

A case report of primary cardiac intimal sarcoma presenting with atrial fibrillation and a left atrial mass

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Background

Intimal sarcoma is an exceedingly rare type of primary cardiac tumour. It is characterized by poorly differentiated spindle-shaped cells that can mimic smooth muscle and is strongly associated with MDM2 genetic amplification. Owing to its rarity and non-distinctive histological features, diagnosis remains a significant challenge.

Case summary

In this case report, we describe a case of primary cardiac intimal sarcoma in a 37-year-old woman who presented with atrial fibrillation (AF) and a left atrial mass. Despite having a histological sample from an excised left atrial mass, the diagnosis was not made until she presented with back pain secondary to metastatic disease to the spine.

Discussion

Primary cardiac intimal sarcoma is an extremely rare diagnosis. The mainstay management of intimal cardiac sarcoma is aggressive surgical resection. Unfortunately, the prognosis of cardiac sarcomas remains very poor, with a mean survival between 3 months and 1 year. This case of cardiac intimal sarcoma highlights the difficulty in establishing a diagnosis, particularly given the unusual presentation of AF.

Keywords

Intimal sarcoma • Cardio-oncology • Cardiac tumour • Atrial fibrillation • Case report

ESC Curriculum

2.2 Echocardiography • 2.3 Cardiac magnetic resonance • 5.3 Atrial fibrillation • 6.8 Cardiac tumours

Learning points

- Despite being a rare aetiology, primary cardiac intimal sarcoma should be considered on the differential of atrial masses.
- Intimal cardiac sarcoma can present with atrial fibrillation as one of the first signs.
- Diagnosis of primary intimal cardiac sarcoma is largely based on MDM2 overexpression.

Introduction

Intimal sarcoma is an exceedingly rare type of primary cardiac tumour. It is characterized by poorly differentiated spindle-shaped cells that can mimic smooth muscle and is strongly associated with MDM2 genetic amplification.¹ Owing to its rarity and non-distinctive histological features, diagnosis remains a significant challenge. In this case report, we describe a case of primary cardiac intimal sarcoma in a 37-year-old woman who presented with atrial fibrillation (AF).

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Timeline

February 2017	The patient was referred to the electrophysiology service for management of paroxysmal atrial fibrillation.
March 2017	An attempt at pulmonary vein isolation was attempted, but the procedure was aborted due to an extremely thick septum.
June 2017	Transoesophageal echocardiogram revealed a sheet-like mass lining the left atrium, suspicious for a thrombus.
June 2018	A cardiac magnetic resonance imaging (MRI) characterized a 4.7×1.3 cm mass in the atrium, believed to be an atrial myxoma.
January 2019	The patient underwent radical excision of the left atrial mass. She was discharged on postoperative day #6.
April 2019	Repeat cardiac MRI revealed complete resection of the left atrial mass, believed to be an organizing thrombus.
May 2020	The patient presented with back pain secondary to T10 and L1 pathological fractures. She underwent vertebral body biopsies and vertebroplasty. Initial pathology suggested a diagnosis of metastatic leiomyosarcoma.
June 2020	Repeat MRI revealed interval increase in the spinal canal encroachment at T10 and L1 vertebral bodies. She underwent surgical decompression and instrumental fusion of the affected vertebral levels.
August 2020	Pathological review of the left atrial mass and vertebral biopsies confirmed the diagnosis of high-grade intimal sarcoma.
September 2020	The patient underwent 6 weeks of stereotactic body radiation therapy.
February 2021	The patient presented with shortness of breath secondary to a large right pleural effusion. Repeat MRI shows progression of an anterior paraspinous soft tissue mass at the T10 and L1 level.
February 2021	The patient was started on an anthracycline-based chemotherapy regimen, including Adriamycin/Ifosfamide mesna for palliation.

Case presentation

A 37-year-old woman was referred to the cardiac electrophysiology service for management of paroxysmal AF. Her past medical history was significant for a remote cholecystectomy. Cardiovascular and respiratory examination did not reveal any abnormal finding. A pulmonary vein isolation ablation was attempted, but an extremely thick inter-atrial septum precluded transseptal puncture and access to the

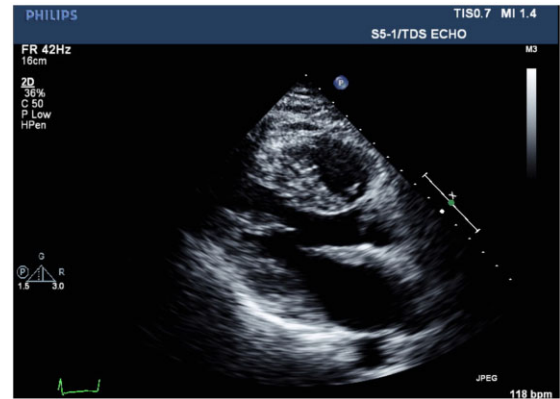


Figure 1 Transthoracic echocardiogram showing a parasternal long-axis view of a thickened anterior mitral valve leaflet and an anterior left atrial wall.

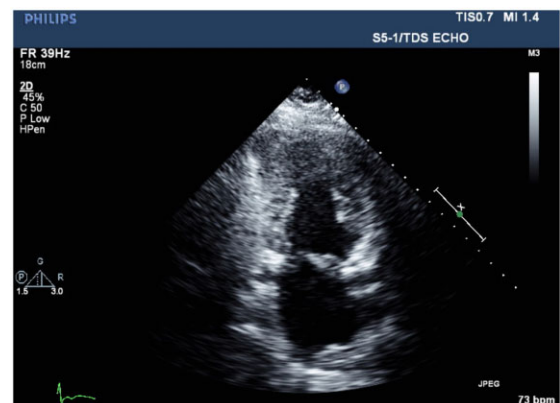


Figure 2 Transthoracic echocardiogram showing an apical two-chamber view of a thickened anterior mitral valve leaflet.

left atrium. The patient's AF was managed with propafenone in the interim.

Transthoracic and transoesophageal echocardiogram revealed a clot-like mass lining almost the entire left atrium, extending into the left atrial appendage (Figures 1–6). A second opinion from a specialist in echocardiography concluded that the differential diagnoses included thrombus, fat, or tumour, and recommended a cardiac magnetic resonance imaging (CMR) for further characterization. Cardiac magnetic resonance imaging revealed a sheet-like mass adherent to the septal side of the left atrial cavity, measuring 4.7×1.3 cm (Figure 7). The mass is isointense to myocardium on pre-contrast T1 imaging, mildly hyperintense to myocardium on the T2-weighted sequence and hyperintense on Short-T1 Inversion Recovery (Figures 7–9). Based on the signal characteristics and enhancement, although the elongated sessile appearance was noted to be atypical, the conclusion was that the mass was most in keeping with an atrial myxoma. The patient underwent open cardiac surgery and excision of the atrial

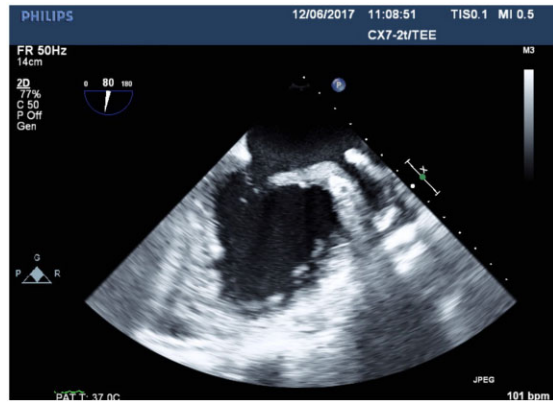


Figure 3 Transoesophageal echocardiogram showing a mid-oesophageal view of a thickened anterior mitral valve leaflet and left atrial appendage.

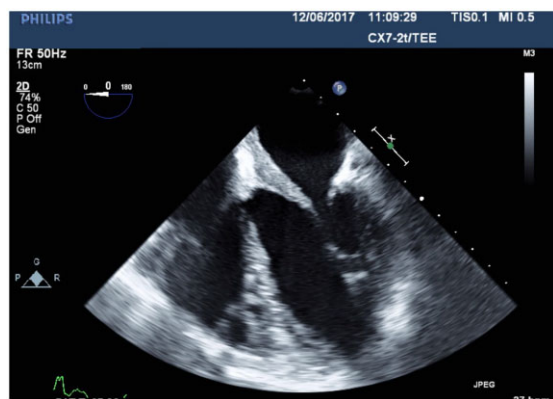


Figure 4 Transoesophageal echocardiogram showing a mid-oesophageal four-chamber view of a thickened anterior mitral valve leaflet.

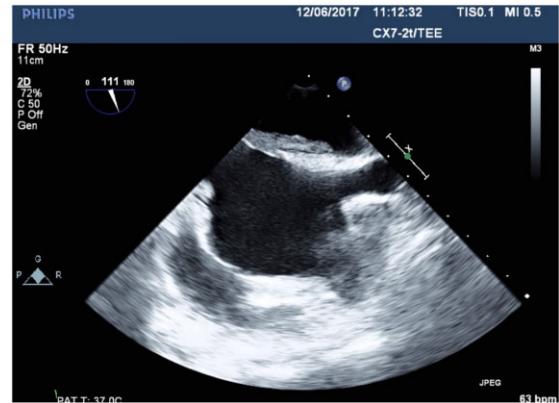


Figure 5 Transoesophageal echocardiogram showing an interatrial septum view of a thickened left atrial wall.

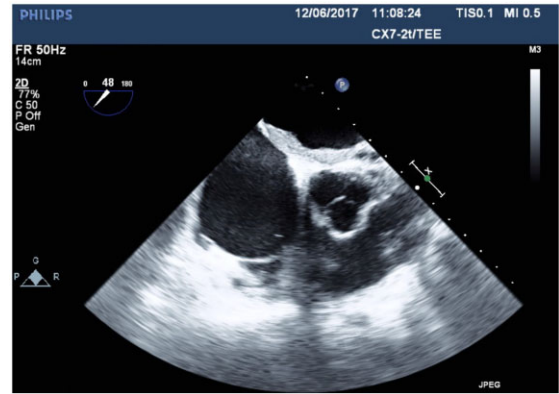


Figure 6 Transoesophageal echocardiogram showing an interatrial septum view of a thickened left atrial wall.

mass (Figure 10). Intra-operatively, the mass was noted to be very fibrotic and densely adherent throughout the left atrial wall extending down towards the mitral leaflets and into each of the pulmonary vein orifices. A frozen section of the mass, after haematoxylin and eosin staining, revealed dense fibrous tissue, with areas of fibrin undergoing organization. As well, there were areas of chronic inflammation and somewhat atypical but reactive appearing stromal cells (Figure 11A and B). There was no cardiac myxoma cells forming ring structures, or other structures that would be diagnostic of an atrial myxoma. Although there is some uncertainty, the tissue was thought to be in keeping with a mural thrombus undergoing organization.

Sixteen months post-surgery, the patient presented to the hospital with severe back pain. A magnetic resonance imaging revealed aggressive lytic pathologic fractures involving the T10 and L1 vertebral bodies, with a paravertebral soft tissue mass at L1, concerning for

metastatic disease. The primary malignancy, however, was unclear. The patient underwent vertebral body biopsies revealing a malignant spindle cell tumour suggestive of smooth muscle differentiation (Figure 11C and D). The tumour cells were positive for muscle markers, desmin, and smooth muscle actin (SMA), pointing towards a leiomyosarcoma. Mammogram, Papanicoulou test, and computed tomography of the chest, abdomen, and pelvis did not identify a primary malignancy.

Due to the lack of a primary malignancy identified and the atypical appearance of the cardiac mass resected a year ago, both the cardiac and vertebral biopsies were sent for further analyses. The atrial mass had foci of moderately atypical spindle-shaped cells with mitotic activity that raised concern for spindle cell sarcoma. The T10 vertebral body also showed similar atypical spindle cells. A series of immunohistochemistry analyses revealed strong nuclear expression of MDM2, with patchy SMA and pankeratin expression. Fluorescence in situ hybridization (FISH) analysis demonstrated convincing evidence of MDM2 genetic amplification, with an MDM2/CEP12 ratio of 7.8.

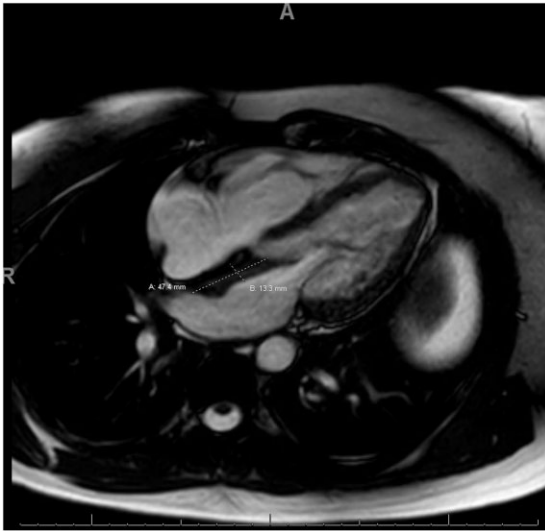


Figure 7 Cardiac magnetic resonance imaging showing an axial view of a sheet-like mass adherent to the septal side of the left atrial cavity.

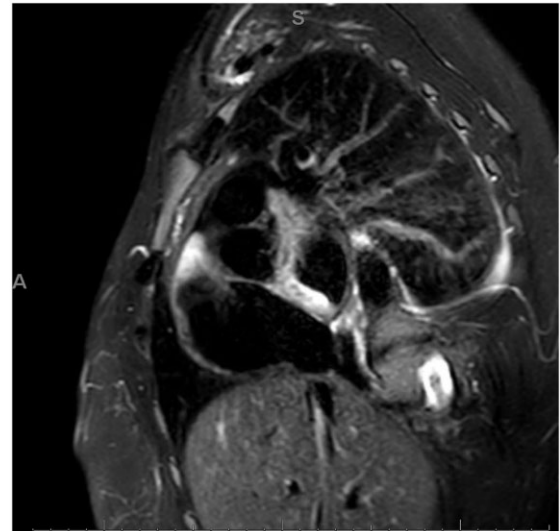


Figure 9 Cardiac magnetic resonance imaging showing a sagittal view of the cardiac mass lining the left atrium. The mass is hyperintense on Short-T1 Inversion Recovery.

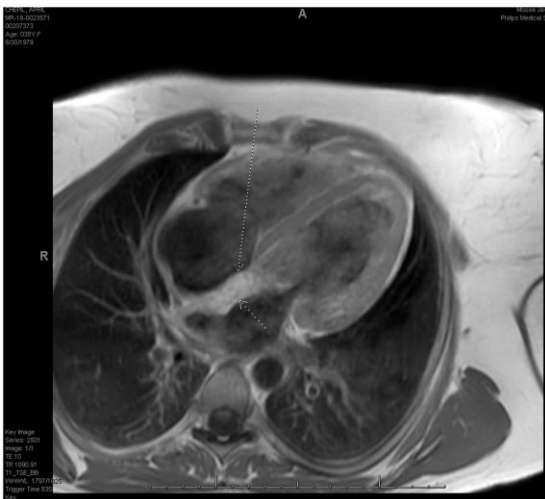


Figure 8 Cardiac magnetic resonance imaging showing an axial view of the mass, which is hyperintense to myocardium on the T2 weighted sequence.

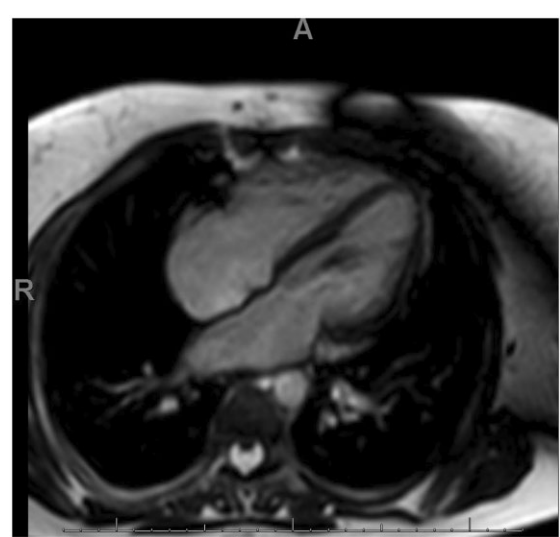


Figure 10 Cardiac magnetic resonance imaging showing an axial view of the heart after surgical excision of the cardiac mass.

These findings supported the diagnosis of an intimal sarcoma of atrial origin, with subsequent metastases to the vertebral bodies.

The patient received 6 weeks of stereotactic body radiation but returned 7 months later with a large pleural effusion and progression of the anterior paraspinal mass. Her case was discussed at Tumour Boards and an anthracycline-based regimen, including Adriamycin/Ifosfamide mesna, and Dacarbazine was initiated for palliation.

Discussion

Primary cardiac tumours are extremely uncommon, with an incidence of 0.001–0.03% based on post-mortem studies.² Approximately a quarter of primary cardiac tumours are malignant, with the majority being sarcomas.³ Intimal sarcoma is a particularly rare subtype, usually encountered in great vessels like the pulmonary artery and aorta, but rarely in the heart.³

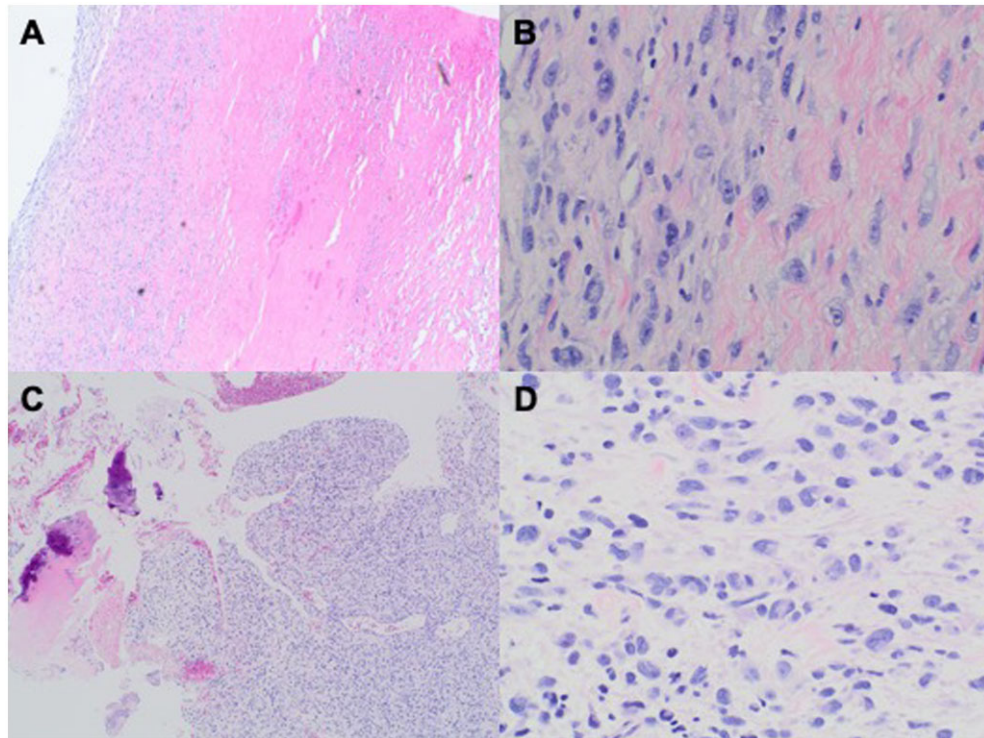


Figure 11 (A) Organizing thrombus with mononuclear infiltrate of large atypical cells (haematoxylin–eosin, original magnification $\times 100$). (B) Organizing thrombus with mononuclear infiltrate of large atypical cells composed of round to polygonal cells with vesicular chromatin, prominent nucleolus and moderate cytoplasm (haematoxylin–eosin, original magnification $400\times$). (C) Similar large atypical cells are present in the metastasis to the T10/L1 vertebral bodies (haematoxylin–eosin, original magnification, $100\times$). (D) Similar large atypical cells are present in the metastasis to the T10/L1 vertebral bodies (haematoxylin–eosin, original magnification $400\times$).

The rarity of this condition and its non-distinctive histological differentiation create a challenge in diagnosing primary cardiac intimal sarcomas. Intimal sarcomas are poorly differentiated mesenchymal tumours, composed of spindle cells with variable degrees of atypia, mitotic activity, necrosis, and nuclear polymorphism.⁴ Most reported cases are immunohistochemically positive for vimentin and alpha-SMA.⁴ There exists significant heterogeneity and uncertainty regarding this diagnosis, with many simply described as undifferentiated pleiomorphic sarcomas.^{5–7} A breakthrough was the discovery of MDM2 overexpression in intimal sarcomas. MDM2 is an oncogene that blocks p53 activity. Neuville *et al.*¹ found that MDM2 overexpression is highly suggestive of the diagnosis of intimal sarcoma and helps to differentiate from other subtypes of cardiac tumours.

The diagnostic challenge of primary intimal cardiac sarcoma is highlighted in this case. The patient's mass was initially thought to be an atrial myxoma on CMR, a differential that is commonly reported in case studies.^{8,9} Atrial myxomas tend to arise from the septum and have a stalk-like base with well-demarcated margins. Malignant tumours, on the other hand, tend to have poorly defined margins and are associated with infiltration into nearby structures. This case highlights that no imaging technique alone can be relied on to discern the nature of a cardiac mass, and an excisional biopsy should be undertaken, particularly in cases with an uncertain diagnosis. The histological findings of the cardiac tumour did not identify any myxoma cells but were thought to be in keeping with an organizing thrombus based

on findings of fibrin. Interestingly, intimal sarcomas, often found in the pulmonary artery, are commonly mistaken as pulmonary embolisms.¹⁰ However, upon further histological review, although there are organizing thrombi present, there are also foci of moderately atypical spindle-shaped cells present, concerning for spindle cell sarcoma. The vertebral body biopsy was initially diagnosed as a leiomyosarcoma, another common differential. Leiomyosarcoma can present similarly to intimal sarcomas with striated spindle cells positive for markers such as vimentin and alpha SMA. Leiomyosarcomas, however, tend to be better differentiated, is positive for desmin or caldesmon, and is commonly found in the vena cava. Nonetheless, these features are non-specific and the diagnosis of intimal sarcoma relies heavily on the overexpression of MDM2. Rare diseases can be difficult to diagnose, and while not every specimen warrants advanced immunohistochemistry or molecular cytogenetic analyses, in cases with atypical presentation and uncertain diagnosis, further investigation is needed and may lead to earlier diagnosis.

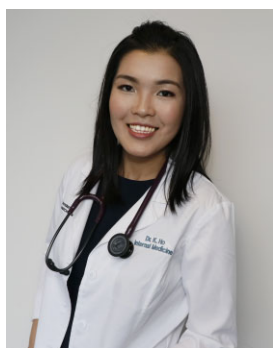
One of the unique aspects of this case was its presentation—paroxysmal AF. Symptoms and signs from cardiac tumours can arise from intracardiac obstruction and systemic embolization. Although cardiac arrhythmias have been mentioned as a symptom, AF has not been reported in primary cardiac intimal sarcomas. Cases in the literature have described dyspnoea,^{7,8} myocardial infarction,⁵ and stroke³ as presenting symptoms. This case reminds clinicians that cardiac tumours can have a wide variety of presentations. As cardiac

tumours, including intimal cardiac sarcomas, commonly arise in the left atrium, the development of AF in a patient should prompt investigation with an echocardiogram.

The mainstay management of intimal cardiac sarcoma is aggressive surgical resection with negative margins. Complete resection, however, is often not feasible due to late diagnosis and large tumour size.⁷ Nonetheless, a retrospective study of 124 patients found that surgical resection, whether complete or partial, was associated with prolonged survival.¹¹ Although chemotherapy and radiotherapy have been reported to have limited benefit,¹² a recent study by Frezza et al.¹³ found a real-world overall response rate of 38% with an anthracycline-based chemotherapy regimen. Unfortunately, the prognosis of cardiac sarcomas remains very poor, with mean survival between 3 months and 1 year.^{14,15} By the time, this case report was submitted, it would have been 48 months since this patient's first presentation, which would make her one of the longer survivors of this disease.

In conclusion, primary cardiac intimal sarcoma is a rare diagnosis. We described a case in a 37-year woman presenting with paroxysmal AF. Although there has been significant advancement in imaging technique, early detection of rare cardiac tumour remains a challenge. Despite having a histological sample from an excised left atrial mass, the diagnosis was not made until she presented with back pain secondary to metastatic disease to the spine. This case of cardiac intimal sarcoma highlights the difficulty in establishing the diagnosis, particularly given the unusual presentation.

Lead author biography



Dr Karen Ho is a 3rd-year Internal Medicine resident at the University of Saskatchewan in Canada. She completed her undergraduate degree at Johns Hopkins University in the USA and her medical degree at the University of Toronto in Canada. She will be pursuing a fellowship in Cardiology at Dalhousie University in Halifax, Canada. She has an interest in women's heart health and quality improvement.

Supplementary material

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

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

Conflict of interest: There is no conflict of interest to declare.

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References

1. Neuville A, Collin F, Bruneval P, Parrons M, Thivolet F, Gomez-Brouchet A et al. Intimal sarcoma is the most frequent primary cardiac sarcoma: clinicopathologic and molecular retrospective analysis of 100 primary cardiac sarcomas. *Am J Surg Pathol* 2014;**38**:461–469.
2. Bussani R, Castrichini M, Restivo L, Fabris E, Porcari A, Ferro F et al. Cardiac tumors: diagnosis, prognosis, and treatment. *Curr Cardiol Rep* 2020;**22**:1–13.
3. Moeri-Schimmel R, Pras E, Desai I, Krol S, Braam P. Primary sarcoma of the heart: case report and literature review. *J Cardiothorac Surg* 2020;**15**:1–6.
4. Ibrahim A, Luk A, Singhal P, Wan B, Zavodni A, Cusimano R et al. Primary intimal (spindle cell) sarcoma of the heart: a case report and review of the literature. *Case Rep Med* 2013;**2013**:461815.
5. Winther C, Timmermans-Wielenga V, Daugaard S, Mortensen SA, Sander K, Andersen CB. Primary cardiac tumors: a clinicopathologic evaluation of four cases. *Cardiovasc Pathol* 2011;**20**:63–67.
6. Agaimy A, Rosch J, Weyand M, Streckler T. Primary and metastatic cardiac sarcomas: a 12-year experience at a German heart center. *Int J Clin Exp Pathol* 2012;**5**:928–938.
7. Cho GJ, Kim HJ, Kang JS. Primary cardiac sarcoma in pregnancy: a case report. *J Korean Med Sci* 2006;**21**:940–943.
8. Li Z, Hsieh T, Hi A. Recurrent cardiac intimal (spindle cell) sarcoma of the left atrium. *J Cardiothorac Vasc Anesth* 2013;**27**:103–107.
9. Modi A, Lipnevicius A, Moorjani N, Haw M. Prolonged survival with left atrial spindle cell sarcoma. *Interact Cardiovasc Thorac Surg* 2009;**8**:703–704.
10. Lu P, Yin B. Misdiagnosis of primary intimal sarcoma of the pulmonary artery as chronic pulmonary embolism: a case report. *World J Clin Cases* 2020;**8**:986–994.
11. 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.
12. Grebenc ML, Rosado de Christenson ML, Burke AP, Green CE, Galvin JR. Primary cardiac and pericardial neoplasms: radiologic-pathologic correlation. *Radiographics* 2000;**20**:1073–1103.
13. Frezza AM, Assi T, Lo Vullo S, Ben-Ami E, Dufresne A, Yonemori K et al. Systemic treatments in MDM2 positive intimal sarcoma: a multicentre experience with anthracycline, gemcitabine, and pazopanib within the World Sarcoma Network. *Cancer* 2020;**126**:98–104.
14. Butany J, Nair V, Naseemuddin A, Nair GM, Catton C, Yau T. Cardiac tumours: diagnosis and management. *Lancet Oncol* 2005;**6**:219–228.
15. Gupta A. Primary cardiac sarcomas. *Expert Rev Cardiovasc Ther* 2008;**6**:1295–1297.