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CASE REPORT
Other

Extensive pulmonary metastases in young boy with primary cardiac angiosarcoma: a case report

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Background Malignant primary cardiac neoplasms are rare and primary cardiac angiosarcoma is the most common and aggressive subtype. It most commonly presents in middle-aged males and due to its non-specific clinical presentation, the diagnosis is often delayed until advanced disease is already present. Clinical presentation is determined by manifestations of local infiltration or metastatic disease and making an early diagnosis is extremely challenging.

Case summary A 15-year-old previously healthy boy was admitted to the emergency department with a history of pathological weight loss and functional decline. The patient was found to have a left-sided pneumothorax as well as bilateral diffusely spread pulmonary nodules on plain chest radiograph. Computed tomography chest confirmed widespread pulmonary metastases and a right atrial filling defect. Echocardiography revealed a right atrial tumour and transvenous endomyocardial biopsy of the tumour was done under fluoroscopic and echocardiographic guidance. A diagnosis of primary cardiac angiosarcoma was made. The patient demised shortly after presentation.

Discussion Primary cardiac angiosarcoma is rare and even more so in patients as young as the case described. The diagnostic process poses several challenges to the clinician, of which the obtaining of a histological sample is one. This case report demonstrates aspects both unique and typical of this rare disease. It also describes an effective option for obtaining tissue for a histological diagnosis in patients whose clinical condition may not allow biopsy under general anaesthesia.

Keywords Case report • Cardiac angiosarcoma • Pulmonary metastases • Right atrial mass • Fluoroscopy-guided biopsy

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Learning points

- Primary cardiac angiosarcoma is one of the commonest causes of malignant primary cardiac neoplasms.
- Presenting symptoms are more commonly those related to local invasion or metastatic spread.
- Echocardiography remains one of the most important diagnostic tools in the evaluation of primary cardiac angiosarcoma.
- Histological confirmation of angiosarcoma remains difficult, but transvenous imaging-guided procedures may assist in making the diagnosis in unstable patients.
- In lieu of the aggressive nature and delayed identification of angiosarcomas, it carries a very poor prognosis.

Introduction

Malignant primary cardiac neoplasms are rare and of them, sarcoma (75–95%) and specifically primary cardiac angiosarcoma (30–40%) is the most common subtype.[1–5] These tumours are known to be aggressive in nature and resistant to chemo- and radiotherapy and are associated with a poor prognosis due to delay in diagnosis and lack of directed therapies.

Clinical presentation depends on tumour location and size and may include dyspnoea, fatigue, cardiac failure, atypical chest pain, and manifestations of metastatic disease. Tissue sampling for a histological diagnosis can be very challenging but is imperative for formulating a definitive therapeutic plan.

We present an unusual case of primary cardiac angiosarcoma in a very young, male patient characterized by a challenging diagnostic process and rapid disease progression following clinical presentation. This case also highlights the potential role of transvenous imaging-guided endomyocardial biopsy as a method to obtain tissue samples where conventional methods may not be feasible.

Timeline

2 weeks prior	Progressive decline with exertional dyspnoea and malaise
Day 0	Acute dyspnoea—pneumothorax related—intercostal drain inserted Initial evaluation started
Day 4	Fluoroscopy and transthoracic echocardiogram guided biopsy of right atrial mass
Day 7	Patient demised

Case presentation

A young 15-year old African boy presented to the emergency centre with sudden onset shortness of breath without any chest pain or associated symptoms. This was preceded by a 2-week history of progressive decline in his functional baseline with a history of exertional dyspnoea (without orthopnoea or paroxysmal nocturnal dyspnoea) and malaise. He reported having lost >6 kg (>10%) of weight during this period but did not report fever or any other constitutional symptoms. He was previously well, and his family history did not include any chronic conditions.

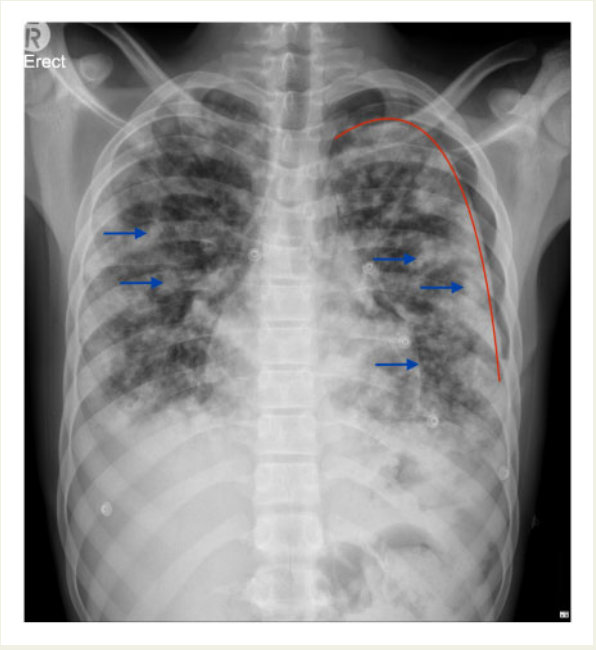


Figure 1 Chest radiograph depicting left-sided pneumothorax (red line) and extensive bilateral nodules (blue arrows).

Clinical examination revealed a thin boy who appeared acutely unwell. He was tachycardic (116 beats per minute) and tachypnoeic (36 breaths per minute), but otherwise had normal vitals. He appeared pale, with no evidence of clubbing and no evidence of lymphadenopathy. Chest auscultation revealed scattered crackles throughout both lung fields. In addition, there was clinical concern about a left-sided pneumothorax. His examination was otherwise unremarkable.

An urgent chest radiograph confirmed a left-sided pneumothorax. In addition, extensive, bilateral nodules highly suggestive of metastases were noted (*Figure 1*). A left-sided intercostal drain was inserted, with improvement in his respiratory status.

Laboratory investigations revealed a haemoglobin of 4.7 g/dL (reference range 13–17 g/dL) [iron 2.3 µmol/L (reference range 11.6–31.3 µmol/L); transferrin 2.42 g/L (reference range 2–3.6 g/L); transferrin saturation 4% (reference range 20–50%); ferritin 110 µg/L (reference range 14–152 µg/L)—a combination of iron deficiency and anaemia of chronic disease] with normal white cell and platelet count. Blood smear suggested an iron-deficiency anaemia with no atypical cells noted. Tumour markers (alpha-feto protein, beta-HCG, and CA 19-9) were not elevated and his human immunodeficiency virus test was negative.

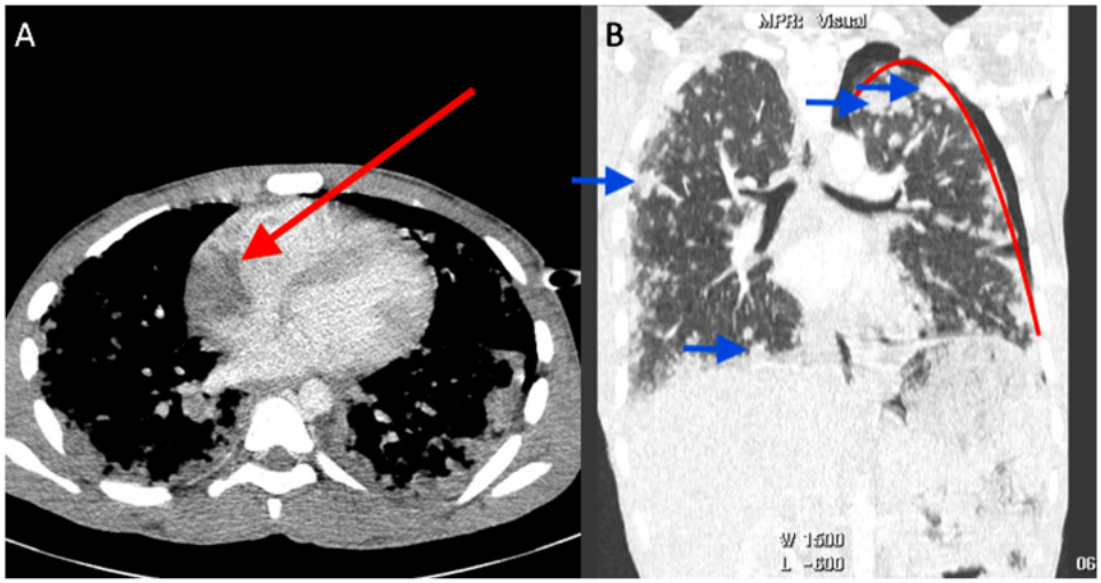


Figure 2 (*A*) Transverse (vascular window) and (*B*) coronal (lung window) views on contrasted computed tomography chest demonstrating the left-sided pneumothorax (red line), bilateral pulmonary nodules (blue arrows), and right atrial mass (red arrow).

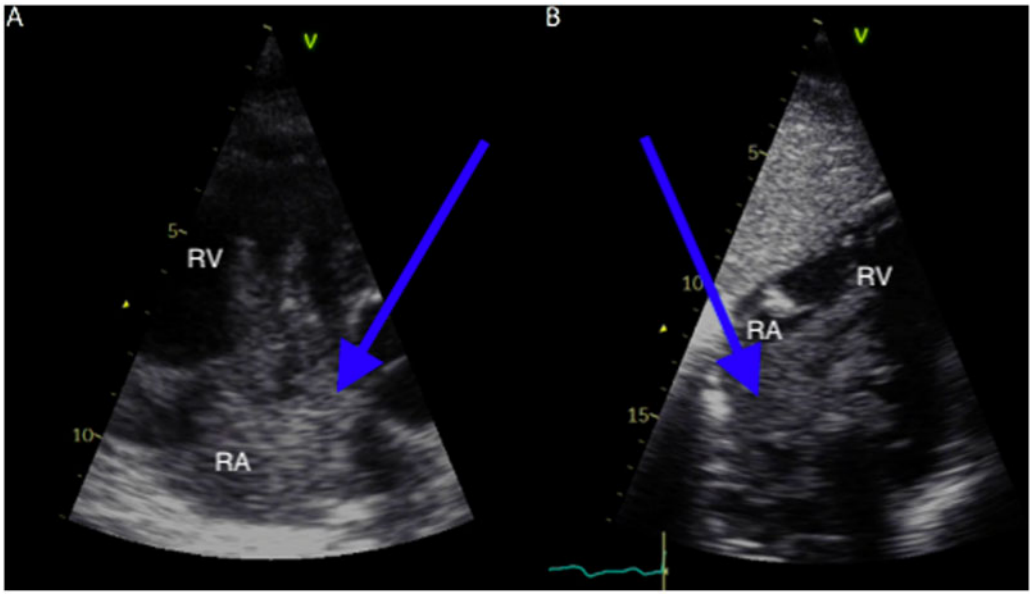
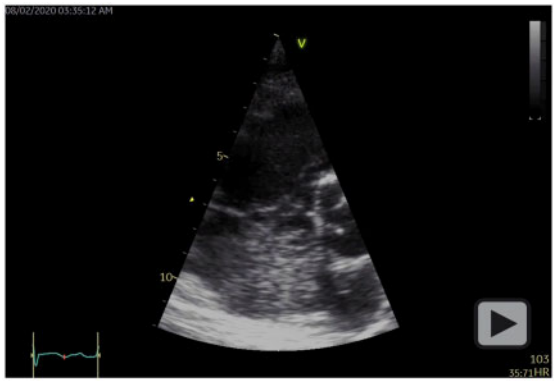


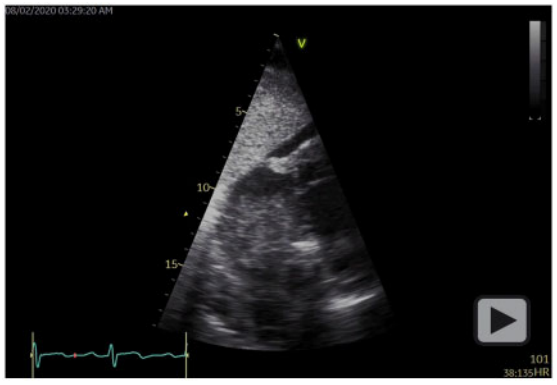
Figure 3 Transthoracic echocardiography with (*A*) modified right ventricular inflow view and (*B*) sub-costal view demonstrating right atrial mass (blue arrow) with frond-like projections prolapsing through tricuspid valve into right ventricle.

Computed tomography (CT) of the chest and abdomen revealed diffuse, solid, well-defined pulmonary nodules throughout both lung fields (*Figure 2A* and *B*). A filling defect was also noted within the right atrium (RA) and the atrial wall was not clearly identified. The other solid organs were normal. An ultrasound of his thyroid and testes were normal and a skeletal survey did not identify any pathology.

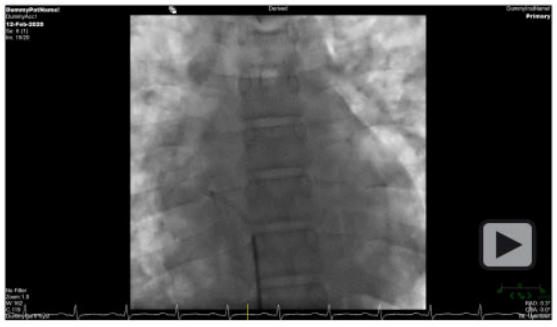
Echocardiography revealed a large inhomogeneous and broad-based mass at the transition between the inferior vena cava (IVC) and RA with frond like projections prolapsing in-and-out through the tricuspid valve (*Figure 3*, *Videos 1* and 2) with minimal tricuspid regurgitation. The IVC was non-dilated with no obvious extension into the IVC noted. A small, circumferential pericardial effusion (not amenable



Video 1 Transthoracic modified right ventricular inflow echocardiographic view demonstrating right atrial mass with frond-like projections.



Video 2 Transthoracic sub-costal echocardiographic view demonstrating right atrial mass with frond-like projections.



Video 3 Fluoroscopy-guided endomyocardial biopsy.

to aspiration) was noted. No attachment points of the mass to the atrial septum were noted. There was otherwise normal cardiac structure and function.

Unfortunately, none of the lung lesions were amenable to transthoracic needle aspiration and his health state was deemed too poor for open lung biopsy. Urgent transfemoral, fluoroscopic and transthoracic echocardiography guided endomyocardial biopsy of the right atrial mass was performed (*Video 3*).

Macroscopically, the specimens were pale-white to translucent with a papillomatous appearance. Intraoperative frozen section revealed sheets of atypical epithelioid cells with hyperchromatic nuclei and areas of necrosis with mitotic activity. Permanent paraffin sections showed a single, small fragment of cardiac muscle and cellular, polypoid tissue fragments with papillary-like projections. Some regions appeared solid, while others had a reticulated pattern. Irregular, vascular-like spaces were also noted, lined by a relatively flattened, single layer of neoplastic cells (*Figure 4A*). The neoplastic cells had predominantly round to occasionally spindled, hyperchromatic nuclei. Cells demonstrated moderate to abundant amounts of clear to light eosinophilic cytoplasm, some with a foamy quality. Karyorrhectic debris was present throughout the tumour, and a focal area of frank necrosis was observed (*Figure 4B*). Mitotic activity was focally seen (*Figure 4C*). The neoplastic cells showed immunohistochemical reactivity for CD31, CD34, FLI-1, and ERG, confirming endothelial differentiation (*Figure 4D*). HHV-8 did not demonstrate immunoreactivity. A diagnosis of angiosarcoma was made.

The young patient's clinical condition deteriorated in the ward and he demised 3 days after the procedure, prior to exploration of any further palliative options.

Discussion

The majority of patients with primary cardiac angiosarcoma present in their 5th or 6th decade of life with a male preponderance (male:female ratio of 2–3:1).[2–4,6] A limited number of cases have been described in adolescents and young adults, but it remains exceedingly rare, with this case being one of the youngest reported cases. Early diagnosis is key to limiting mortality, but due to the non-specific presenting symptoms and its aggressive nature, diagnosis is often made with significant local extension or metastatic spread already evident.[1,4,7,8]

Echocardiography is considered the first line of investigation as it is inexpensive and readily available. Moreover, these tumours have characteristics that distinguish them from other cardiac masses on echocardiography.[1,3,4,6] The differential diagnosis for cardiac masses include tumours (primary and secondary), vegetations, thrombi and structural causes (*Figure 5*). Angiosarcomas most frequently originate in the RA (90%) and have a distinct irregular, broad-based appearance.[1,2,4,6] The presence of a pericardial effusion, which is common and present in about 60% of patients at the time of diagnosis, suggests extension beyond the myocardial walls and is associated with a poorer prognosis.[4] Cardiac CT, magnetic resonance imaging, and positron emission tomography can be used as adjunctive imaging modalities to further delineate anatomy and local extension as well as identify possible metastatic deposits.[1,4,6]

Obtaining a histological diagnosis often proves to be a difficult endeavour due to the location of the primary tumour as well as the

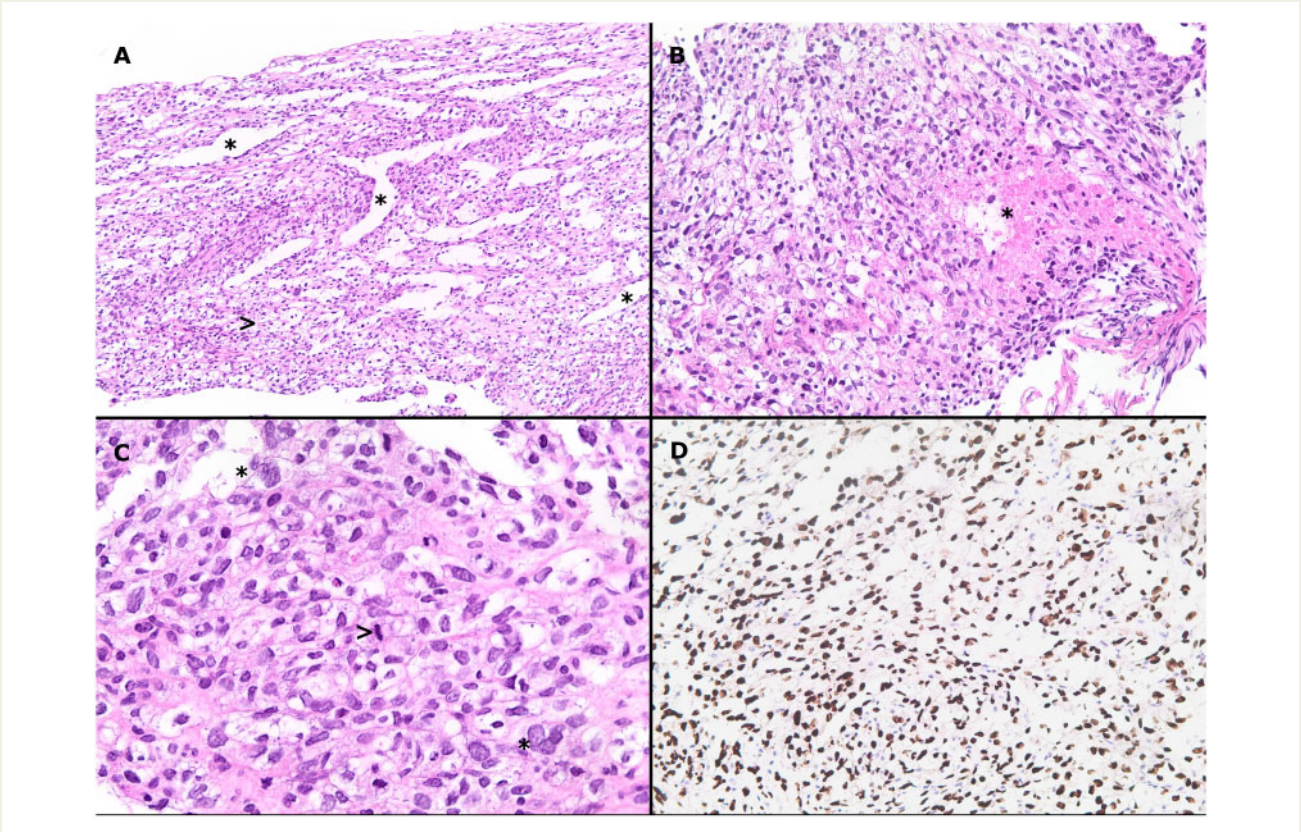


Figure 4 (*A*) Tumour demonstrating areas of reticulated growth (open arrowhead) with irregular vascular channels (asterisks) (haematoxylin and eosin stain, ×100 magnification). (*B*) Tumour cells with hyperchromatic nuclei and clear cytoplasm growing in sheets. A focal area of necrosis is present (asterisk) (haematoxylin and eosin stain, ×200 magnification). (*C*) Tumour cells displaying marked nuclear pleomorphism and hyperchromatism (asterisks). A mitotic figure is seen in the centre of the field (open arrowhead) (haematoxylin and eosin stain, ×400 magnification). (*D*) ERG immunohistochemical staining demonstrating strong, diffuse nuclear positivity (×200 magnification).

invasive nature of procedures done to acquire a tissue specimen. Performing diagnostic pericardiocentesis may be unrewarding due to difficulty in accessing the pericardial space as well as poor sensitivity of pericardial fluid cytological analyses.[4,6,7,9,10] If biopsy of these tumours or metastases is undertaken, it often carries a considerable amount of procedural risk. Although previously described, transvenous endomyocardial biopsy of the mass is not commonly performed.[11] Where options for the obtaining of tissue for a histological diagnosis are limited, this method provides an effective alternative. The advantage of the transvenous, imaging-guided technique employed in this case is that it can be performed in patients of high-anaesthetic risk, as this procedure is performed under local anaesthetic. Moreover, live imaging allows for efficient sampling of the mass and early identification of possible complications of the procedure.

Histologically, angiosarcomas may have a wide array of morphological appearances. Anastomosing vascular channels and poorly differentiated areas with solid growth, may be seen.[4,6,8] Solid areas can consist of epithelioid or spindle-shaped cells, or a combination thereof.[4,6] Spindled areas can closely resemble Kaposi sarcoma, commonly seen in patients with HIV/AIDS.[4] Areas of necrosis and haemorrhage are commonly seen.[4] Immunohistochemistry is used to further differentiate angiosarcoma from other soft tissue and vascular tumours. Angiosarcoma usually stains positive for CD31, FLI-1, CD34, ERG, and von Willebrand factor.[4,8]

Angiosarcomas, in addition to the aforementioned non-specific symptoms, more commonly present with clinical manifestations of local infiltration or metastatic disease as with our case. Pericardial effusions with heart failure symptoms and cardiac tamponade are not uncommon findings. In addition, right-sided angiosarcomas commonly metastasise to the lungs via haematogenous spread. Rare reports of systemic embolization of left-sided tumours with resultant cerebrovascular accidents, myocardial infarctions and acute limb ischaemia have been reported.[3,4]

The overall prognosis of angiosarcomas is known to be extremely poor, with the survival rates since time of diagnosis measured in months.[1–4,6] This is due its aggressive nature, the difficulty in diagnosing it at an early stage, as well as resistance to chemotherapy and radiation. Surgical excision is the mainstay of therapy but obtaining adequate tumour-free margins is challenging due to tumour location and its proximity to vital structures. Local recurrence is common.[1,4] An effective, evidence-based treatment regimen has yet to be formulated but remains extremely challenging due to the rarity of these tumours.

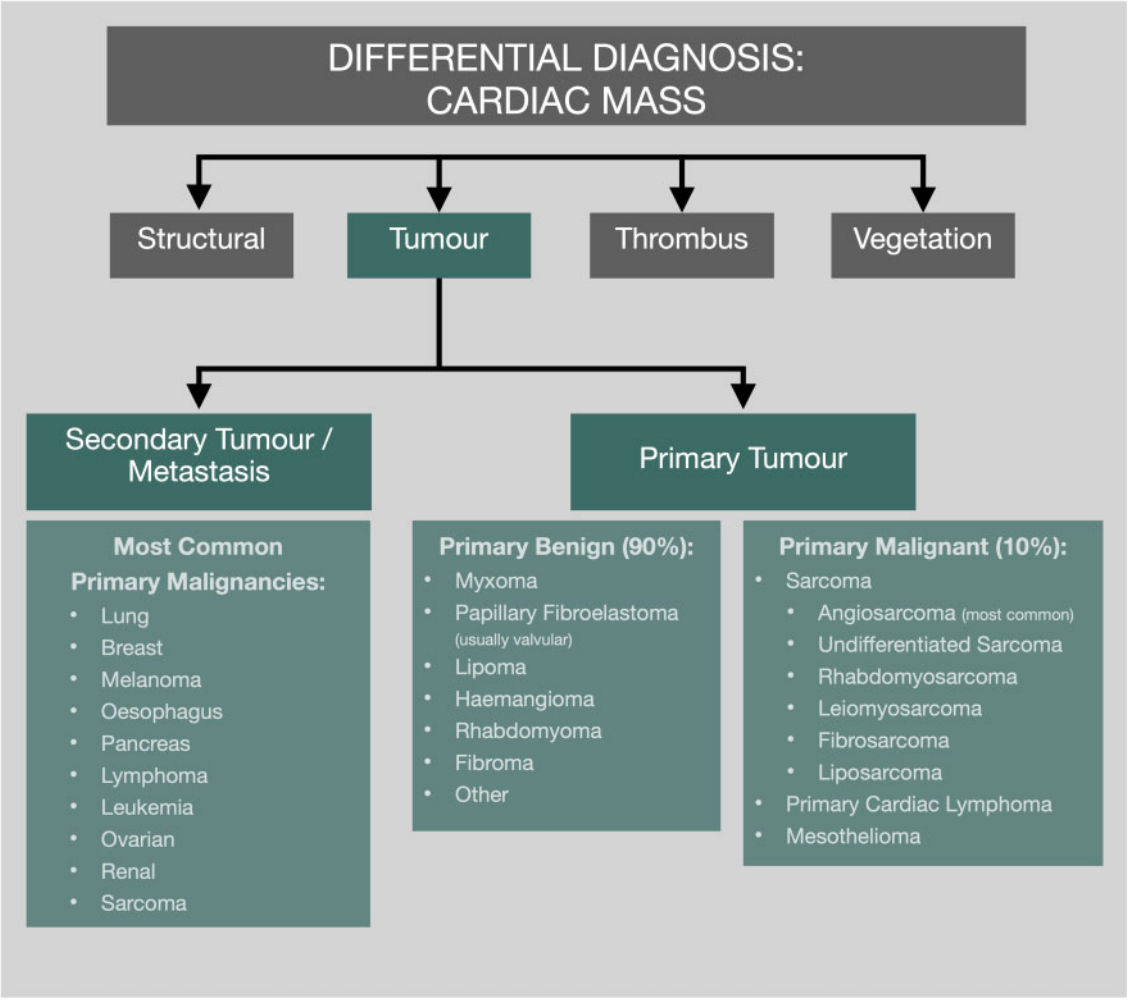


Figure 5 Differential diagnosis for cardiac masses.

Health research and ethics approval

This manuscript has been approved by the Stellenbosch University Health Research and Ethics Committee. HREC Reference No: C20/08/026.

Lead author biography

Dr Gerhard van Wyk is a medical officer at the Department of Internal Medicine of Karl Bremer Hospital in Cape Town, South Africa. He obtained his MBChB degree at the Stellenbosch University, Faculty of Medicine and Health Sciences in 2014.

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 author/s confirm that written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patient's next-of-kin in line with COPE guidance.

Conflict of interest: none declared.

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