Multimodal Imaging for the Assessment of a Cardiac Mass - A Case of Primary Cardiac Sarcoma

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ABSTRACT

We present a case of an 85-year-old patient who underwent clinical work-up for chronic heart failure, acute coronary syndrome, and pulmonary embolism, until she was diagnosed with a cardiac mass that was histologically identified as sarcoma. The aim of this educational case report is to raise awareness of cardiac masses and to point out diagnostic hints towards a cardiac tumor on chest X-ray, coronary angiography, echocardiography, and chest CT. Moreover, the vital role of cardiac magnetic resonance for the diagnosis of a cardiac mass is highlighted.

CASE REPORT

CASE REPORT

An 85-year-old woman presented to an outside hospital with dyspnea on exertion. Left-ventricular dilation was noted on her chest X-ray, a new finding compared to a chest X-ray four years before (Fig 1-A and 1-B). At echocardiography, mitral regurgitation was detected, and the patient was diagnosed with chronic heart failure (NYHA II-III). Her symptoms improved with diuretic medication so she could be discharged.

Four months later, the patient presented to our hospital due to recurrent atypical chest pain, slight ST-segment alterations and a mildly increased troponin T level (0.027 ng/dl, reference level <0.014 ng/dl). Coronary angiography was performed for suspicion of coronary artery disease. In the cath lab, a left main (LM) coronary artery stenosis was found and treated with a drug eluting stent. Additionally, atypical vessels deriving from an atrial branch of the right coronary artery (RCA) were visualized (Fig 1-D). This finding was interpreted as an arteriovenous fistula (AV fistula). The patient was discharged in a stable condition on platelet aggregation inhibitors (aspirin and ticagrelor).

Two weeks later, the patient presented to another hospital with acute dyspnea. On physical examination, her respiratory rate was increased. Her lab values showed elevated D dimers (2.1 mg/l, reference level <0.5 mg/l). Thoracic computed tomography angiography (CTA) was performed and pulmonary embolism was ruled out, but a large cardiac mass with left ventricular compression was found (Fig 1-E). Regarding her previous coronary intervention, her anti platelet aggregation medication, and mild anemia (hemoglobin 10.4 g/dl, reference level 12.0-16.0 g/dl), the suspicion of a pericardial hematoma was raised and the patient was referred to our institution.

On admission to our hospital, the patient was in mild respiratory distress, blood pressure was 152/90 mmHg, heart rate was 81 bpm, and electrocardiogram showed sinus rhythm

without ST segment deviation. Her current chest X-ray (Fig 1-C) showed a progressive increase in cardiac diameter compared to previous examinations. A transesophageal echocardiography revealed a normal ejection fraction and a mass in the left atrium with hyperechogenic and isoechogenic components (Fig 1-F).

Cardiac magnetic resonance imaging (CMR) was indicated to further assess the extent of the mass and to rule out intracardiac thrombus, pericardial hematoma and myocardial laceration. CMR revealed a large solid mass that had most likely developed from the left atrial wall or lateral left ventricular wall and extended into the left atrium and pericardium (Fig 2-A, B, C, D).

As the patient increasingly suffered from left ventricular compression, surgery was performed to relief her symptoms. During surgery, the finding of a solid tumor was confirmed. Tumor debulking was done, but because of considerable adhesions and a pronounced bleeding tendency, complete tumor extirpation was not possible.

Histopathologic assessment revealed a sarcoma (Fig 3-A, B), resembling a leiomyogenic subtype; however, as immunohistochemistry was only positive for actin and CD99, but negative for desmin, h-Caldesmon, AE1/AE3 and S100, the tumor was classified as undifferentiated sarcoma. The proliferative index was high, accounting for 30-40% of tumor cells.

The patient was discharged in a stable condition 8 days after her surgery and was still alive after 3 months of follow-up.

DISCUSSION

Etiology & Demographics:

Primary cardiac tumors occur in approximately 0.02 % autopsy series, whereas secondary tumors (metastases) to the heart are reported to be 20 times more frequent (1,2). Approximately 90% of primary cardiac tumors are benign (e.g. myxoma, papillary fibroelastoma, rhabdomyoma, lipoma) and 10% are malignant (2). Malignant primary cardiac tumors include sarcoma (undifferentiated sarcoma, angiosarcoma, leiomyosarcoma, rhabdomyosarcoma, myxofibrosarcoma, osteosarcoma, synovial sarcoma), germ cell tumors (teratoma and yolk sac tumor), and lymphoma (2). These tumor entities can present in different locations, but some of them have preferential sites of manifestation: Undifferentiated sarcoma, leiomyosarcoma and myxofibrosarcoma are most commonly found in the left atrium (3), rhabdomyosarcoma in the left ventricle, angiosarcoma and synovial sarcoma in the right atrium, lymphoma in the right atrium or right ventricle. Undifferentiated sarcoma, the most common subtype of sarcoma, develop from mesenchymal cells. The mean age of manifestation is approximately 45 years. There is no gender predilection and no known risk factors (3).

Clinical & Imaging Findings:

Dyspnea on exertion and atypical chest pain usually do not raise suspicion of a cardiac mass in the first place, since masses are rare entities among a plethora of pathologies responsible for thoracic discomfort. As illustrated by this case, diagnosing a cardiac tumor can be a challenge, in light of a broad spectrum of clinical presentations that range from asymptomatic to dyspnea, chest pain and to sudden cardiac death (4). Clinical features reflect location, size and the extent of the tumor. The diagnosis of a cardiac tumor is typically made utilizing a combination of multiple imaging studies (2):

(I.) **Chest X-ray** is the most cost-effective and widely used imaging tool in dyspnea and atypical chest pain. It allows for a detection of an increase in heart size, which, however, is non-specific and can also be observed in chronic heart failure or pericardial effusion. In our case, an increase of the patient's heart size was initially attributed to chronic heart failure due to mitral valve insufficiency, but can retrospectively also be explained by tumor growth.

(II.) **Coronary angiography** may visualize abnormal tumor vasculature. In the presented case, abnormal vessels originating from a prominent atrial branch of the distal RCA were found in addition to a significant LM stenosis. This finding was initially interpreted as an AV fistula (5). Retrospectively, the abnormal vessels can be attributed to tumor vasculature (6).

(III.) **Transthoracic and transesophageal echocardiography** are appropriate modalities to detect a cardiac mass. Thrombi, vegetations and myxoma need to be considered as most important differentials for malignancy. Image quality, acoustic window as well as artifacts may restrict detailed assessment (7). In our case, echocardiography revealed a hyperechogenic mass, raising suspicion of a cardiac mass and prompting further imaging.

(IV.) **CT angiography** is the imaging modality of choice in patients with severe dyspnea or chest pain to visualize pulmonary embolism or aortic dissection. It is also able to detect a cardiac mass, calcifications within, and – depending on contrast phase – tumor vascularization (8). Following coronary intervention or cardiac surgery, a coronary or myocardial laceration with contrast extravasation and pericardial hematoma needs to be considered as a differential diagnosis (9,10). In the presented case, differentiation between highly concentrated contrast material and cardiac calcifications was difficult, because there was only an arterial phase and no unenhanced phase available. Therefore, further imaging by cardiac MRI was indicated.

(V.) **Cardiac MRI** (CMR) is the best tool for soft tissue characterization (11,12) and assessment of tumor infiltration of the myocardium, pericardium and intracardial cavities (13,14). Also, CMR, has established as the gold standard for cardiac function analysis. In correlation with CT, T1- and T2-hypointense inclusions within a cardiac mass as well as absence of susceptibility artifacts, made an acute hematoma unlikely. Moreover, an extensive mass with irregular borders, heterogeneous T1- and T2-signal, infiltration of left atrial and

ventricular wall, pericardial involvement, left ventricular wall motion impairment on CINE sequences, and contrast uptake on early enhancement and late enhancement sequences are typical features of a cardiac malignancy, so a benign cardiac tumor can be excluded. Of note, contrast enhanced T1w sequences with frequency selective fat suppression are very useful to highlight contrast-enhancing lesions, whereas non-selective short-tau-inversion-recovery sequence (STIR) should not be used after contrast application because not only fat signal but also contrast enhancement is suppressed by the inversion pulse. Given unifocal tumor manifestation (involving the left atrium and ventricle) no history of underlying tumor disease or multifocal metastases, a primary cardiac malignancy could be considered more likely than a secondary cardiac malignancy in the presented case. As illustrated by this case, utilization of CMR improves diagnostic certainty compared with echocardiography and CT alone, and allows for a firm diagnosis on which cardiac surgery decision and planning of surgery can be based. New CMR techniques, such as T1 and T2 mapping, may yield valuable additional information (15) and improve diagnostic certainty in the non-invasive diagnosis of cardiac masses. As to date, cardiac masses account for approximately 1% of CMR scans in Europe (16). Broader availability and increasing use of CMR in clinical practice may help detect cardiac tumors at earlier stages.

Treatment & Prognosis:

The best treatment of cardiac sarcoma is not yet well defined. At an early stage and absence of tumor spread, radical resection is the best therapeutic approach (17). However, complete excision is possible in less than half of the patients. In most cases, due to nonspecific symptoms, the diagnosis is often delayed until the tumor is at an advanced stage and complete resection is not possible (17,18). Palliative treatment options include tumor debulking surgery, radiotherapy and chemotherapy. The prognosis is poor. Most patients die within 2 years despite surgical resection. The mean survival time after diagnosis is between 7 months and 2 years.

Differential Diagnosis:

Differential diagnoses of a cardiac mass other than pericardial effusion and pericardial cyst include:

(I.) Pericardial hematoma can occur spontaneously in patients with coagulopathy or in consequence of a trauma (e.g. iatrogenic, following coronary intervention). On chest X-ray, an increase in heart size may be noted. On echocardiography, hematomas can show heterogeneous echogenicity. On CT, acute hematomas are hyperdense, chronic hematoma mixed or hypodense. On CMR, a hematoma shows susceptibility artifacts (especially on T2*w gradient echo sequences) and heterogeneous T1 and T2 signal intensity, depending on the age of the hematoma. Hematomas do not show contrast uptake or myocardial infiltration.

(II.) Intracardiac thrombi are the most common intracardiac masses (2) and represent a frequent source for stroke and other arterial embolic events. Thrombi are most often located in the atria, especially the left or right auricle, and are associated with atrial fibrillation. Ventricular thrombi in patients with ischemic heart disease are preferentially located near the apex. On chest X-ray, thrombi are not directly visualized. On echocardiography, thrombi are hyperechoic. On thoracic CT with contrast, thrombi are hypodense to blood. On CMR, T1 and T2 signal intensity is heterogeneous, depending on thrombus age; on CINE sequences, a thrombus is usually isointense to myocardium and hypointense to blood. Most thrombi do not show contrast enhancement, but enhancement is possible in chronic thrombi. A mural thrombus is best revealed by early contrast-enhanced inversion recovery MR sequences because the myocardium and the cardiac cavity show high signal intensities immediately after contrast injection whereas thrombi appear hypointense (19).

(III.) Cardiac myxoma are the most common primary cardiac tumors (20). The average age of presentation is approximately 50 years. There is a female predilection. Most patients are asymptomatic (incidental finding), but large tumors may cause valve obstruction, embolism, or arrhythmia. The typical location of a myxoma is the left atrium (75%), atypical locations are the right atrium (20%) and ventricles (5%). Chest X-ray is usually unremarkable. On echocardiography, a hyperechoic, well-circumscribed atrial mass can be found. On CT, myxoma are hypodense to blood; they may contain hyperdense calcifications. On CMR, myxoma tend to be T1 hypointense to isointense, T2 hyperintense, with moderate enhancement post contrast (2,13). Curative therapy is complete resection, with low recurrence rates.

(IV.) Benign cardiac tumors other than myxoma: this group includes lipoma, rhabdomyoma, papillary fibroelastoma and other rare entities (e.g. cardiac hemangioma, calcified amorphous tumors, fibroma, inflammatory myofibroblastic tumor, hamartoma, pericardial germ cell tumor) (13,20). Lipoma are most often localized at the interatrial septum; they are hyperechoic on echocardiography, hypodense on CT, and hyperintense on T1 and T2w CMR (13,20). Papillary fibroelastoma are typically small tumors with a stalk, heterogeneous on echocardiography, CT, and CMR (13,20). Rhabdomyoma are the most common primary cardiac tumors in young children (up to 90%) (2). They are usually asymptomatic, but some may cause valve obstruction. Rhabdomyoma are hyperechoic on echocardiography, hypodense on CT, isointense to myocardium on T1w and hyperintense on T2w CMR (20). Most often no treatment is required due to and the tumor can regress spontaneously.

(V.) Secondary cardiac tumors (cardiac metastasis) are approximately 20 times more frequent then primary cardiac malignancies (1,2,21). Depending on the primary tumor entity, cardiac metastases show various echogenicity, CT density and CMR signal intensity. Common features are infiltrative growth and contrast uptake. Metastases can manifest in any location and multiple sites of the heart (13).

In the presented case, the combination of imaging features ruled out intracavitary thrombus and pericardial hematoma (contrast enhancement of the mass) and the tumor was easy to distinguish from a benign mass by its considerable increase in size on chest X-ray within 4 months, its infiltrative growth and its heterogeneous contrast uptake on CMR. A secondary cardiac tumor was considered unlikely because the patient had no known primary malignancy.

TEACHING POINT

Utilization of multimodal imaging is key in the diagnosis of a cardiac tumor. An increase in heart size on chest X-ray, a calcified mass on echocardiography or chest CT, and abnormal vessels on coronary angiography (in patients with suspected coronary artery disease) can give useful hints towards a cardiac tumor, whereas CMR is the best tool to make the definite diagnosis and for further tumor characterization.

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FIGURES

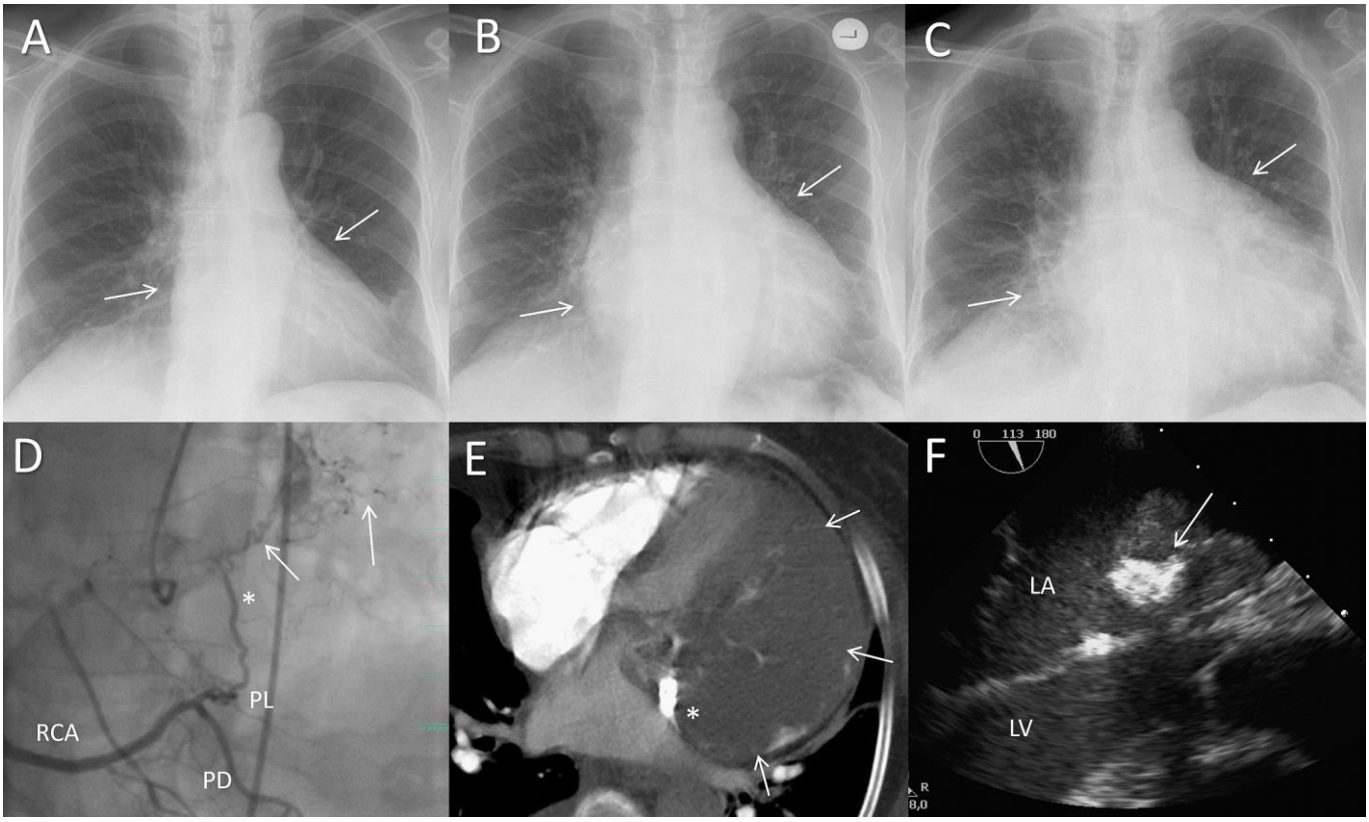

Figure 1: 85 y/o female with cardiac sarcoma.
(1-A, B, C) Technique: Chest X-ray performed with CR 85-X, AGFA HealthCare, Bonn, Germany, 115 keV, automatic mAs.
Findings: Chest X-ray 4 years ago (A), chest X-ray 4 months ago (B) and chest X-ray now (C) show an increase in heart size (arrows).
(1-D) Technique: Coronary angiography performed with AXIOM-Artis, Siemens Healthcare, Forchheim, Germany.
Findings: visualization of the right coronary artery (RCA) with posterolateral branch (PL), posterior descending artery (PD) and abnormal vessels (arrows) arising from a prominent right atrial branch (asterisk).
(1-E) Technique: Chest computed tomography angiography (CTA) performed with GE Optima CT520 Series (100 kV, automatic mAs) in pulmonary artery phase after IV contrast injection of 70 mL iodinated contrast (Ultravist 300, Bayer HealthCare, Germany), slice thickness 2.5 mm.
Findings: CTA shows a large left-pericardial mass (arrows) with hyperdense inclusions (asterisk), resembling calcifications.
(1-F) Technique: Transesophageal echocardiography performed with CX50 Philips (X7-2T transducer, sector phased, 7-2 Mhz), Best, Netherlands.
Findings: hyperechogenic mass adjacent to the left atrium (arrow), representing calcified tumor components.

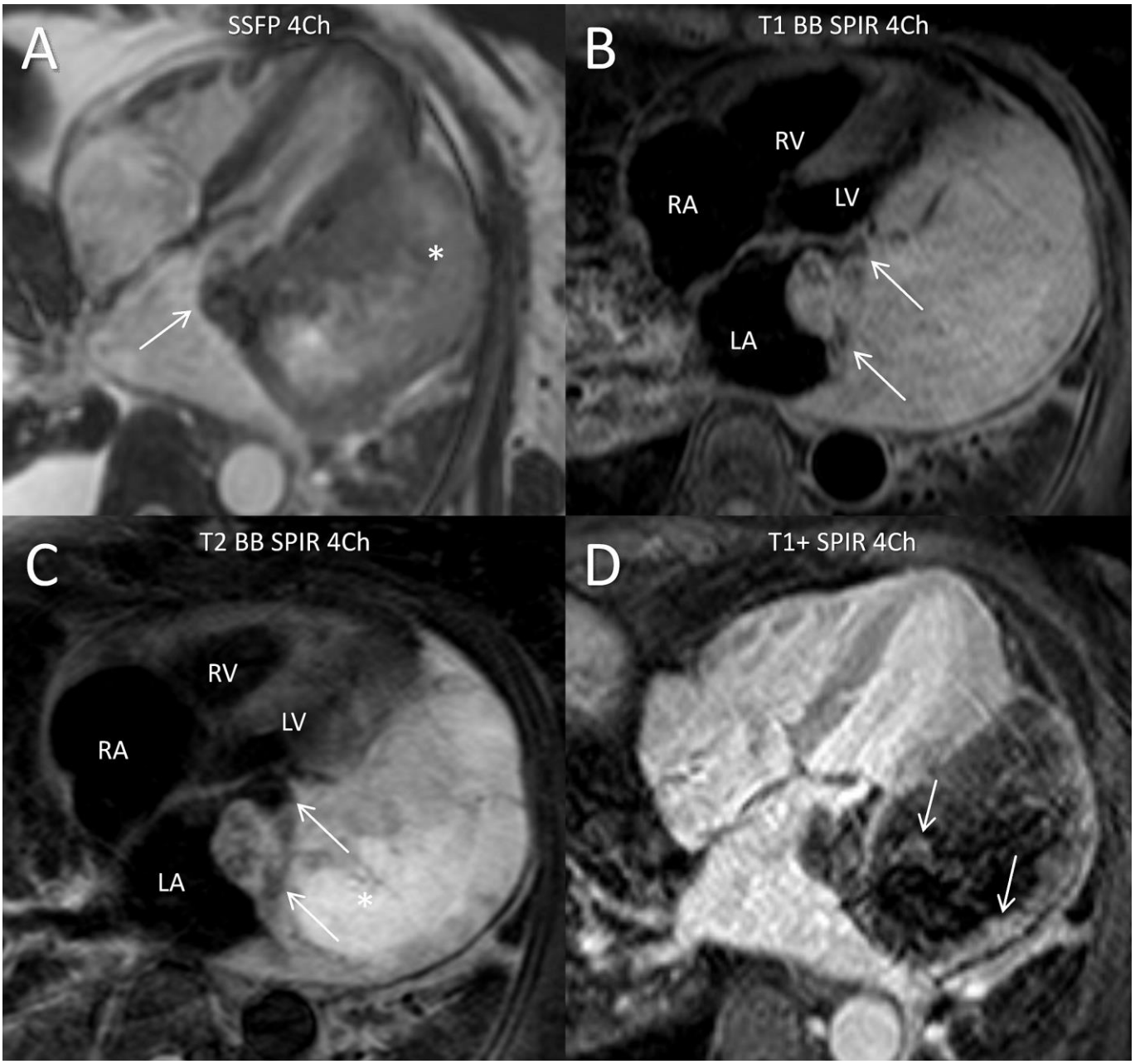

Figure 2: 85 y/o female with cardiac sarcoma.
Technique: Cardiac MRI: Philips Intera 1.5 T, Best, Netherlands (receiving coil "cardiac-SENSE" with parallel imaging). Pre and post IV contrast administration (12 ml Gadovist, 1 mmol/ml, Bayer HealthCare, Germany).
Findings: (2-A) Steady-state-free-precession (balanced fast field echo bFFE, TR 2.7 ms, TE 1.4 ms, flip angle 60°) sequence in four chamber view (4Ch) shows a solid mass (12.8 x 12.2 x 5.7 cm) that had developed from the left atrial or left lateral ventricular wall and extends into the left atrium (arrow) and pericardium (asterisk), causing left lateral wall motion impairment. (2-B) T1w black blood sequence with spectral-presaturation-inversion-recovery for fat suppression (T1 BB SPIR 4Ch, TR 1000, TE 20, flip angle 90°) and (2-C) T2w black blood sequence (T2 BB 4Ch, TR 2000, TE 80, flip angle 90°) show hypointense inclusions within the tumor (arrows), compatible with calcifications - in correlation with the CT findings. T2-hyperintense areas within the tumor (asterisk) may represent edema or mucoid tumor components. (2-D) T1w sequence post contrast with spectral fat suppression (T1+ TFE SPIR 4Ch, TR 3.8, TE 1.3, flip angle 20°) shows heterogeneous contrast uptake of the tumor (arrows).

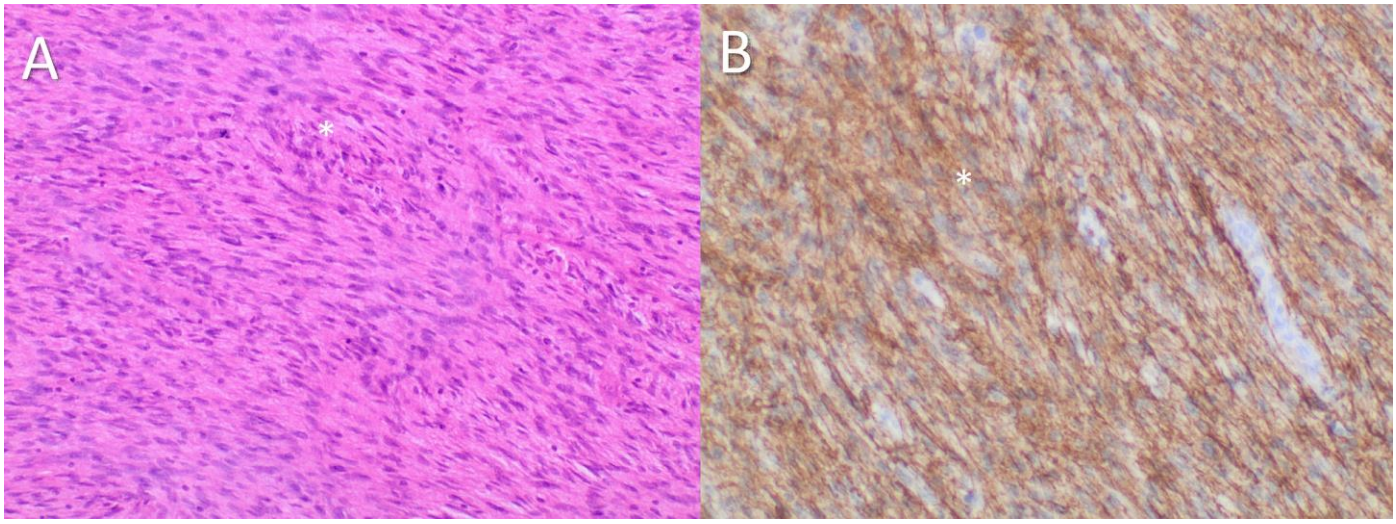

Figure 3: 85 y/o female with cardiac sarcoma.
Technique: Histopathologic analysis: hematoxylin-eosin (HE) stain and Immunohistochemistry for actin.
Findings: HE stain (3-A) shows a tumor consisting of interweaving fascicles of moderately pleomorphic spindle cells ("storiform pattern", asterisk) with high mitotic activity. (3-B) Immunohistochemistry confirming a high actin expression (asterisk), which in conjunction with the missing expression of desmin was classified as undifferentiated sarcoma.

Etiology	Mutation, unknown
Incidence	<0.02
Gender ratio	No predilection
Age predilection	Mean age 45 years
Risk factors	No known risk factors
Treatment	Resection (if possible)
Prognosis	Poor (< 2 years survival)
Findings on imaging	X-ray, echocardiography, CT: mass effect, possible calcification; MRI: heterogeneous signal, infiltrative growth, enhancement

Table 1: Summary table for primary cardiac sarcoma.

	X-ray	**Echo**	**CT**	**MR**	**Most common location and characteristics**
Primary Cardiac Tumor, malignant (undifferentiated sarcoma, leiomyosarcoma, angiosarcoma, rhabdomyosarcoma)	Gradual to fast increase in heart size	Isoechogenic to hyperechogenic (calcifications)	Isodense to myocardium, may contain calcification	T1: isointense or heterogeneous; T2: isointense to hyperintense; CINE: restricted wall motion; Enhancement: diffuse, strong	Left atrium (undifferentiated sarcoma, leiomyosarcoma), right atrium (angiosarcoma), left ventricle (rhabdomyosarcoma)
Primary Cardiac Lymphoma	Gradual to fast increase in heart size	Isoechogenic wall thickening, pericardial effusion	Hypo- to isodense	T1: hypointense; T2: hyperintense; CINE: may show systolic dysfunction; Enhancement: variable	Right cavities, mediastinal extension
Secondary Cardiac Tumor (metastasis)	Gradual to fast increase in heart size	Isoechogenic to hyperechogenic (calcifications)	Isodense to myocardium, may contain calcification	T1: mostly hypointense to isointense; T2: mostly isointense to hyperintense; CINE: restricted motion of infiltrated wall; Enhancement: heterogeneous, mostly strong	Multilocular
Benign Cardiac Tumor: Myxoma	Normal, or indirect signs of valve obstruction	Hyperechoic, intracavitary, lobular border	Hypodense, calcifications	T1 hypointense to isointense, T2: hyperintense, calcifications hypointense CINE: mass effect may lead to valve obstruction; Enhancement: moderate	Left atrium (75%), right atrium (20%), ventricles (5%)
Benign cardiac tumors, other than myxoma (e.g. lipoma, papillary fibroelastoma, rhabdomyoma)	Normal, or indirect signs of valve obstruction	Hyperechoic; (lipoma, rhabdomyoma); heterogeneous (papillary fibroelastoma)	Hypodense (lipoma, rhabdomyoma), heterogeneous (papillary fibroelastoma)	T1 and T2 hyperintense (lipoma); T1 and T2 heterogeneous (papillary fibroelastoma); T1 isointense, T2 hyperintense (rhabdomyoma); Enhancement: none or minimal (lipoma, papillary fibroelastoma, rhabdomyoma) to moderate (fibroma)	Interatrial wall (lipoma); valves (papillary fibroelastoma); multiple locations (rhabdomyoma)
Pericardial hematoma	Gradual to fast increase in heart size	Heterogeneous (depending on age)	Heterogeneous (depending on age)	T1, T2: heterogeneous (depending on age); Enhancement: none	pericardial
Intracardiac Thrombus	Normal	Intracavitary hyperechogenic lesion	Hypodense intracavitary lesion	T1, T2: heterogeneous (depending on age); CINE: isointense to myocardium, hypointense to blood; Enhancement: no early enhancement, late enhancement possible if chronic	Intracavitary, mostly left or right auricles, apical thrombus after myocardial infarction

Table 2: Differential diagnosis table for primary cardiac tumor.

ABBREVIATIONS

4Ch = four chamber view
CMR = cardiac magnetic resonance imaging
CT = computed tomography
CTA = computed tomography angiography
LM = left main
RCA = right coronary artery
SA = short axis view
SPIR = spectral-presaturation-inversion-recovery
SSFP = steady-state-free-precession
STIR = short-tau-inversion-recovery

KEYWORDS

cardiac mass; cardiac tumor; cardiac sarcoma; magnetic resonance imaging; MRI; cardiac MRI; cardiovascular MR; CMR; computed tomography; CT; echocardiography; coronary angiography; chest X-ray; multimodal imaging

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