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CARDIO-ONCOLOGY

CLINICAL CASE

1-Month Relapse of Undifferentiated Sarcoma in the Left Atrium

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ABSTRACT

Primary cardiac sarcomas are extremely rare. Echocardiography provides initial information about tumor location and size. However, due to the frequent resemblance to benign myxomas or thrombotic formations, the correct diagnosis often requires a multimodal approach. We report a case of undifferentiated cardiac sarcoma in a 46-year-old woman who underwent surgical resection. One month after the operation, echocardiography revealed disease recurrence. The patient underwent chemotherapy and hypofractionated radiotherapy with significant reduction of mass size. Primary cardiac sarcomas may be suspected by multimodality imaging tests, but the definitive diagnosis is histologic. There is still no international agreement about imaging criteria to define these tumors or optimal treatment. Radical surgery is potentially the best therapeutic option, but it is still burdened by high recurrence rates; radiotherapy, chemotherapy and immunotherapy appear promising, especially when used in combination. (JACC Case Rep. 2025;30:103861)

Primary cardiac tumors are extremely rare with an incidence of clinical diagnosis of approximately 1.38 of 100,000 inhabitants per year[1] and from 0.001% to 0.03% in autopsy series.[2] Of these, 75% are benign and only 25% are malignant: mainly sarcomas of various histotypes (75%),[3] the most common being angiosarcoma.[2]

Clinical presentations of primary cardiac sarcomas (PCSs) include valvular dysfunctions, arrhythmias, congestive heart failure, and central/peripheral embolisms (ie, cerebrovascular accident or pulmonary embolism).[4] Echocardiography usually provides initial information about tumor location and size; however, the correct diagnosis may be hindered by similarities to benign myxomas or thrombotic formations. Therefore, a multimodality approach with

TAKE-HOME MESSAGES

- Echocardiography is essential to provide initial information about primary cardiac sarcomas; however, a multimodality approach with second-level imaging techniques and histologic analysis is frequently needed to establish a definitive diagnosis.
- There is still no international agreement about treatment.
- Radical surgery is potentially the best therapeutic option, but it is still burdened by high recurrence rates, thus a close follow-up is essential; radiotherapy, chemotherapy and immunotherapy appear promising, especially when used in combination.

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ABBREVIATIONS AND ACRONYMS

CMR = cardiac magnetic resonance

CT = computed tomography

FDG = fluorodeoxyglucose

LA = left atrium

PCS = primary cardiac sarcoma

PET = positron emission tomography

TTE = transthoracic echocardiography

second level imaging techniques is frequently needed.[5] Cardiac magnetic resonance (CMR) is considered the gold standard for comprehensive assessment and tissue characterization, whereas computed tomography (CT), either combined with CMR or as an alternative, plays a critical role in specific cases and presurgical planning. When results are inconclusive, 18F-fluorodeoxyglucose (FDG) positron emission tomography (PET) is valuable for identifying malignancy and staging malignant cardiac tumors. Additionally, the diagnostic approach often depends on the availability of local resources and expertise.[5]

The very low incidence of these tumors makes it hard to conduct randomized controlled trials; therefore, no standard treatment strategy has been established yet.

Surgery is the only treatment that potentially increases survival; however, a complete tumor resection is not easy to obtain because, in many cases, infiltration does not offer adequate cleavage plans or involves structures that cannot be removed and replaced.[6] After surgery, adjuvant therapies such as radiotherapy, chemotherapy, and immunotherapy may be used, the latter two targeting the specific histologic subtype of the tumor. Nevertheless, prognosis in PCSs is very poor with a mean survival of 11 months.[7]

We report a case of early relapse of undifferentiated PCS after surgical resection.

HISTORY OF PRESENTATION

A 46-year-old woman presented with chest pain, dyspnea, and palpitations. The patient was hemodynamically stable. Physical examination revealed 4/6 systolic murmur at apex and diffuse crackles on lung auscultation.

VISUAL SUMMARY Timeline of Diagnostic and Therapeutic Procedures

Date	Event
Day 0	Emergency surgical resection of the mass
Day 9	TTE: no residual disease
Day 39	Started chemotherapy (Doxorubicin- Ifosfamide-Mesna)
Day 40	TTE: recurrence of cardiac mass in the left atrium PET-CT with FDG: intense metabolic activity (SUVmax 6) in correspondence to the known formation
Day 51 to 65	Hypofractionated radiotherapy treatment (5 sessions, total dose of 3500 cGy
Day 75	TTE: impressive reduction in the size of the atrial mass
Day 107	CT: Further significant reduction in the size of the atrial mass
Day 199	CT: almost complete disappearance of the known lesion with a residual minimal thickening along the posterior and posteroinferior wall of the left atrium

PAST MEDICAL HISTORY

The patient had no past medical history and no cardiovascular risk factors.

DIFFERENTIAL DIAGNOSIS

The presentation could be due to a series of conditions including acute aortic syndrome, pulmonary embolism, myocardial infarction, pericarditis, or valvular disease.

INVESTIGATIONS

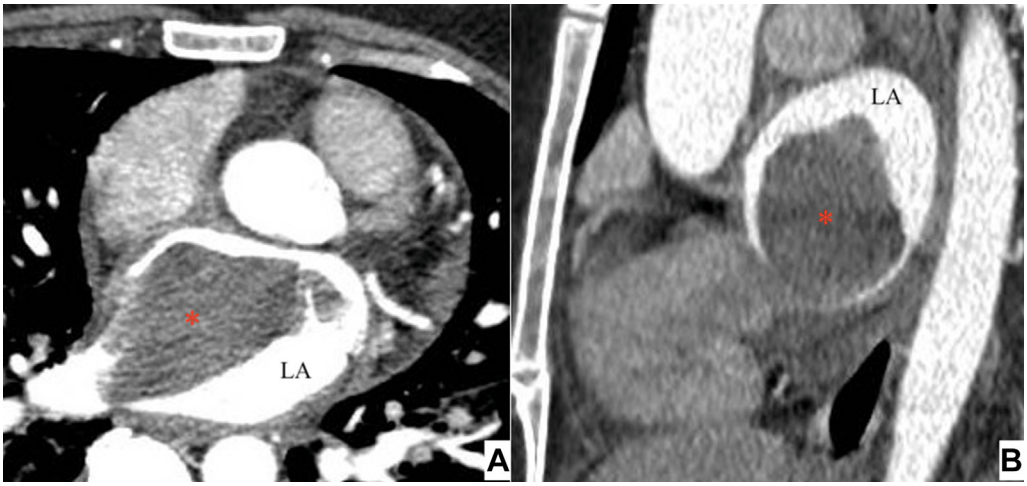
Electrocardiogram showed sinus tachycardia (heart rate, 130 beats/min) and nonspecific abnormalities of ventricular repolarization. On blood tests, the pathologic results were: high-sensitivity troponin I 240-278 ng/L (I and II determination; reference values [ref], <42 ng/L), N-terminal pro-B-type natriuretic peptide 1,002 pg/mL (ref, <150 pg/mL), D-dimer 3,627 ng/mL (ref, <750 ng/mL), polymerase chain reaction 53.5 mg/L (ref, <5 mg/L), white blood cells 10.86 $\times$ 10^9/L (ref, <10 $\times$ 10^9/L); hemoglobin 10.4 g/dL (ref, >12 g/dL). Contrast-enhanced chest CT was immediately performed to rule out pulmonary embolism and/or acute aortic syndrome and it showed a gross mass in the left atrium extending to the right pulmonary veins and through the mitral valve into the left ventricle for approximately 4 cm, compatible with thrombus, with no contrast-enhancement (**Figure 1**).

A transthoracic echocardiogram (TTE) showed a voluminous isohyperechoic formation with irregular margins (maximum diameter 35 mm) in the left atrium in relation to the anterior leaflet of the mitral valve, very mobile with excursion into the left ventricle, leading to a mild increase in the transvalvular gradient (mean gradient 4 mm Hg) and severe regurgitation. The first diagnostic hypothesis was thrombotic formation. The hemodynamic impact of the mass was not relevant; however, the high mobility was concerning.

MANAGEMENT

The case was evaluated by the cardiac surgery team. Because CMR was not available in the emergency setting and due to the high embolic risk of the mass, the team decided for urgent surgical resection. Intraprocedural transesophageal echocardiogram was performed, confirming the presence of a large, very

FIGURE 1 **Contrast-Enhanced Chest Computed Tomography**

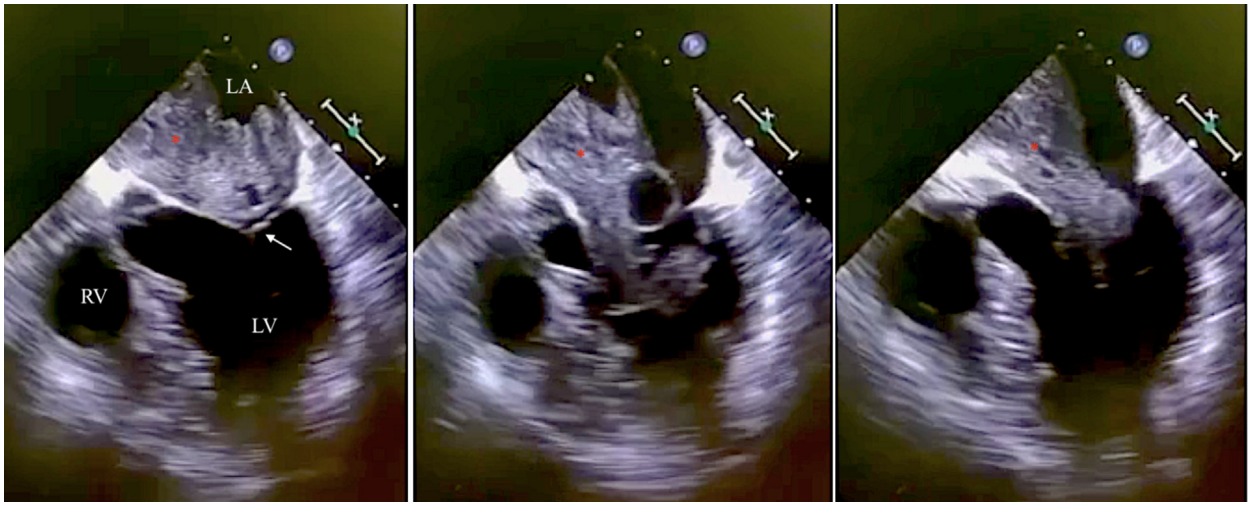


A gross mass (red asterisk) compatible with thrombus in the left atrium extending to the right pulmonary veins is shown. (A) Transverse section. (B) Sagittal section. LA = left atrium.

mobile mass in the left atrium with irregular margins and nonhomogeneous echostructure (Figure 2).

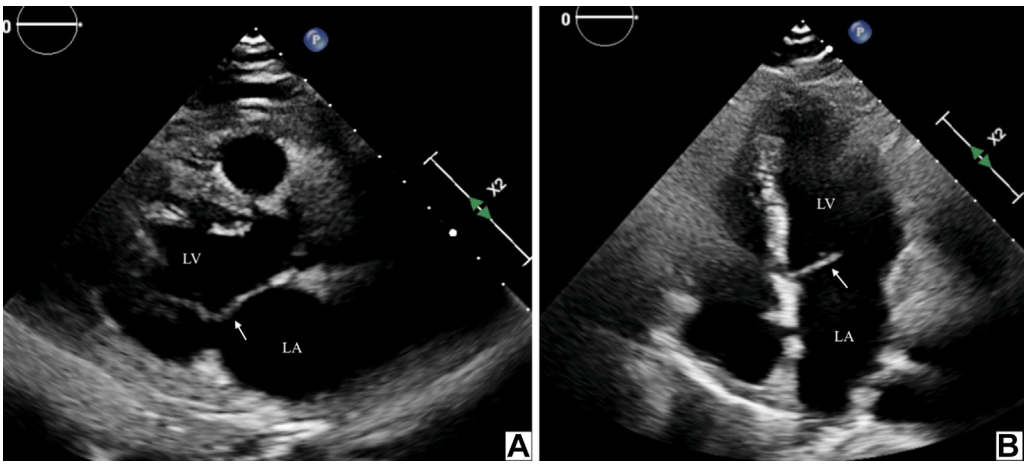
During resection, a biopsy sample was obtained for histologic examination. Upon extemporaneous examination, the finding was compatible with neoplastic tissue. Although further studies on post-fixation tissue were needed, the patient underwent a complete surgical resection of the cardiac mass and, after 2 weeks of cardiologic rehabilitation, she was discharged.

FIGURE 2 **Intraoperative Transesophageal Echocardiography**



A large, very mobile mass (red asterisk) in the left atrium with irregular margins and non-homogeneous echostructure. LV = left ventricle; RV = right ventricle; other abbreviation as in Figure 1.

FIGURE 3 Transthoracic Echocardiogram With No Residual Disease



Transthoracic echocardiogram performed during rehabilitation (9 days after surgery) showing no residual disease. (A) Parasternal long-axis view. (B) Apical 4-chamber view. White arrow indicates the mitral valve. Abbreviations as in Figures 1 and 2.

FOLLOW-UP

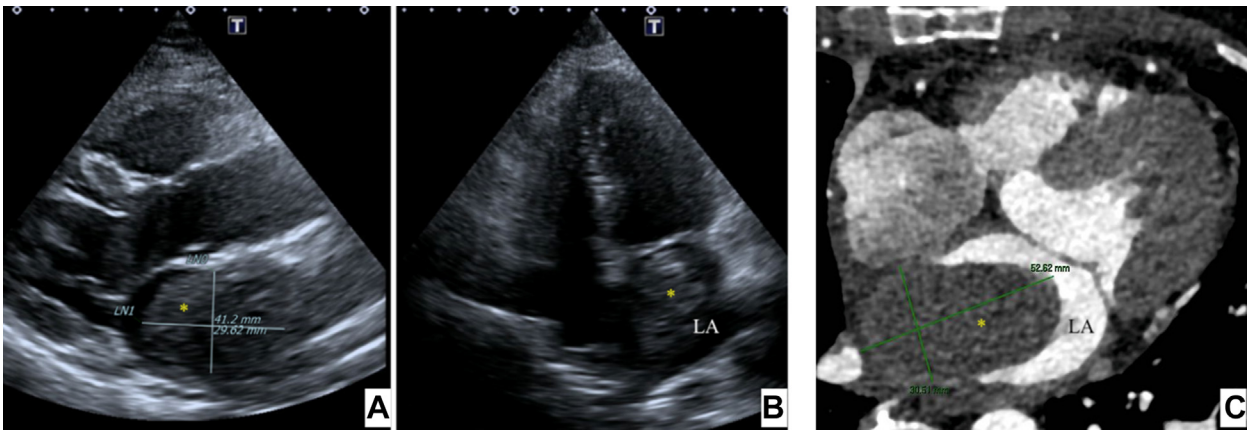
The TTE performed during rehabilitation (9 days after surgery) showed no residual disease (Figure 3).

Pathology revealed undifferentiated sarcoma (widespread positivity for vimentin and negativity for S100, CD45LCA, AE1/3, CD34, CD31, factor VII, thrombomodulin ERG, Fly1, MyoD1, myogenin, and myoglobin); therefore, the patient was re-admitted and started chemotherapy (doxorubicin-ifosfamide-mesna) almost 40 days after surgery. On that occasion, the patient underwent a new TTE revealing recurrence of cardiac mass in the left atrium confirmed by the angio-CT scan (Figure 4).

The PET-CT with FDG documented intense metabolic activity (maximum standardized uptake value, 6) at the level of the left atrium corresponding to the known formation and at the level of almost all the skeletal segments examined in relation to bone marrow activation secondary to postsurgical anemia. No further localizations of disease were detected (Figure 5).

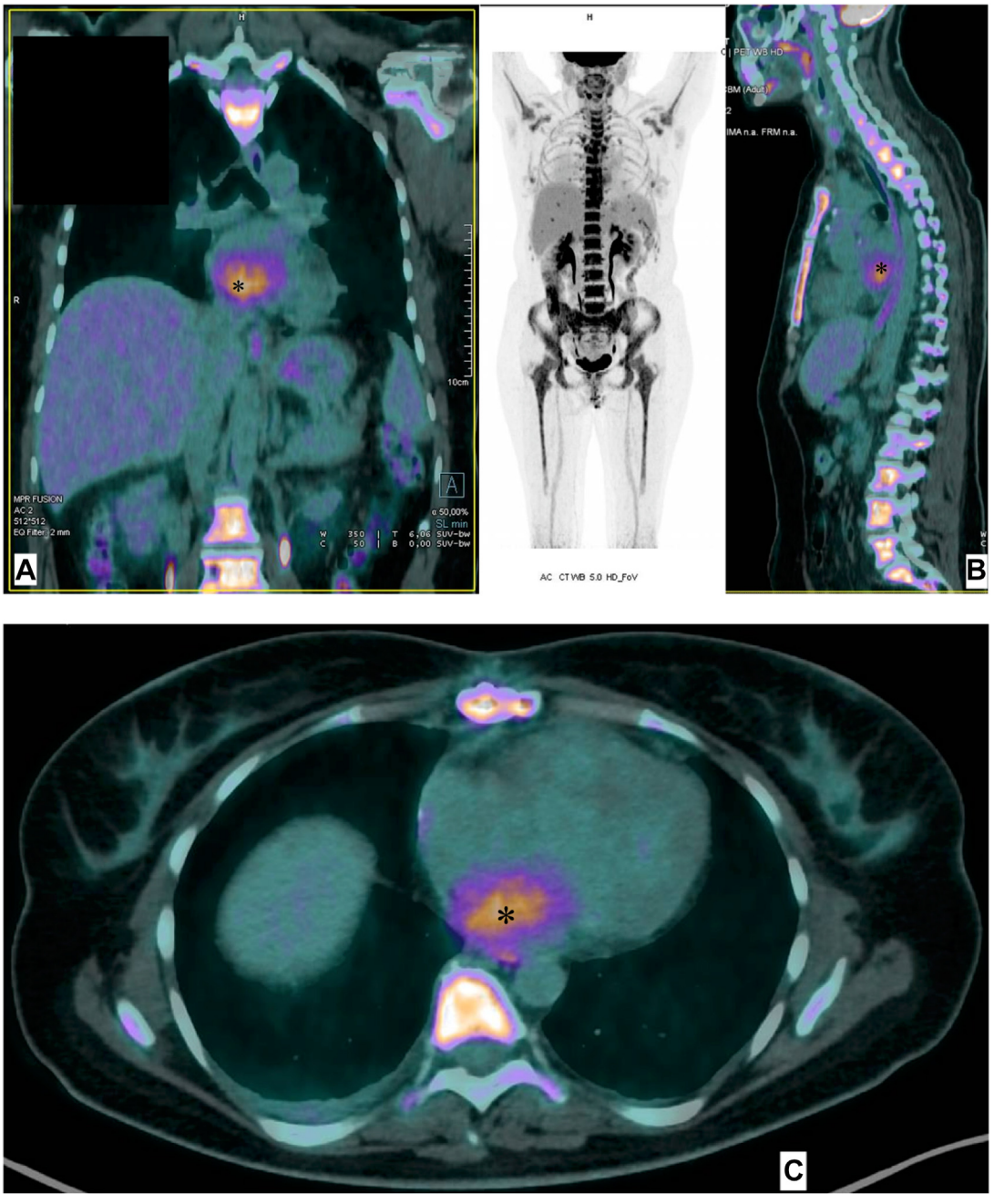
After multidisciplinary evaluation, redo surgery was excluded and the patient was referred to

FIGURE 4 Transthoracic Echocardiogram Showing Recurrence



A cardiac mass (yellow asterisk) is shown in the LA (A) Parasternal long-axis view. (B) Apical 4-chamber view. (C) Mass is confirmed by the angio-computed tomography scan (transversal plane). Abbreviation as in Figure 1.

FIGURE 5 **Positron Emission Tomography/Computed Tomography With Fluorodeoxyglucose**

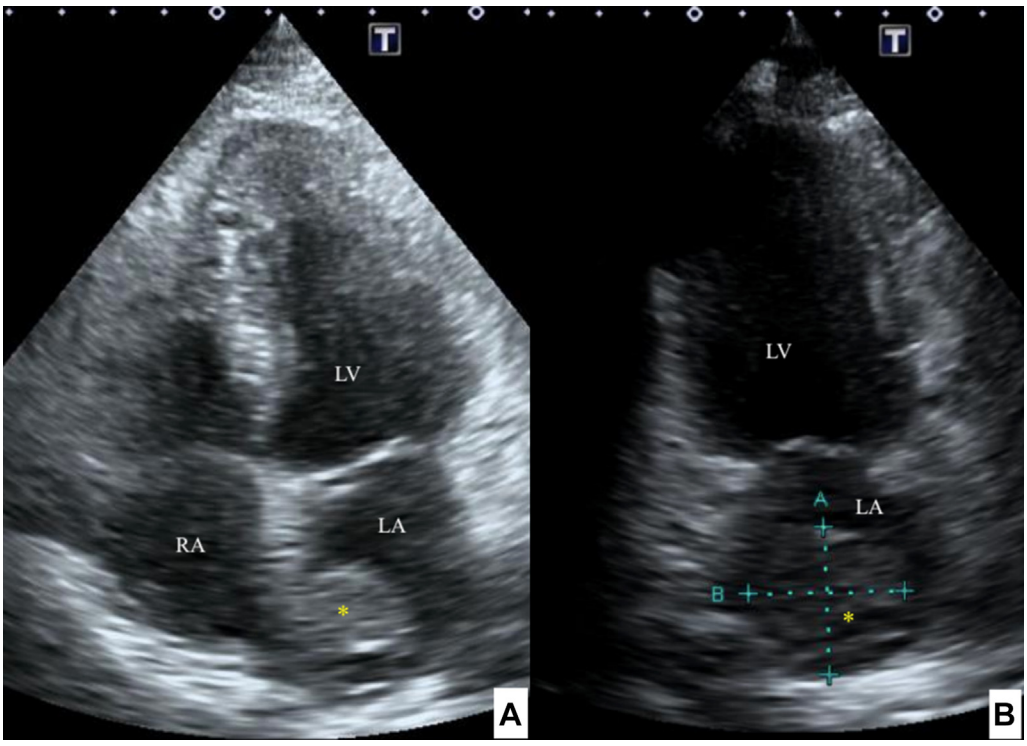


Intense metabolic activity (maximum standardized uptake value 6) at the level of the LA corresponding with to the known formation (black asterisk) and at the level of almost all the skeletal segments examined in relation to bone marrow activation secondary to postsurgical anemia. (A) Coronal plane. (B) Sagittal plane. (C) Transverse plane.

hypofractionated radiotherapy treatment (5 sessions, total dose of 3,500 cGy), complicated by one single episode of chest pain and dyspnea, with no signs of acute ischemia on electrocardiogram and laboratory tests and with no hemodynamic instability.

One month after detection of disease recurrence, during a new hospitalization to perform the second cycle of chemotherapy, the patient underwent a new TTE documenting impressive reduction in the size of the atrial mass (Figure 6).

FIGURE 6 Transthoracic Echocardiogram After 1 Month



Transthoracic echocardiogram performed 1 month after detection of disease recurrence documenting impressive reduction in the size of the atrial mass (yellow asterisk). (A) Apical 4-chamber view. (B) Apical 2-chamber view. Abbreviations as in Figures 1 and 2.

Further significant reduction was documented on control CT performed 2 months after the recurrence diagnosis (Figure 7).

Five months after the recurrence (after 6 cycles of chemotherapy and 5 sessions of hypofractionated radiotherapy treatment), CT showed almost complete disappearance of the known lesion with a residual minimal thickening along the posterior and posteroinferior wall of the left atrium (Figure 8).

Unfortunately, 2 months later the patient died due to a spontaneous cerebral hemorrhage.

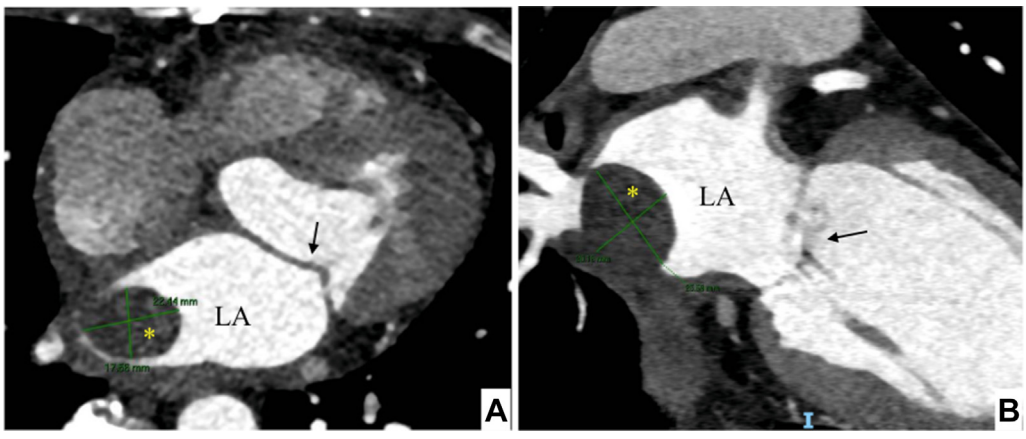
DISCUSSION

Although the incidence and survival of malignant cardiac tumors has shown an increasing trend over the past 50 years, they remain a very infrequent disease, with very poor prognosis.

PCSs mostly affect women, with mean presenting age of 47 years, and they are mostly localized in the left atrium, especially involving the posterior wall with an infiltrative pattern.[8] Tumor location and size determine presenting symptoms more than tumor histology. Left heart sarcomas commonly present with dyspnea due to the obstruction of transmitral blood flow, whereas right heart tumors are bulkier and usually determine nonspecific symptoms. Also, it is not unusual that the first incidental finding of disease is related to metastasis because up to 80% of PCSs are metastatic at diagnosis.[2] Another reported type of clinical presentation is related to embolic phenomena such as stroke and pulmonary embolism but also embolization in bones and adrenal glands.[8] Finally, PCSs can also simulate a pericardial disease and are often associated pericardial effusion.

Imaging techniques are essential in the diagnostic process. Echocardiography, widely available, usually provides initial information about tumor location and its size; however, the correct diagnosis may be hindered by similarities to benign myxomas or thrombotic formations. Several echocardiographic hallmarks of malignancy have been proposed and integrated into scoring systems, which have been shown to enhance the diagnostic accuracy of echocardiography in detecting cardiac masses' malignancy and ruling out thrombotic lesions.[9]

FIGURE 7 Computed Tomography After 2 Months

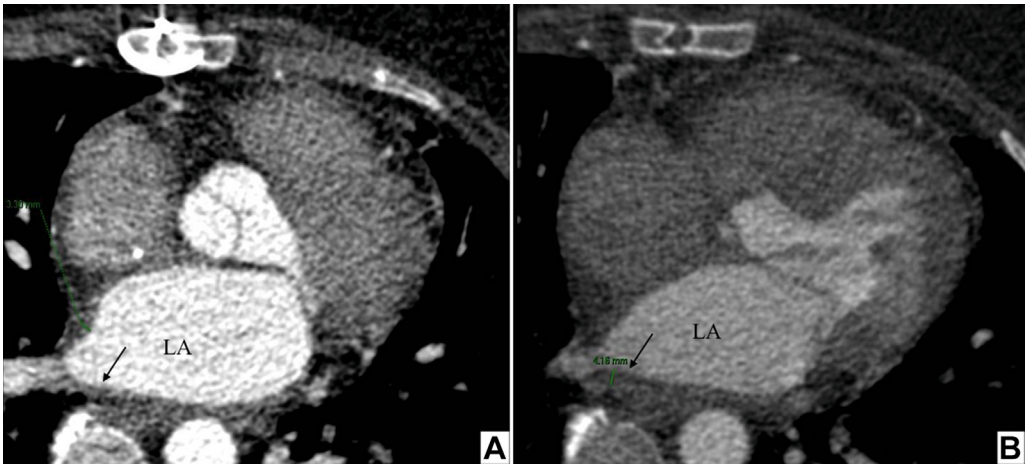


Computed tomography performed 2 months after the recurrence diagnosis documenting further significant reduction in the size of the atrial mass (yellow asterisk). (A) Transverse plane. (B) Sagittal plane. Black arrow indicates the mitral valve. Abbreviation as in Figure 1.

Nowadays, CMR is considered the gold standard technique for cardiac masses, offering tissue characterization and additional prognostic insights.[10] Integrated management using CT-PET is a valuable second-choice diagnostic tool for cardiac tumors. Unfortunately, CMR and PET are often unavailable in the emergency setting.

Beyond the diagnostic intent, imaging techniques are essential also to assess the possibilities of cardiac surgery because radical surgery is first-line therapy for cardiac sarcomas when it is feasible, potentially increasing survival. Nevertheless, patients who have no evidence of distant metastases who undergo an R0 resection still have a high probability of recurrence

FIGURE 8 Computed Tomography After 5 Months



Computed tomography performed 5 months after the recurrence (after 6 cycles of chemotherapy and 5 sessions of hypofractionated radiotherapy treatment) showing almost complete disappearance of the known lesion with a residual minimal thickening along the posterior and posteroinferior wall of the LA (black arrow). (A) Transverse plane, arterial phase. (B) Transverse plane, venous phase. Abbreviation as in Figure 1.

and, if this happens, reoperation is not associated with a significant increase in prognosis.[11] When the curative intent is not achievable, surgery can still be used for palliative purposes.

Furthermore, there is no consensus on adjuvant therapies. Chemotherapy can be used before and after the surgery, and multiple therapy has potentially greater chances than a single therapy, but evidence is still lacking. However, the use of neoadjuvant chemotherapy is extremely rare because it requires histologic diagnosis for which surgery is often the only option. The same goes for radiotherapy, with only an adjuvant intent. Immunotherapy appears to be promising but further studies are needed.

CONCLUSIONS

PCS is a rare disease that predominantly affects adults in the fifth decade of life with a very poor prognosis. Symptoms depend on the size and location of the tumor and may be nonspecific up to the advanced stages. Diagnosis may be suspected by TTE or CT, but it may also be hampered by resemblance to benign myxomas or thrombus; thus, histologic diagnosis is often essential. There is no standard treatment. Surgery is potentially the best treatment option, followed by radiotherapy, chemotherapy, and immunotherapy targeted to the specific histologic subtype of the tumor, but further studies are needed.

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