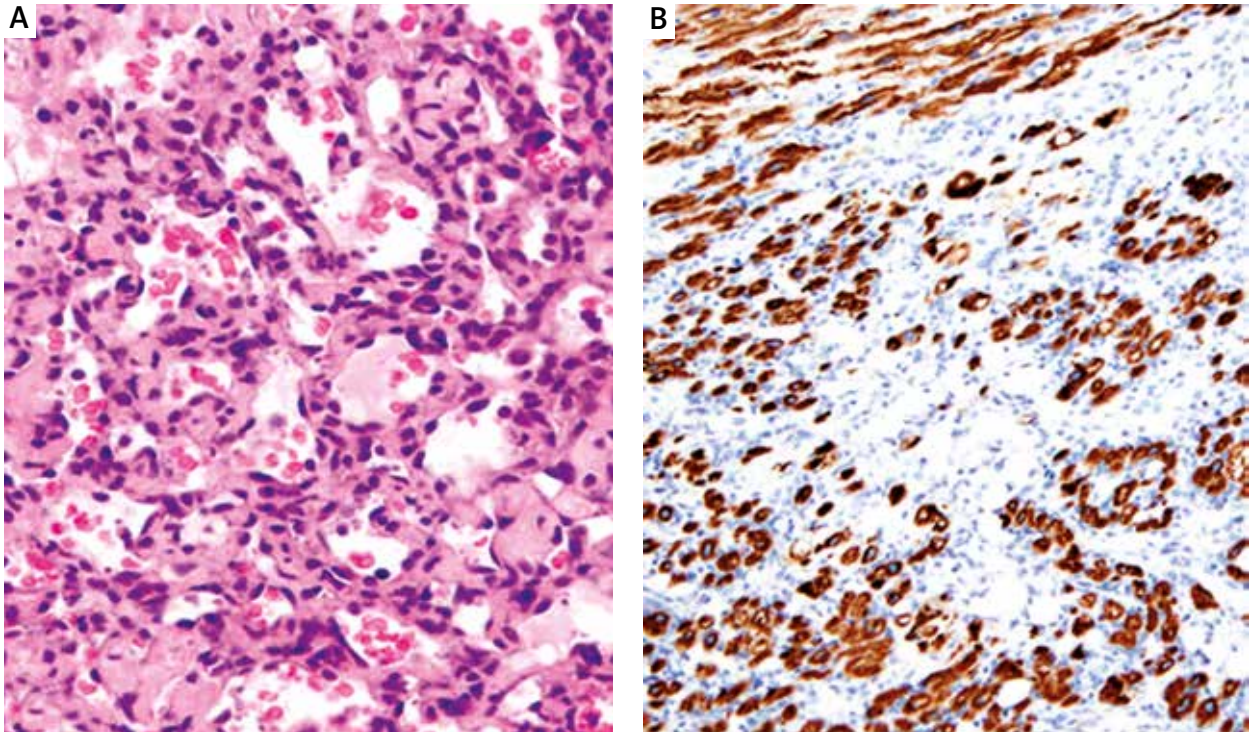

Fig. 1. A) Histology (haematoxylin-eosin staining) of a poorly differentiated, well-vascularized malignant angiosarcoma; **B**) Immunohistochemical positivity for CD34

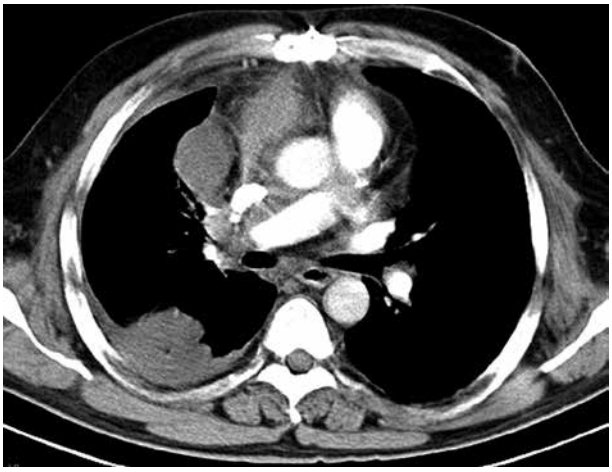

Fig. 2. Thoracic computerized tomography (CT) shows mass in the right atrium expanding in the right hemithorax with fluidothorax

four-month follow up, the patient was symptom-free with a complete remission of the disease confirmed by CT-scan. Four months later, a mass of size 80 mm × 50 mm × 140 mm in the wall of the right chamber, expanding in the right hemithorax was found (Fig. 2). Also there were two in the right-lung, five in the liver metastasis and massive packets of mediastinal lymph nodes confirmed. The local progression and dissemination of the disease contraindicated to surgical treatment and the patient's status did not allow palliative chemotherapy. The patient died due to multi-organ failure 11 months after diagnosis.

Case report II

A 35-year-old woman admitted to the internal ward for dyspnoea. The patient's medical and family history was negative for malignancy or heart disease. No fever, weight loss, syncope nor unconsciousness was reported. The physical examination showed only dyspnoea at rest, blood pressure 150/90 mm Hg and a heart rate of 85 beats per minute. Electrocardiogram and routine laboratory studies were normal. A chest X-ray confirmed fluidopericard, and after conduction of the pericardial drainage about 1400 ml of fluid was drained. A cytological examination was negative for malignant cells. Transesophageal echocardiography showed a mass in the right atrium, and because of malignancy suspicion a PET-scan was performed. This confirmed a highly vascularized and highly glucose-accumulated tumour in the right atrium, sized 45 mm × 50 mm × 40 mm (Fig. 3). Massive metastatic disease of the lungs and the retroperitoneal area were also found. The patient underwent a cardiosurgical operation to take a biopsy sample and to try a debulking operation, but the local finding was that it was inoperable. Histologically, the tumour sections showed a poorly differentiated malignant neoplasm composed of spindled cells with a high marker of mitosis. The immunohistochemical stain showed that the tumour cells were positive for CD34, CD31, fVIII and desmin and negative for Aktin S, Myoglobin, S100 and AE 1–3 (Fig. 4). The patient's status was defined as inoperable, so systematic treatment was indicated. The patient underwent 6 cycles of palliative chemotherapy, doxorubicin with cardio-protective dexrazoxane. A PET-scan after the first line of chemotherapy showed no change in metabolic

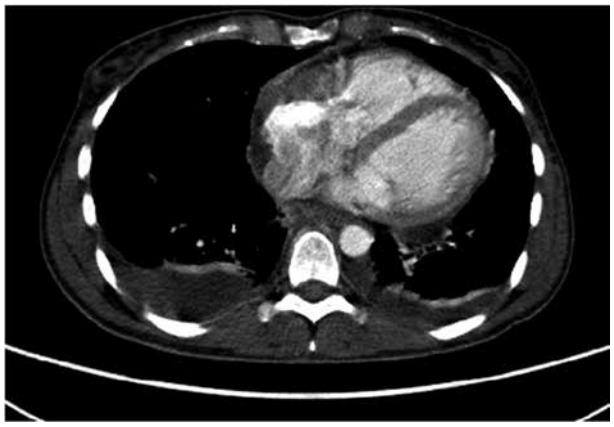

Fig. 3. Thoracic computerized tomography (CT) shows a mass in the right atrium and massive metastatic disease of the lungs

activity, but partial progression of origin tumour size. The lung metastases reduced their size by one third, but the liver metastases stayed unchanged. Chemotherapy was changed to cisDDP + etoposide. After 4 cycles the chemotherapy had to be changed to etoposide monotherapy due to the poor clinical status of the patient. After the next 3 cycles, a CT-scan was performed. It confirmed progression in size and metabolic activity of the origin and number of metastases in the lung as well as the liver. The local progression, dissemination of the disease and the patient's status were contraindications to a third line of palliative chemotherapy. The patient died due to multi-organ failure 13 months after diagnosis.

Discussion

Primary cardiac tumour in adults is a very rare diagnosis. Routine autopsy studies confirm the incidence to be about 0.001–0.3% [1, 2]. About 75% of primary heart tumours are benign, with myxoma as the most common histological type. More than a third of the remaining 25% are angiosarcomas [1, 2]. This histologic type is the most common malignant primary heart tumour. The other histological types of malignant tumours are rhabdomyosarcoma, osteosarcoma, leiomyosarcoma, undifferentiated sarcoma and primary cardiac lymphoma [3–5]. Primary angiosarcoma of the heart is common in males and in the 3rd–5th decades of life. About 90% of the tumours arise from the lateral wall of the right atrium [6]. Metastases are found in almost 89% of patients at the time of diagnosis. Primary angiosarcoma of the heart most commonly metastasizes to the lungs and mediastinal lymph nodes, occasionally to bones, liver, brain, pleura and kidney [7, 8]. The clinical diagnosis of this disease is very difficult because of its non-specific signs and symptoms. The main symptoms are, in order, tumour localization, its size, degree of tissue infiltration and the presence of metastasis. Because of the localization of tumours in the right atrium, the first symptoms can be right heart symptoms, vena cava obstruction or cardiac tamponade [9]. The most common symptoms are not so urgent, but also nonspecific such as chest pain, haemoptysis, orthostatic hypotension, emesis, fever, anorexia, dyspnoea or arrhythmia [10]. For the diagnosis of cardiac tumours, echocardiography (transesophageal or transthoracic) is the modality of choice for the initial evaluation. It is useful to describe the location of the mass and pericardial effusion. For the staging of the disease, CT scan or MRI are usable. It should be noted that the CT scan is less precise to describe a tumour, because of heart movement, while the MRI has more advantages for diagnosis by tissue characterization and the possibility to differ between the blood stream and highly vascularised masses of angiosarcoma [9, 10]. Because of these factors the best way to diagnose the tumour is histology with immunohistochemical staining for CD31, CD34, factor

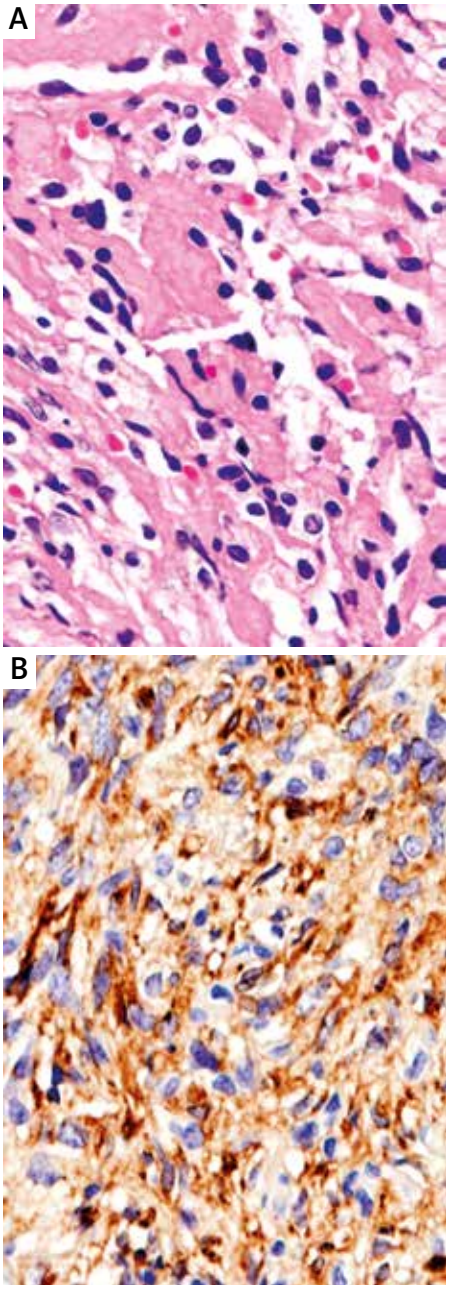

Fig. 4. A) Histology (haematoxylin-eosin staining) of a poorly differentiated malignant neoplasm composed of spindled cells; **B**) Immunohistochemical positivity for fVIII

VIII and vimentin [11]. Therapy of primary angiosarcoma of the heart has the same principles as therapy of sarcomas with a different site of origin. The initial and only method with any possibility to cure this disease is surgery [12, 13]. Complete resection of a tumour is indicated with no signs of dissemination of disease and with resectable local findings [14]. A few case reports also describe heart transplantation as threat possibility [15]. However it's radical tumour resection, overall survival is weighted by a high incidence of local relapse. After surgical resection adjuvant radiotherapy or chemotherapy is recommended. The final radiotherapy dose range is about 50 Gy. This modality is unfortunately weighted by many difficulties such as inaccuracies with the concentration of the dose of radiation on just the tumour or on the entire site of tumour resection due to movement of the heart. The second major complication is the toxicity of radiation to healthy tissue of critical organs in this location [16, 17]. Chemotherapy could be used as neo/adjuvant or palliative modality. The limited experience caused by the rarity of this disease leads to uncertainty about the efficiency of different drugs. By the known effect on sarcomas from different origin, were used and reported: doxorubicin, cyclophosphamide, ifosfamide, docetaxel, paclitaxel, cisplatin and etoposide [18–20]. The response to chemotherapy is poor and more knowledge about the effect of chemotherapy is weighted by tumour rarity. The same problem complicates obtaining objective data about using multikinase inhibitors such as sorafenib or anti-VEGFs such as bevacuzimab [21, 22]. The survival rate for patients with primary angiosarcoma of the heart remains unchanged in the range from 6 to 13 months [21, 23].

In conclusions, our patients confirmed very poor response to adjuvant chemotherapy in angiosarcoma of the heart in palliative treatment.

The authors declare no conflict of interest.

References

1. Burke A, Virmani R. Primary cardiac sarcomas. Atlas of tumor pathology. Tumors of the heart and great vessels 1990; 16: 127-70.
2. Patel J, Sheppard MN. Pathological study of primary cardiac and pericardial tumours in a specialist UK centre: surgical and autopsy series. Cardiovasc Pathol 2010; 19: 343-52.
3. Hamidi M, Moody JS, Weigel TL, Kozak KR. Primary cardiac sarcoma. Ann Thorac Surg 2010; 90: 176-81.
4. Reynen K. Frequency of primary tumor of the heart. Am J Cardiol 1996; 77: 107.
5. Pigott C, Welker M, Khosla P, Higgins RS. Improved outcome with multimodality therapy in primary cardiac angiosarcoma. Nat Clin Pract Oncol 2008; 5: 112-5.
6. Kodali D, Seetharaman K. Primary cardiac angiosarcoma. Sarcoma 2006; 2006: 39130.
7. Janigan DT, Husain A, Robinson NA. Cardiac angiosarcomas. A review and a case report. Cancer 1986; 57: 852-9.
8. Burke AP, Virmani R. Tumors and tumor-like conditions of the heart. Cardiovasc Pathol 2001; 583-605.
9. Grebenc ML, Rosado de Christenson ML, Burke AP, Green CE, Galvin JR. Primary cardiac and pericardial neoplasms: radiologic-pathologic correlation. Radiographics 2000; 20: 1073-103.
10. El-Osta HE, Yammine YS, Chehab BM, Fields AS, Moore DF Jr, Mattar BI. Unexplained hemopericardium as a presenting feature of primary cardiac angiosarcoma: a case report and a review of the diagnostic dilemma. J Thorac Oncol 2008; 7: 800-2.
11. Tremaine LA, Gaertner EM. Persistent hemopericardial effusion in a 54-year-old man. Arch Pathol Lab Med 2005; 129: 223-30.
12. Gong Y, Hong T, Chen M, Huo Y. A right heart angiosarcoma with rapidly progressing hemorrhagic pericardial effusion. Intern Med 2011; 50: 455-8.
13. Timóteo AT, Branco LM, Bravio I, Pinto E, Timoteo T, Matos P, Ferreira RC. Primary angiosarcoma of the pericardium: case report and review of the literature. Kardiol Pol 2010; 68: 802-5.
14. Grande AM, Ragni T, Vigan M. Primary cardiac tumors. A clinical experience of 12 years. Tex Heart Inst J 1993; 20: 223-30.
15. Gowdamarajan A, Michler RE. Therapy for primary cardiac tumors: is there a role for heart transplantation? Curr Opin Cardiol 2000; 15: 121-5.
16. Butany J, Nair V, Naseemuddin A, Nair GM, Catton C, Yau T. Cardiac tumors: diagnosis and management. Lancet Oncol 2005; 6: 219-28.
17. Prosnitz RG, Chen YH, Marks LB. Cardiac toxicity following thoracic radiation. Semin Oncol 2005; 32: 71-80.
18. Nakamura-Horigome M, Koyama J, Eizawa T, et al. Successful treatment of primary cardiac angiosarcoma with docetaxel and radiotherapy. Angiology 2008; 59: 368-71.
19. Llombart-Cussac A, Pivot X, Contesso G, Rhor-Alvarado A, Delord JP, Spielmann M, Türsz T, Le Cesne A. Adjuvant chemotherapy for primary cardiac sarcoma: the IGR experience. Br J Cancer 1998; 78: 1624-8.
20. Simpson L, Kumar SK, Okuno SH, Schaff HV, Porrata LF, Buckner JC, Moynihan TJ. Malignant primary cardiac tumors: review of a single institution experience. Cancer 2008; 112: 2440-6.
21. Bakaeen FG, Jaroszewski DE, Rice DC, et al. Outcomes after surgical resection of cardiac sarcoma in the multimodality treatment era. J Thorac Cardiovasc Surg 2009; 137: 1454-60.
22. Penel N, Marréaud S, Robin YM, Hohenberger P. Angiosarcoma: state of the art and perspectives. Crit Rev Oncol Hematol 2011; 80: 257-63.
23. Kakizaki S, Takagi H, Hosaka Y. Cardiac angiosarcoma responding to multidisciplinary treatment. Int J Cardiol 1997; 62: 273-5.

Address for correspondence

Dr. **Vit Martin Matejka**
Department of Oncology and Radiotherapy
University Hospital in Pilsen
323 00 Pilsen, Czech Republic
tel. +420377105534, +420608607259,
fax +420377105545
e-mail: matejkavm@fnplzen.cz, vit.martin.matejka@centrum.cz

Submitted: 11.03.2013
Accepted: 5.09.2013