

Right atrium angiosarcoma with feeding vessels from right coronary artery: a case report

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Background Primary cardiac angiosarcoma is a rare primary cardiac malignancy. Biopsy of such vascular-rich tumours may result in serious complications.

Case summary This is a case of a 43-year-old woman who presented with syncope. According to clinical history, she initially had massive pericardial effusion, with an uncertain aetiology. Multimodality imaging at our hospital revealed a cauliflower-like tumour in the right atrium. Coronary angiography results confirmed multiple feeding vessels from the right coronary artery to the tumour. Thoracoscopic biopsy resulted in a massive bleeding requiring haemostasis via thoracotomy. Histopathological examination of the specimen showed an angiosarcoma with atypical cells and spindle cells in a myxomatous background. Treatment with systemic targeted therapy and chemotherapy was initiated, and the patient is still under active treatment.

Discussion Cardiac angiosarcomas most commonly arise from the right atrium and may be hard to detect with transthoracic echocardiography. Biopsy of primary cardiac angiosarcomas requires careful planning because they are highly vascularized. Currently, no guidelines regarding the treatment of such tumours exist, and a multidisciplinary treatment is needed.

Keywords Case report • Cardiac angiosarcoma • Multimodality imaging • Pericardial effusion

ESC Curriculum 6.6 Pericardial disease • 6.8 Cardiac tumours

Learning points

- Refractory bloody pericardial effusion could be the manifestation of malignancy involving the pericardium.
- Right atrium angiosarcoma with epicardial extension may be unremarkable on transthoracic echocardiography.
- Post-biopsy haemorrhage should be concerning for angiosarcoma with feeding vessels from the coronary artery. Biopsy confirmation from metastatic site is an alternative approach.

Introduction

Cardiac tumours can be classified into primary and secondary neoplasms on the basis of their origins. Primary cardiac tumours are extremely rare (incidence: 0.0001–0.0030%), and the majority (75%)

are benign.^{1,2} Of all the malignant primary cardiac tumours, 95% are sarcomas, with angiosarcomas being the most common tissue subtype.^{3,4} This article reports the case of a 43-year-old woman with epigastric pain and unexplained pericardial effusion, highlighting the diagnostic and treatment aspects of primary cardiac angiosarcoma.

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Timeline

Four months prior to admission	Presented with dyspnoea and epigastric pain. Pericardiocentesis to drain large amount of pericardial effusion.
Clinical presentation at admission	Syncope
1 week after admission	Diagnosis and thoracoscopic biopsy of a right atrial mass are complicated by massive bleeding requiring thoracotomy for haemostasis
3 weeks after admission	Histopathological diagnosis of primary right atrium angiosarcoma
5 weeks after admission	First cycle of weekly paclitaxel and tri-weekly bevacizumab
10 months after diagnosis	New pulmonary nodule observed during routine follow-up
11 months after diagnosis	Pulmonary metastasectomy
12 months to 18 months after diagnosis	Oral pazopanib
18 months after diagnosis	Monthly ifosfamide plus doxorubicin

Case presentation

This is the case of a 43-year-old woman who presented with syncope. Four months before admission, she had dyspnoea and epigastric discomfort and was hospitalized after contrast-enhanced abdominal computed tomography (CT) that showed a large pericardial effusion, which was confirmed by a subsequent contrast-enhanced chest CT (Figure 1A and B). Pericardiocentesis yielded 600 mL of bloody pericardial fluid, and biochemistry, microbiology, and cytology analyses were negative. Blood tests for autoimmune disease, thyroid function, and screening of tumour markers revealed negative results as well. A pigtail catheter was inserted into the pericardial space for drainage. A fluorodeoxy-glucose-18-positron emission tomography-computer tomography (FDG-PET-CT) scanning showed hypermetabolism only in the right cardiac region, suggestive of malignancy. No other extracardiac hypermetabolic sites were observed (Figure 1C). No medications were prescribed because of the unknown aetiology of the pericardial effusion, and the pigtail catheter was removed upon discharge.

At the time of admission, the patient experienced syncope without prodrome for 10 s. Physical examination showed no relevant findings. Haematologic analysis showed microcytic anaemia. Biochemical analysis was unremarkable. Electrocardiography findings showed sinus rhythm. Chest radiograph results revealed an enlarged cardiac

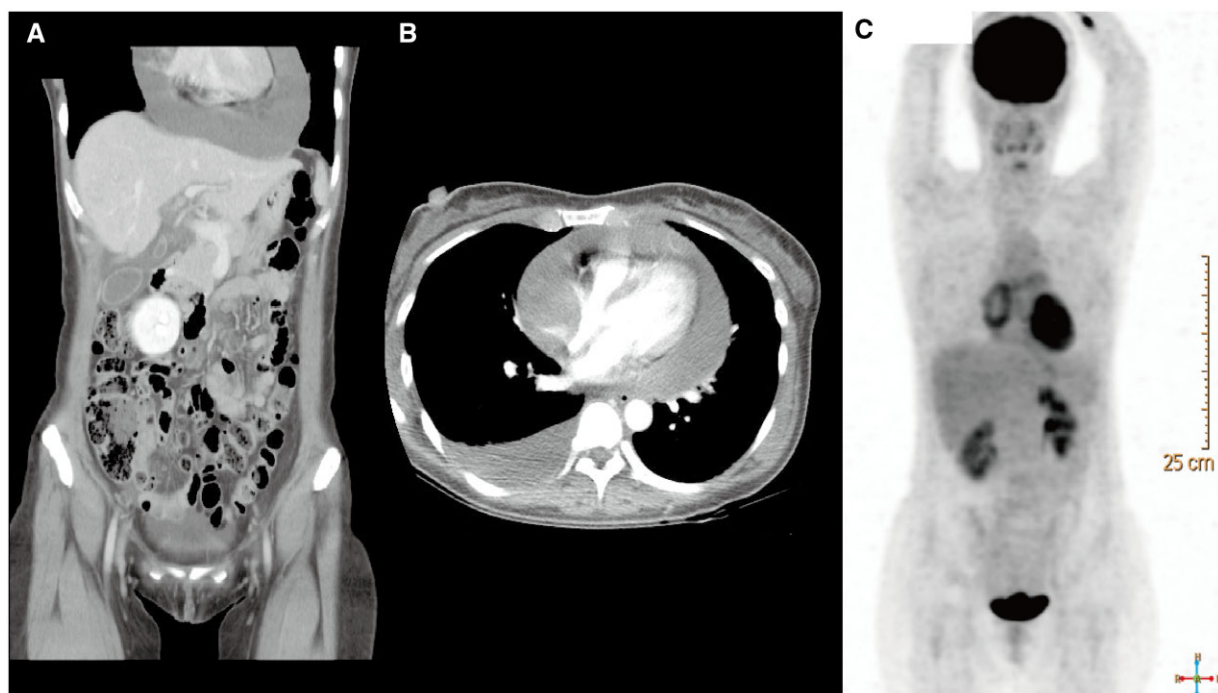


Figure 1 Images performed at 4 months before admission. (A, B) Contrast-enhanced abdominal and chest computed tomography findings showed a large pericardial effusion. (C) Fluorodeoxy-glucose-18-positron emission tomography-computer tomography scanning showed hypermetabolism only in the right cardiac region.

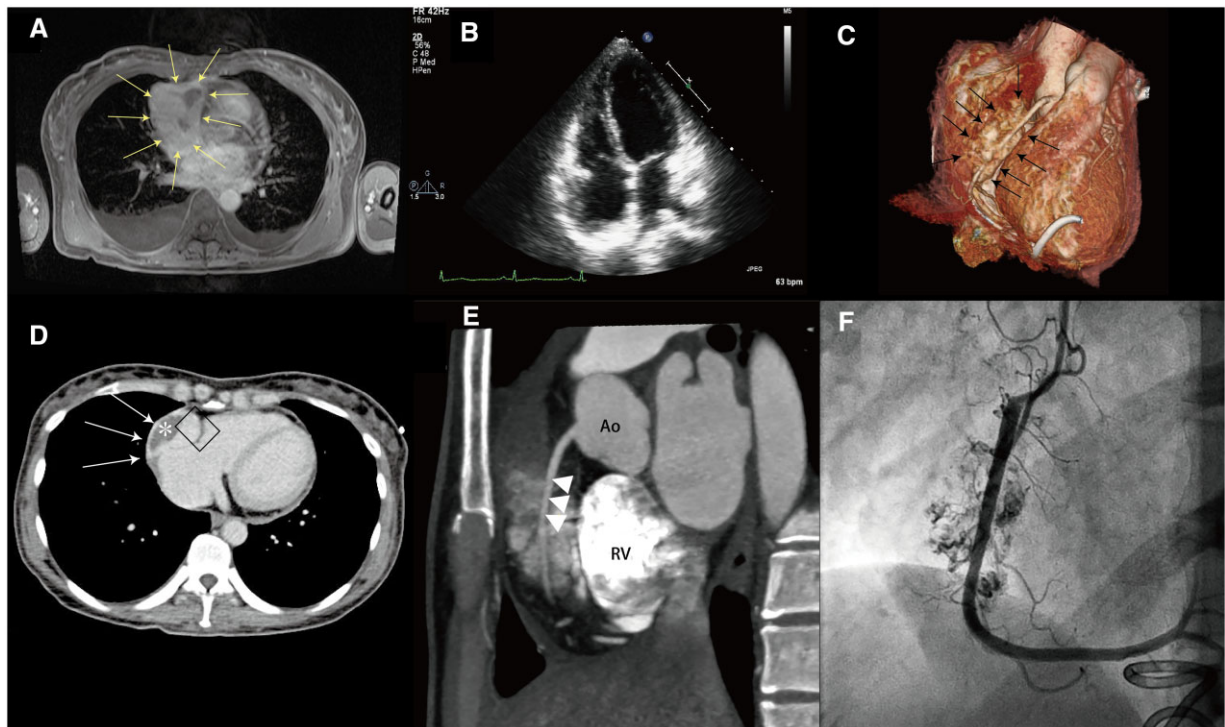
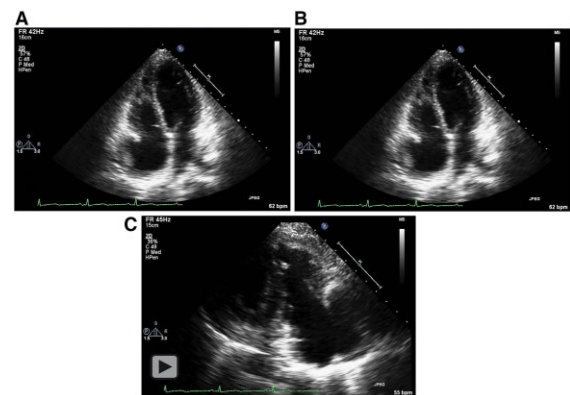


Figure 2 Cardiac magnetic resonance imaging, echocardiogram, coronary computer tomography angiography, chest computer tomography, and coronary angiography at presentation. (A) Black blood T1-weighted inversion-recovery cardiac magnetic resonance imaging with fat suppression showed a tumour in the right atrium with heterogeneous intensity (yellow arrows) and thick pericardium. (B) Apical four-chamber view showed unremarkable findings. (C) Three-dimensional reconstruction showed the tumour involving the right atrium (black arrows) and right coronary artery. (D) Non-electrocardiogram-gated chest computer tomography showed a tumour with right atrium thrombus (asterisk), right atrium anterior wall aneurysm formation (white arrows), and obliteration of fat plane at the right atrioventricular groove (black square). (E) Electrocardiogram-gated coronary computer tomography angiography showed a tumour encasing the right coronary artery (white arrowhead). (F) Coronary angiography showed multiple feeding arteries from the right coronary artery to the tumour. Ao, aorta; RV, right ventricle.

silhouette. Transthoracic echocardiography (TTE) once again showed a large pericardial effusion, and pericardiocentesis was performed. Black blood T1-weighted inversion-recovery cardiac magnetic resonance imaging (MRI) with fat suppression showed a 3.8 cm × 5.8 cm × 6.8 cm lesion arising from the right atrium (RA) with thick pericardium (Figure 2A, yellow arrows). The patient was referred to our institution for further evaluation.

At our hospital, repeat echocardiography showed minimal pericardial effusion without remarkable abnormalities (Figure 2B, Video 1). Electrocardiogram (ECG)-gated coronary CT angiography followed by non-ECG-gated chest CT using high-pitch scan mode showed a large (3.8 cm × 6 cm × 7.7 cm), cauliflower-like tumour located mainly in the RA (Figure 2C, black arrows), with inner thrombus formation (Figure 2D, white asterisk), RA anterior wall aneurysm formation (Figure 2D), and obliteration of fat plane at the right atrioventricular groove (Figure 2D, black square) and epicardial extension along with encasement of the middle portion of the right coronary artery (RCA) (Figure 2E, white arrowheads). A primary cardiac tumour was



Video 1 Transthoracic echocardiography at presentation: (A) Apical four-chamber view. (B) Modified short-axis view. (C) Right ventricle inlet view.

suspected based on previous FDG–PET–CT results. Since the tumour arose from the RA and is extended to the atrioventricular groove, initial differential diagnoses include angiosarcoma, paraganglioma, and lymphoma. Coronary angiography findings revealed multiple feeding arteries originating from the RCA to the tumour (Figure 2F). Blocking of the feeding arteries by placing a cover stent in the main trunk of the RCA up to the bifurcation of the posterior longus and posterior descending arteries was considered but not performed because of the lack of stents with a suitable size.

Thoracoscopic biopsy resulted in massive bleeding because of the high vascularity of the tumour, and conversion to thoracotomy for haemostasis after completion of biopsy was required. Biopsy within the perimeter of a pre-emptively created ring of purse-string suture was performed. Histopathology findings revealed atypical cells with mild nuclear atypia arranged in cords, small nests, glandular-like structures, and vascular channels mixed with fibrinoid material and spindle cells arranged haphazardly in a myxomatous background. Immunohistochemistry yielded positive results for CD34 and CD31 and negative for calretinin (Figure 3). Thus, the final diagnosis was angiosarcoma. Tumour resection was not performed because of the infiltrative involvement into the RA, the right ventricle, and the RCA when visualized directly during biopsy. Fluorodeoxy-glucose-18-positron emission tomography–computer tomography findings showed bilateral lung nodules, which were suspected as metastases (Figure 4, black arrowhead). The patient was treated with a combination of paclitaxel (90 mg/m²) and bevacizumab (10 mg/kg). At 10 months' follow-up, the patient received a total of 23 and 13 courses of paclitaxel and bevacizumab, respectively. Non-ECG-gated contrast-enhanced chest CT using high-pitch scan mode revealed an interval decrease of the primary tumour size (Figure 5) and a new

well-enhanced pulmonary nodule (1.2 cm) over the left upper lobe. Surgical resection of the nodule confirmed the diagnosis of metastatic angiosarcoma. At 12 months' follow-up, the patient's anti-cancer treatment was shifted to oral pazopanib (800 mg/day) after an abdominal ultrasound showed liver metastases. At 18 months' follow-up, oral pazopanib was shifted to monthly ifosfamide (1500 mg/m²) and doxorubicin (25 mg/m²) after chest CT confirmed the presence of progressive disease. Up to the present, the patient is still under active treatment.

Discussion

Angiosarcomas are more often diagnosed in males than in females (males to females: 2–3.5 to 1), and most were diagnosed before the age of 65 years.^{5,6} The most common location of primary cardiac angiosarcoma is the RA, with the clinical presentation most commonly being heart failure and pericardial effusion with or without cardiac tamponade.^{3,6} The diagnostic sensitivity of TTE was 75%, whereas pericardial fluid cytology was found to be negative in most cases.⁷ Over half (56%) of the patients had metastases upon diagnosis, and the median survival time was 13–20 months.^{6,8} Though the prognosis is poor, surgical resection with free margins can potentially cure the disease and improve survival.⁶ Other comprehensive treatments include chemotherapy, target therapy, radiotherapy, and heart transplantation.⁹

Transthoracic echocardiography is an initial modality to evaluate cardiac tumours, and angiosarcomas could be presented as a mass that infiltrate the RA free wall and protrude into the RA chamber on TTE.¹⁰ In our case, the angiosarcoma that originated from the RA

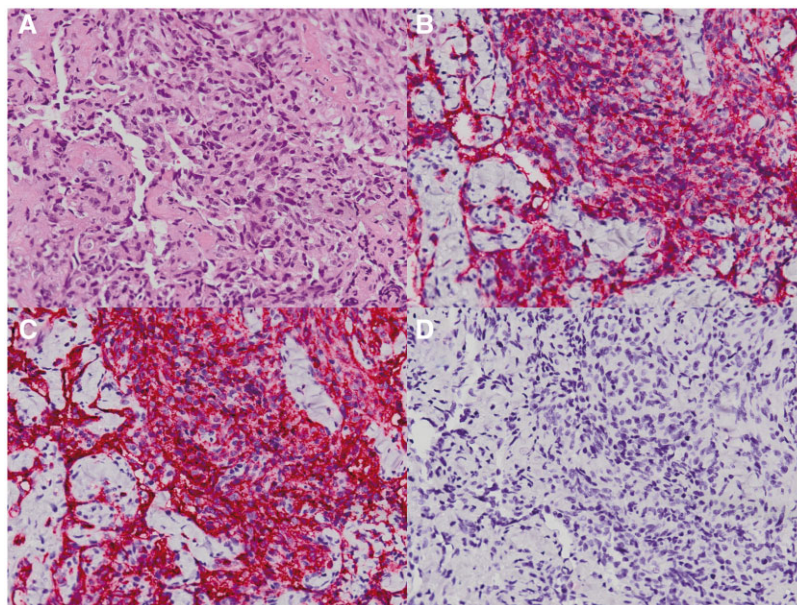


Figure 3 Histological and immunohistochemical analysis of the specimen. (A) Pleomorphic spindle cells forming atypical vascular channels. (B) Positive immunohistochemical reaction with CD34 200 \times . (C) Positive immunohistochemical reaction with CD31 200 \times . (D) Negative immunohistochemical reaction with calretinin 200 \times .

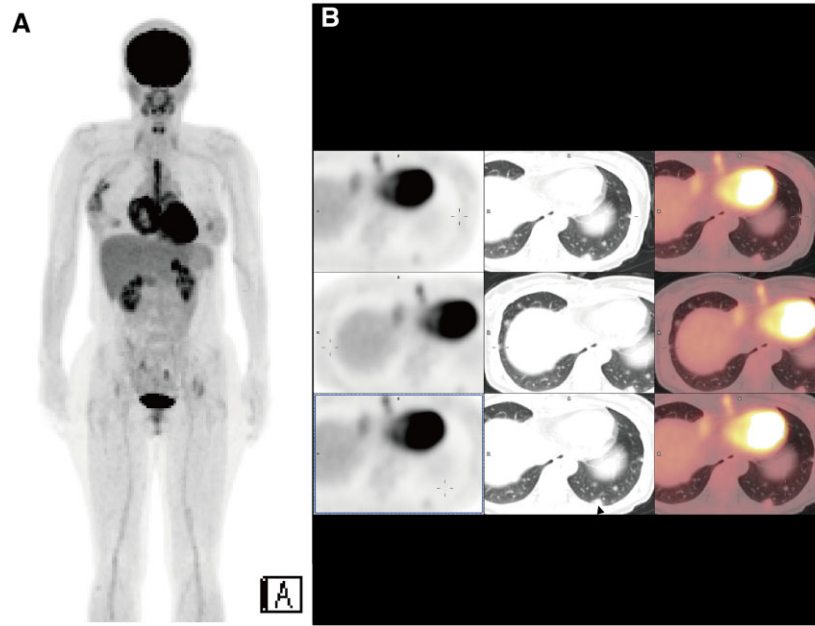


Figure 4 Fluorodeoxy-glucose-18-positron emission tomography-computer tomography at the time of diagnosis. (A) Fluorodeoxy-glucose-18-positron emission tomography-computer tomography findings showed a tumour with increased uptake in the right atrium. (B) Multiple pulmonary nodules in the left lower lobe with increased fluorodeoxy-glucose-18 uptake (black arrowhead).

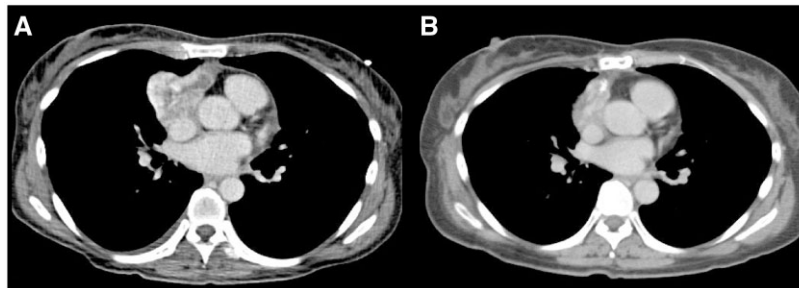


Figure 5 Non-electrocardiogram-gated chest computer tomography at presentation and at 7 months' follow-up. (A) Right atrium tumour with heterogeneous enhancement at presentation. (B) A significant decrease in the size of the tumour at 7 months' follow-up.

free wall and extending toward the pericardium was unremarkable on standard TTE views because of the absence of a mass protruding into the RA chamber.

Cardiac MRI provides a comprehensive evaluation of the cardiac mass since it provides information regarding the anatomic location of the mass, its tissue characteristics, and its relation with nearby structures. Angiosarcomas typically present with heterogeneous signals on T1- and T2-weighted images, reflecting a combination of tumour mass, tissue necrosis, and haemorrhage.¹¹

Although biopsy remains the gold standard of diagnosis of a cardiac mass, the biopsy of our patient resulted in severe haemorrhage because of the high vascularity of the tumour and severe adhesions to adjacent structures. Since over half of the patients with angiosarcoma

had metastasis at the time of diagnosis, a biopsy of metastatic lesions may also be confirmatory.¹² Transoesophageal echocardiography-guided transvenous endomyocardial biopsy has also been reported to successfully diagnose cardiac angiosarcomas¹³ and could be an alternative method to traditional methods.

No standardized systemic therapy regimens exist for cardiac angiosarcomas. Weekly paclitaxel and bevacizumab, oral pazopanib, and monthly ifosfamide plus doxorubicin have all been shown as an active regimen and are in line with major guidelines.^{14,15} The tumour response of our patient was well.

Surgery with or without clear margins has been shown to improve the prognosis of cardiac angiosarcomas.⁶ The goal of our treatment is to reduce the size of the tumour to enable the patient to undergo

surgery. Radiotherapy has been shown to improve the long-term survival of patients with primary cardiac angiosarcomas¹⁶ but may cause fibrosis of the area and complicate the future surgery process. Therefore, radiotherapy was not ordered for our patient.

Stent graft placement in the left circumflex coronary artery had been reported to successfully treat cardiac haemangioma with tumour blush.¹⁷ Though evidence of blocking the feeding arteries of primary cardiac angiosarcomas is currently lacking, it may be combined with systemic therapy to debulk the tumour so that surgical resection may be possible, since surgical resection remains the treatment that warrants the best prognosis.⁶

In conclusion, a refractory bloody pericardial effusion in the absence of an obvious cause should prompt the clinicians to search for tumours involving the pericardium that may be obscured on standard TTE views. The combination of tumours arising from the RA and in close proximity to the atrioventricular groove and encasement of and stealing blood from the RCA should raise the suspicion of cardiac angiosarcoma. Once suspected, imaging studies to identify possible metastases should be conducted, because metastases could serve as alternatives to the primary tumour for tissue proof. Biopsy of cardiac angiosarcoma carries bleeding risks because of its high vascularity. Thoracoscopic biopsy is a reasonable option because it is less invasive. Although surgical resection could not be performed on our patient, the combination of chemotherapy and targeted therapy successfully improved our patient's survival.

Lead author biography



Jian-Kuan Yeh graduated from the National Cheng Kung University College of Medicine in Taiwan in 2017. He is currently a junior internal medicine resident at National Cheng Kung University Hospital. His field of interest includes cardiac imaging, pulmonary embolism, and cardio-oncology.

Supplementary material

Supplementary material is available at *European Heart Journal—Case Reports online*.

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as [Supplementary data](#).

Consent: The authors confirm that written consent for submission and publication of this case report including images and asso-

ciated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: none declared.

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References

- Centofanti P, Di Rosa E, Deorsola L, Dato GM, Patane F, La Torre M et al. Primary cardiac tumors: early and late results of surgical treatment in 91 patients. *Ann Thorac Surg* 1999;**68**:1236–1241.
- Kodali D, Seetharaman K. Primary cardiac angiosarcoma. *Sarcoma* 2006;**2006**:39130.
- Patel SD, Peterson A, Bartczak A, Lee S, Chojnowski S, Gajewski P et al. Primary cardiac angiosarcoma - a review. *Med Sci Monit* 2014;**20**:103–109.
- Isambert N, Ray-Coquard I, Italiano A, Rios M, Kerbrat P, Gauthier M et al. Primary cardiac sarcomas: a retrospective study of the French Sarcoma Group. *Eur J Cancer* 2014;**50**:128–136.
- Antonuzzo L, Rotella V, Mazzoni F, Doni L, Bianchini D, Garbini F et al. Primary cardiac angiosarcoma: a fatal disease. *Case Rep Med* 2009;**2009**:591512.
- Look Hong NJ, Pandalai PK, Hornick JL, Shekar PS, Harmon DC, Chen YL et al. Cardiac angiosarcoma management and outcomes: 20-year single-institution experience. *Ann Surg Oncol* 2012;**19**:2707–2715.
- Kupsky DF, Newman DB, Kumar G, Maleszewski JJ, Edwards WD, Klarich KW. Echocardiographic features of cardiac angiosarcomas: the Mayo Clinic experience (1976–2013). *Echocardiography* 2016;**33**:186–192.
- Ramlawi B, Leja MJ, Abu Saleh WK, Al Jabbari O, Benjamin R, Ravi V et al. Surgical treatment of primary cardiac sarcomas: review of a single-institution experience. *Ann Thorac Surg* 2016;**101**:698–702.
- Uberfuhr P, Meiser B, Fuchs A, Schulze C, Reichenspurner H, Falk M et al. Heart transplantation: an approach to treating primary cardiac sarcoma? *J Heart Lung Transplant* 2002;**21**:1135–1139.
- Bouma W, Lexis CPH, Willems TP, Suurmeijer AJH, van der Horst ICC, Ebels T et al. Successful surgical excision of primary right atrial angiosarcoma. *J Cardiothorac Surg* 2011;**6**:47.
- Motwani M, Kidambi A, Herzog BA, Uddin A, Greenwood JP, Plein S. MR imaging of cardiac tumors and masses: a review of methods and clinical applications. *Radiology* 2013;**268**:26–43.
- Liu C, Zhao Y, Yin Z, Hu T, Ren J, Wei J et al. Right atrial epithelioid angiosarcoma with multiple pulmonary metastasis confirmed by multimodality imaging-guided pulmonary biopsy: a case report and literature review. *Medicine (Baltimore)* 2018;**97**:e11588.
- Hammoddeh AJ, Chaaban F, Watson RM, Millman A. Transesophageal echocardiography-guided transvenous endomyocardial biopsy used to diagnose primary cardiac angiosarcoma. *Cathet Cardiovasc Diagn* 1996;**37**:347–349.
- Ray-Coquard IL, Domont J, Tresch-Bruneel E, Bompas E, Cassier PA, Mir O et al. Paclitaxel given once per week with or without bevacizumab in patients with advanced angiosarcoma: a randomized phase II trial. *J Clin Oncol* 2015;**33**:2797–2802.
- Network NCC. NCCN clinical practice guidelines in oncology: soft tissue sarcoma (Version 2.2020). https://www.nccn.org/professionals/physician_gls/pdf/sarcoma.pdf. (20 January 2020)
- Zhang C, Huang C, Zhang X, Zhao L, Pan D. Clinical characteristics associated with primary cardiac angiosarcoma outcomes: a surveillance, epidemiology and end result analysis. *Eur J Med Res* 2019;**24**:29.
- Liao CT, Shih JY, Chen ZC, Chang JM, Wu WL, Wu WS. Management of a primary cardiac neoplasm with tumor blush by a stent graft. *Acta Cardiol Sin* 2015;**31**:164–167.