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GRAND ROUND
Heart failure

A mimicker of constriction: a case report of a rare case of cardiac angiosarcoma

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Background Cardiac angiosarcoma is an exceptionally rare primary malignant tumour with an aggressive course and typically poor prognosis. Diagnosis is difficult, and patients often present with metastatic disease. We report the rare case of a patient with cardiac angiosarcoma who presents with constrictive physiology due to tumour encasement.

Case summary A 65-year-old female with a past medical history of Hodgkin's lymphoma and limited scleroderma presented with progressive dyspnoea on exertion. Multimodality imaging and haemodynamics with echocardiography, cardiac magnetic resonance imaging (MRI), and cardiac catheterization showed findings of constrictive physiology. Cardiac MRI showed areas of pericardial enhancement, so she was initially started on colchicine, prednisone, and mycophenolate mofetil to treat pericardial inflammation. However, her symptoms progressed, and she underwent pericardiectomy with cardiac surgery. Pericardium was noted to be thickened and a mass-like substance was densely adherent and potentially invading the heart itself and could not be dissected free. Surgical pathology showed features consistent with epithelioid angiosarcoma. Patient had rapid progression of her disease and was started on chemotherapy. Her course, however, was complicated by acute gastrointestinal bleeding, atrial fibrillation with rapid rates, and persistent volume overload. She elected for comfort measures and passed away shortly after her diagnosis.

Discussion Our case shows an extremely rare diagnosis, cardiac angiosarcoma, presenting with typical findings of constrictive physiology. The case shows the typical features of constrictive physiology using multimodality imaging and haemodynamics and emphasizes the need to always think broadly in creating a differential diagnosis for constriction to ensure that rare diseases are considered.

Keywords Constrictive • Multimodality imaging • Haemodynamics • Cardio-oncology • Case report

ESC Curriculum 2.1 Imaging modalities • 2.2 Echocardiography • 2.3 Cardiac magnetic resonance • 6.6 Pericardial disease • 6.8 Cardiac tumours

Learning points

To understand the typical features of constrictive physiology using multimodality imaging and haemodynamics.
To recognize cardiac angiosarcoma as a rare aetiology of constrictive physiology.
To realize the need to always think broadly when creating a differential diagnosis to ensure rare diseases are considered.

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Introduction

Cardiac angiosarcoma is an extremely rare and aggressive primary cardiac malignancy with typically poor prognosis.[1–3] Symptoms are typically non-specific and are associated with recurrent pericardial effusions and invasion of adjacent structures. We report a case of a patient with cardiac angiosarcoma who presented with progressive dyspnoea on exertion and was found to have constrictive physiology, initially presumed to be due to calcific constrictive pericarditis. With this case report, we aim to not only show the typical findings of constrictive physiology using multimodality imaging and haemodynamics but also to demonstrate cardiac angiosarcoma as an aetiology of constriction that has only rarely been reported in the literature.[4,5]

Timeline

Time point	Event
April 2020	Symptom onset. Patient began experiencing dyspnoea on exertion and shoulder pain. She initially attributed these symptoms to her kyphosis.
August 2020	Symptoms worsened. Presented to an outside institution and found to have large pericardial effusion with tamponade physiology and underwent pericardial window. Pericardial fluid negative for infection or malignancy. Started on colchicine for pericardial inflammation.
December 2020	Symptom recurrence. Patient started having worsening palpitations and shortness of breath on exertion with decreasing exercise tolerance.
March 2021	Patient presented to our institution. She underwent repeat transthoracic echocardiogram, cardiac magnetic resonance imaging, and cardiac catheterization with findings consistent with constrictive physiology.
April 2021	Patient seen by Rheumatology. Patient was continued on colchicine and sequentially started on prednisone and mycophenolate mofetil for pericardial inflammation.
May 2021	Patient admitted with persistent heart failure symptoms. She underwent pericardiectomy with cardiac surgery. Surgical pathology showed cardiac angiosarcoma. Hospital course post-operatively was complicated by volume overload, and she was diuresed aggressively with intravenous diuretics. Oncology was consulted, but palliative chemotherapy deferred for 3 weeks to allow time for wound healing.
June 2021	Patient was re-admitted with worsening heart failure symptoms. Repeat cardiac magnetic resonance imaging showed progression of disease. Started on inpatient chemotherapy, but course complicated by acute gastrointestinal bleeding, atrial fibrillation, and persistent volume overload. Patient and family elected for comfort measure. Patient passed away.

Case presentation

A 65-year-old female presented with a 3-month history of progressive exertional dyspnoea. The patient's past medical history was notable for a history of a large pericardial effusion surgically managed with the formation of a pericardial window, Hodgkin's lymphoma (diagnosed in 1986 and subsequently requiring surgical treatment, high-dose mantle radiation therapy, and chemotherapy), limited scleroderma, and paroxysmal atrial fibrillation. One year prior to her current presentation, the patient began experiencing symptoms of dyspnoea on exertion and shoulder pain that she initially attributed to deconditioning during the Coronavirus disease of 2019 (COVID-19) pandemic and her long-standing kyphosis. After 3 months of progressive symptoms, she presented to the Emergency Department and was noted to have a large pericardial effusion complicated by cardiac tamponade and underwent a pericardial window. Pericardial fluid studies at that time were negative for malignant cells or infection. Surgical pathology showed acute neutrophilic and chronic lymphocytic inflammatory infiltrates, but no diagnostic evidence of a lymphoproliferative disorder or of malignancy. She developed post-operative atrial fibrillation and was placed on amiodarone. She was prescribed colchicine for pericardial inflammation. She did well until 3 months prior to her current presentation when she had recurrent shortness of breath, lower extremity oedema, and palpitations and presented to our cardiology clinic for a second opinion. Transthoracic echocardiography (TTE) at an outside institution showed a left ventricular (LV) ejection fraction of 55%, septal wall dyskinesia, and moderate tricuspid regurgitation. There was no pericardial effusion. Myocardial perfusion imaging showed no evidence of inducible ischaemia. Holter monitor showed frequent episodes of atrial fibrillation with arrhythmia burden of 26% in 24 h. Physical exam was notable for 1+ bilateral lower extremity oedema. Cardiac ausculation was normal. Lungs were clear to auscultation bilaterally. Laboratory studies showed normal blood counts, electrolytes, and kidney function. Constrictive pericarditis secondary to prior radiation use was suspected vs. secondary to underlying autoimmune disease.

Transthoracic echocardiography was repeated at our institution and showed normal global left ventricular (LV) function and reduced right ventricular function (by visual estimate). There was septal flattening suggestive of right ventricular overload and a septal bounce in some beats suggestive of constrictive physiology (see *Figure 1A* and *B*). There was a small, localized pericardial effusion posterior to the LV and pericardial thickening measuring up to 0.8 cm anterior to the right ventricle (RV). There was also marked respirophasic variability of the transmitral diastolic velocities consistent with constrictive physiology (see *Figure 1C*). She also underwent cardiac magnetic resonance imaging (MRI) that showed diffusely thickened pericardium (maximum thickness 0.7–0.8 cm) with pericardial enhancement suggestive of inflammation or pericarditis. There was exaggerated septal motion suggestive of constrictive physiology. Finally, the patient underwent right and left heart catheterization that showed an increase in superior vena cava pressures with deep inspiration (consistent with Kussmaul's sign), right atrial pressure waveform with W-pattern and prominent x- and y-descents, right ventricular waveform with intermittent dip and plateau during diastole (consistent with square root sign), and on simultaneous LV and RV pressure tracings, evidence of systolic pressure discordance with inspiration (see *Figure 2*). These were all consistent with constrictive physiology.

Patient was seen by Rheumatology and restarted on colchicine given pericardial inflammation noted on MRI and started on prednisone 20 mg daily for recurrent pericarditis. Given concern for an autoimmune component, she was started on mycophenolate mofetil 500 mg twice a day as a trial of medical therapy. Despite this therapy, the patient had progressively worsening symptoms and soon after required readmission to the hospital. Cardiothoracic surgery was consulted, and she underwent pericardial stripping due to persistent symptoms. Pre-operatively, patient underwent computed tomography scan of her chest to assess the degree of

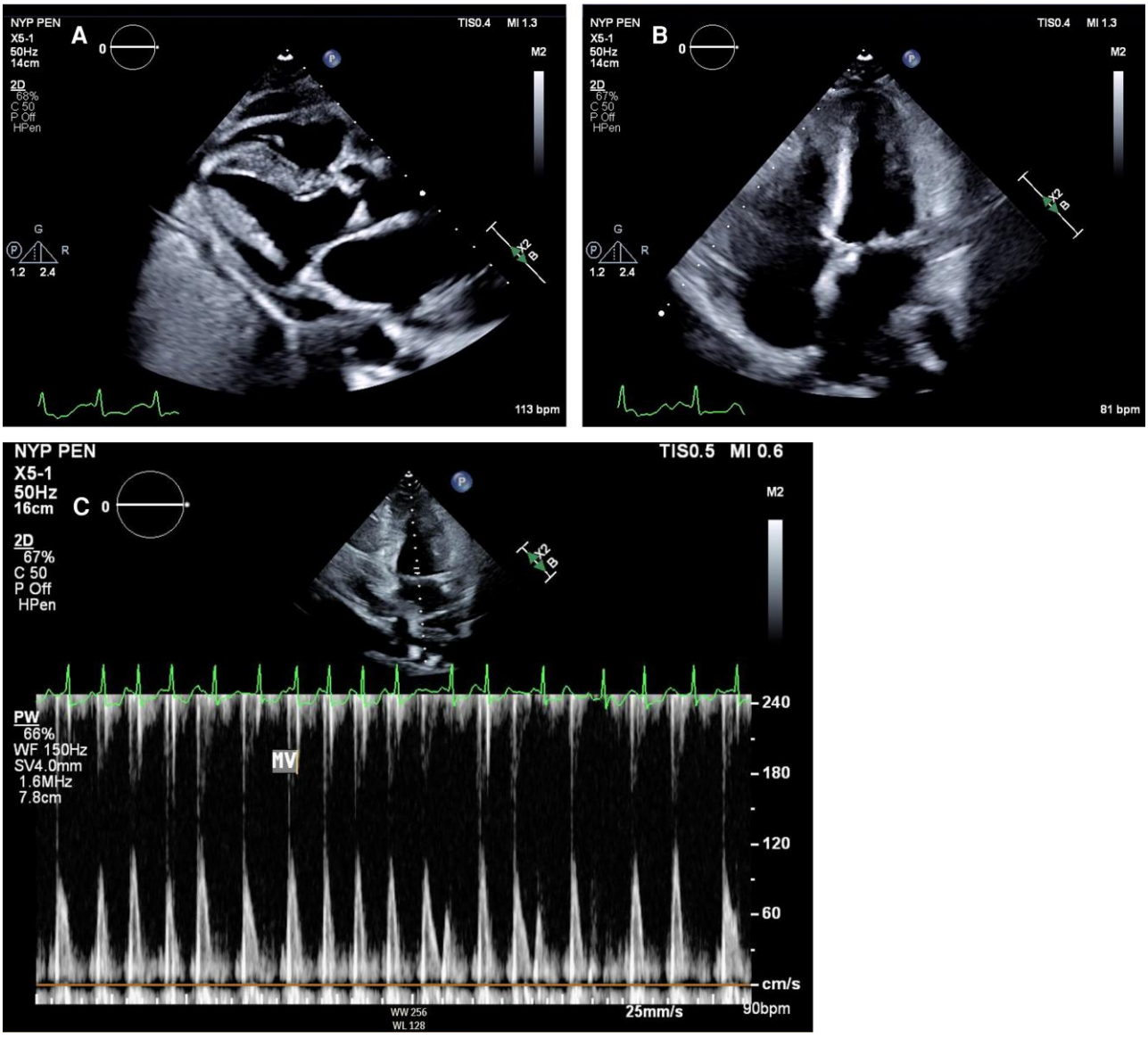

Figure 1 Transthoracic echocardiogram. (*A*) Parasternal long-axis view showing normal left ventricle function and small localized pericardial effusion posterior to the left ventricle. Pericardial thickening measuring up to 0.8 cm anterior to the right ventricle. Septal flattening suggesting right ventricular overload. (*B*) Four-chamber view showing a septal bounce in some views. See videos in Supplementary material online, *Files*. (*C*) Transmitral diastolic velocities showing marked respirophasic variation consistent with constrictive physiology.

pericardial thickening and showed circumferential nodular thickening of the pericardium and a more focal mass-like area within the left superior mediastinum that was thought to represent a component of pericardial thickening or secondary to prior left upper lobe surgery radiation. Haematology/Oncology was consulted regarding whether these findings could be due to a recurrence of her Hodgkin's lymphoma. They believed this was unlikely in the absence of lymphadenopathy or organomegaly. In the operating room, the anterior pericardium was noted to be thickened with loculated masses on the pericardium. The pericardium was pliable and did not have the fibrous appearance usually associated with pericardial constriction. There were also irregular, lobulated, and firm epicardial masses on the anterior surface of the heart. The mass-like substance on the epicardial surface of the heart was densely adherent and potentially invading the heart itself and could not be completely dissected (see *Figure 3*). Pathology of surgical specimens showed tumour composed of epithelioid cells and high-grade sarcoma positive for vimentin, ERG, and CD34 and negative for calretinin and Wilms' tumor 1 (WT-1). This supported a diagnosis of a high-grade sarcoma with epithelioid features consistent with epithelioid angiosarcoma (see *Figure 4*).

Post-operatively, oncology was consulted and recommended palliative systemic chemotherapy, but decision was made to wait 3 weeks to allow for wound healing following her surgery. She was discharged home on high-dose bumetanide but continued to have volume overload and was readmitted to the hospital for acute decompensated heart failure. Repeat cardiac MRI was obtained and showed significant progression of disease with pericardial thickening that extended throughout the inferior and superior aspects of the pericardium and

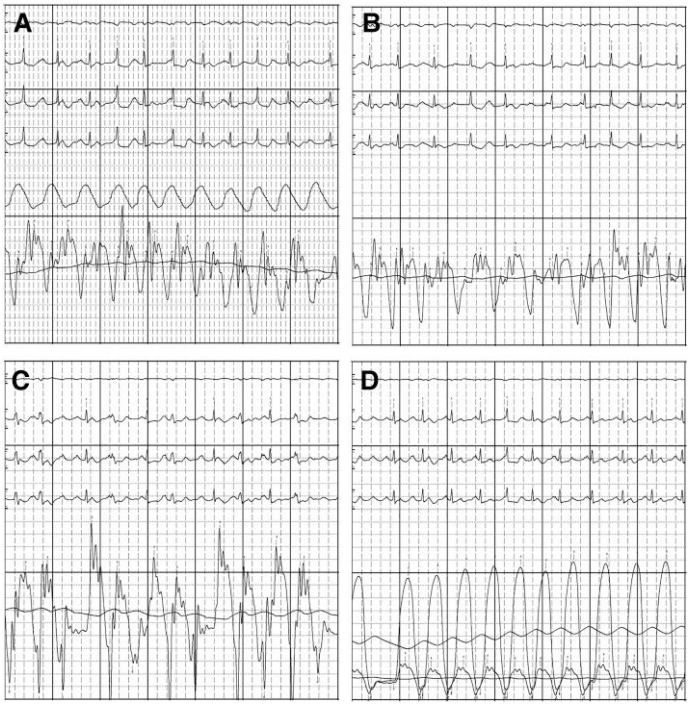

Figure 2 Cardiac catheterization. (*A*) Superior vena cava pressure wave form showing an increase with deep inspiration consistent with Kussmaul's sign. (*B*) Right atrial pressure waveform with W-pattern and prominent x- and y-descents. (*C*) Right ventricular waveform with intermittent dip and plateau during diastolic consistent with square root sign. (*D*) Simultaneous left ventricular and right ventricular pressure tracing showing evidence of systolic pressure discordance with inspiration (ventricular interdependence).

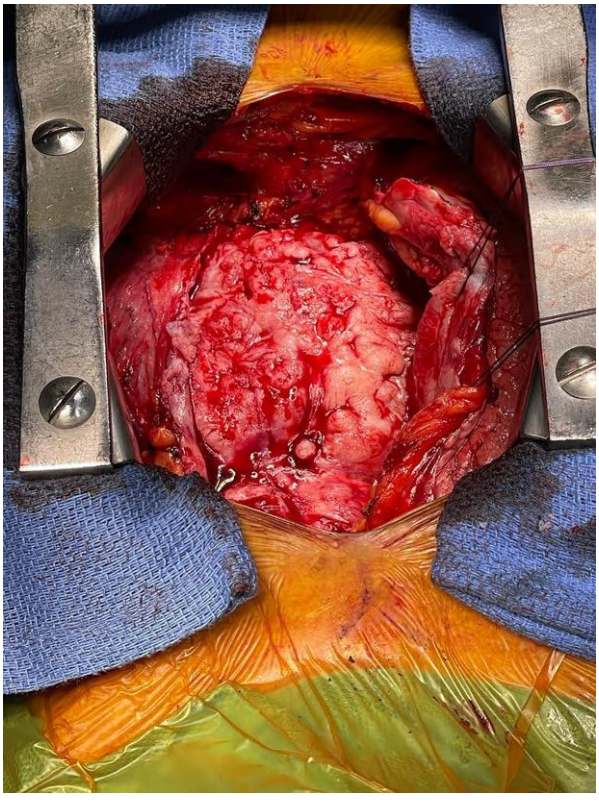

Figure 3 Intraoperative findings. Intraoperative images showing irregular, lobulated, firm epicardial masses along most of the anterior surface of the heart.

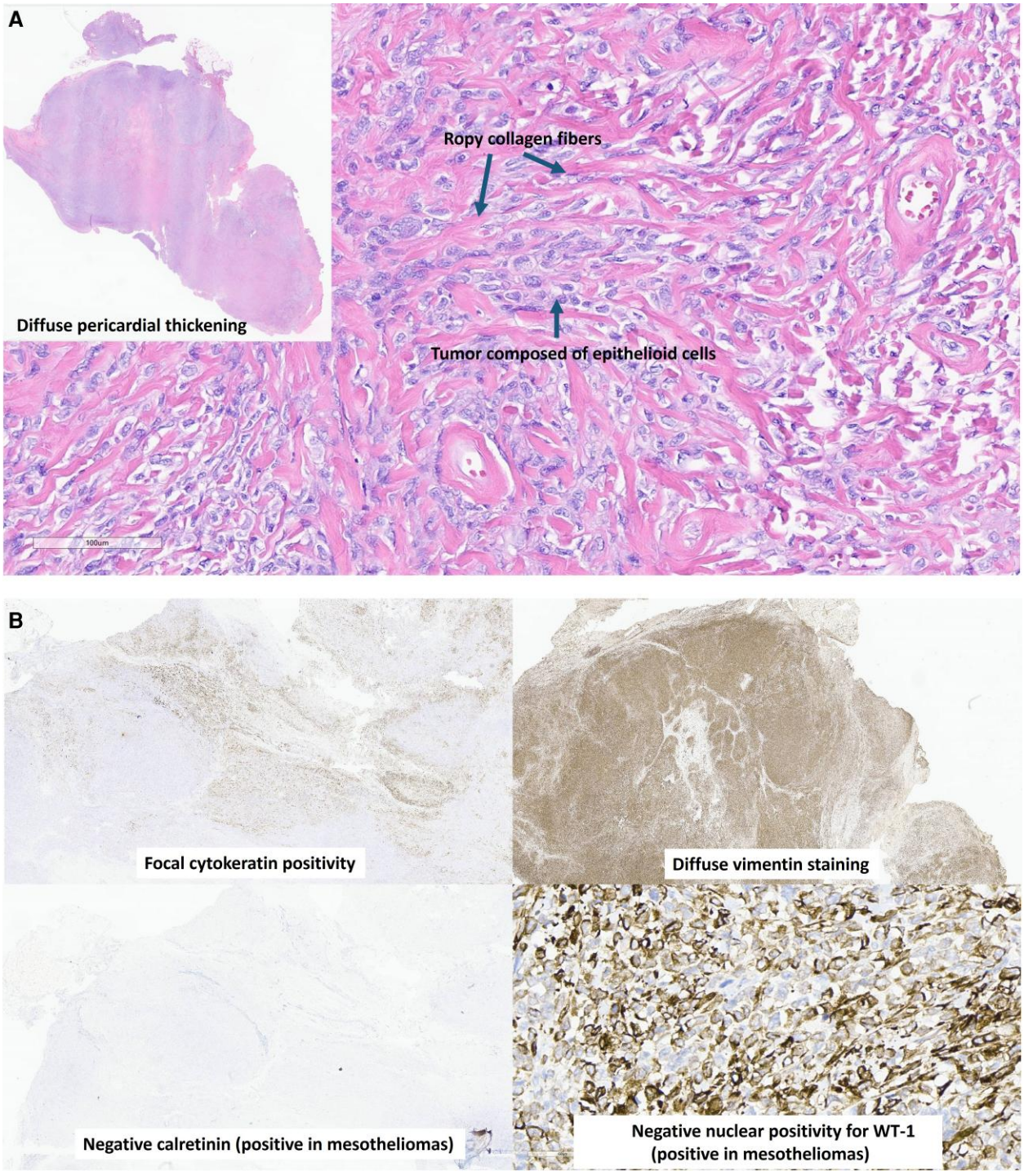

Figure 4 Surgical pathology. (*A*) Surgical pathology showed pericardial thickening with ropy collagen fibres and tumour composed of epithelioid cells. (*B*) Immunohistochemical staining showed positivity for endothelial markers found in sarcomas (cytokeratin and vimentin) and negative for epithelial markers seen in mesotheliomas (calretinin and Wilms' tumor 1 [WT-1]).

surrounded the great vessels (see *Figure 5*). Given her persistent and progressive symptoms, constrictive physiology was most likely secondary to encasement of heart in tumour, not pericarditis. Given rapid progression of disease, she was started on inpatient chemotherapy with gemcitabine and docetaxel, but course was complicated by acute gastrointestinal bleeding, atrial fibrillation with rapid ventricular rates, and persistent volume overload. Goals of care were discussed with family, and decision was made to transition to comfort measures. The patient passed away comfortably with her family present at the bedside.

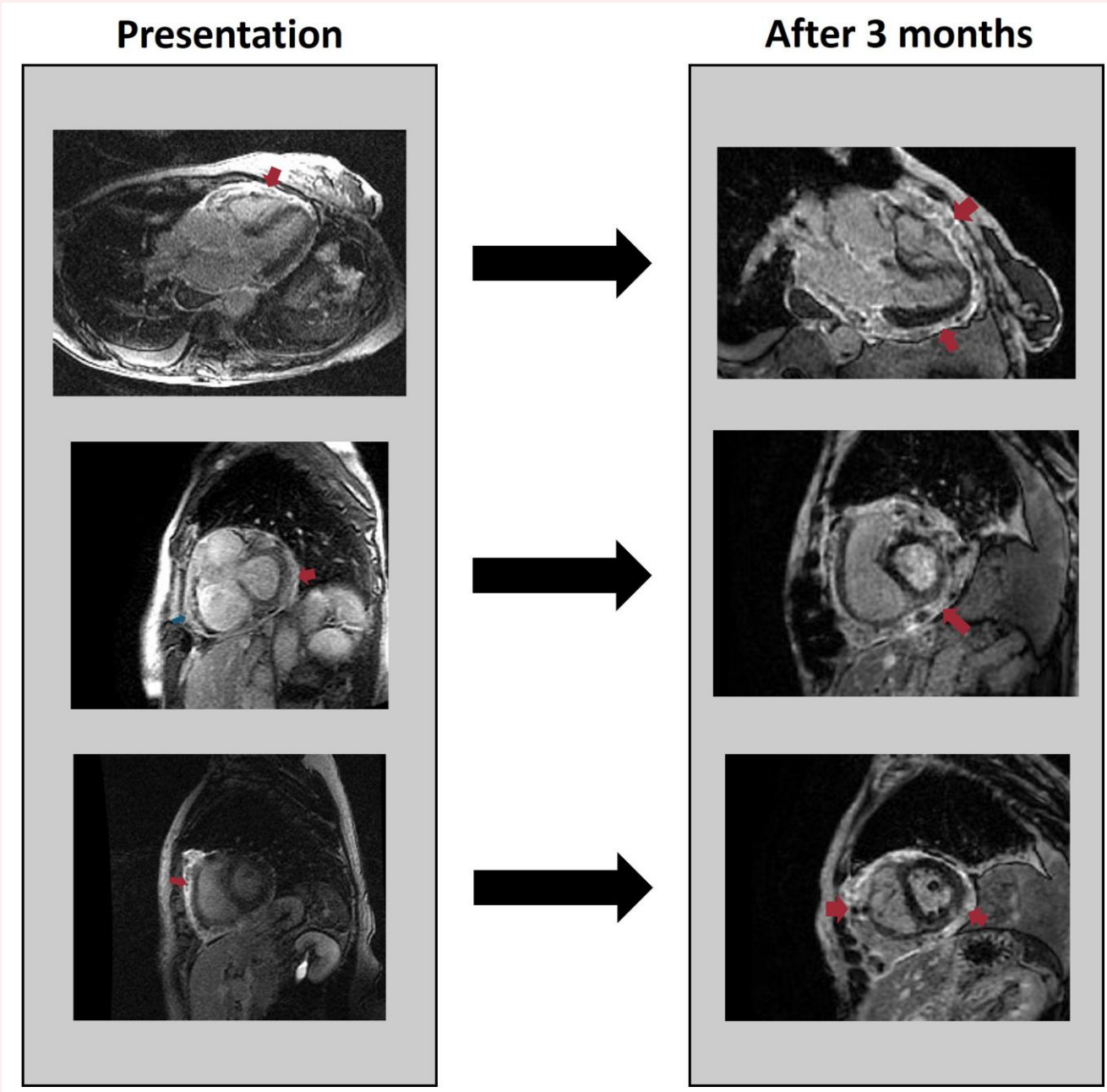

Figure 5 Cardiac magnetic resonance imaging. Cardiac magnetic resonance imaging at initial presentation and 3 months into patient's course. Initial magnetic resonance imaging showed diffusely thickened pericardium with pericardial enhancement suggestive of inflammation. Repeat scan showed increase in pericardial thickening (0.7–1.4 cm anterior thickness) and prominent pericardial enhancement together with scattered areas of hypo-enhancements, consistent with neoplasm. The representative images shown below are T1-weighted late gadolinium enhancement sequences.

Discussion

This is a rare case of constrictive physiology secondary to epithelioid angiosarcoma, confirmed by post-operative pathology. Prior to surgery, the patient's constrictive physiology was thought to be due to pericarditis secondary to her history of mediastinal radiation therapy or her underlying rheumatologic condition; however, an alternate aetiology was confirmed with surgical pathology.

Cardiac angiosarcomas, the most common primary malignant cardiac tumours, are exceptionally rare with rates of 0.0002–0.03% on autopsy series.[1] The most common aetiologies are exposure to vinyl chloride or mediastinal radiation.[2,3,5] Given that aggressive tumours have an initial silent evolution, metastatic disease is common at the time of diagnosis.[2,3] Symptoms, although non-specific, are associated with recurrent pericardial effusions, pericarditis, and invasion of adjacent structures and include progressive dyspnoea, chest pain, and malaise.[2] The diagnosis is difficult to make since repeated pericardiocentesis often fails to exhibit malignant cells and TTE usually fails to show an echogenic mass.[1,3] Mean survival is typically only 6–14 months and tumours generally respond poorly to chemotherapy and radiation.[2,3] Chemotherapeutic regimens can

include adriamycin, ifosfamide, cyclophosphamide, vincristine, or dacarbazine.[6] Cardiac transplantation has been reported if extracardiac metastases are not present, but outcomes remain poor with mean survival of 12 months.[7]

Conclusions

Cardiac angiosarcoma is a rare aetiology of constrictive physiology. Diagnosis can be difficult due to silent evolution of disease and prognosis is typically poor. The diagnosis should be considered if there is a prior history of mediastinal radiation.

Lead author biography

Adam Vohra is a fourth-year cardiovascular disease fellow at New York-Presbyterian Weill Cornell Medicine. His research interests include the interaction between health care policy and cardiovascular outcomes, specifically the effects of hospital market concentration. Prior to fellowship, Dr Vohra completed internal medicine residency at the University of Chicago. He also received his medical doctorate (MD) and Master of Business Administration (MBA) at the University of Chicago Pritzker School of Medicine and Booth School of Business, respectively. He received a Bachelor of Arts from Northwestern University. He plans to start subspeciality training in interventional cardiology at Weill Cornell Medicine in July 2023.

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: Written consent for submission and publication of this case report, including images, was obtained from the patient's next of kin in accordance with Committee on Publication Ethics (COPE) guidelines.

Conflict of interest: No conflicts of interests relevant to the contents of this article.

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Data availability

The data underlying this article are available in the article and in its online supplementary material.

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