Radiology Case Reports 19 (2024) 1200–1207

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/radcr

Case Report

Clinical presentation, diagnostic evaluation, and management of undifferentiated/unclassified cardiac sarcoma: A case report and literature review ☆

Aynaz Mohammadi[a,1], *Mohammad Mohammadi*[a,1], *Mahboubeh Pazoki*[b], *Mohammad reza Ayoubpour*[c], *Pegah Babaheidarian*[d], *Sam Zeraatian Nejad Davani*[e], *Reza Ghaderi*[f,*]

[a] *School of Medicine, Iran University of Medical Sciences, Tehran, Iran*
[b] *Department of Cardiology, School of Medicine, Hazrat-e Rasool General Hospital Iran University of medical sciences, Tehran, Iran*
[c] *Department of Radiology, School of Medicine, Hazrat-e Rasool General Hospital Iran University of medical sciences, Tehran, Iran*
[d] *Department of Pathology, School of Medicine, Hazrat-e Rasool General Hospital Iran University of medical sciences, Tehran, Iran*
[e] *Department of Cardiovascular Surgery, School of Medicine, Hazrat-e Rasool General Hospital, Iran University of Medical Sciences, Tehran, Iran*
[f] *Department of Internal Medicine, School of Medicine, Hazrat-e Rasool General Hospital, Iran University of Medical Sciences, Tehran, Iran*

ARTICLE INFO

Article history:
Received 22 October 2023
Revised 24 November 2023
Accepted 25 November 2023
Available online 4 January 2024

ABSTRACT

This case report details a challenging instance of undifferentiated/unclassified cardiac sarcoma in a 28-year-old female, presenting with diverse symptoms like muscle weakness, shortness of breath, and hemoptysis. Diagnostic hurdles led to an initial misdiagnosis of granulomatosis with polyangiitis before discovering a sizable left atrial mass, ultimately diagnosed as high-grade undifferentiated/unclassified sarcoma. Despite initial surgical intervention, the patient's condition worsened, underscoring the complexities in managing such cases involving cardiac sarcomas. This case emphasizes the diagnostic complexities

☆ Competing Interests: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

* Corresponding author.
E-mail address: Rezaghaderi1355@gmail.com (R. Ghaderi).

[1] The authors share the first authorship.

https://doi.org/10.1016/j.radcr.2023.11.065

Keywords:
Cardiac tumors
Undifferentiated sarcoma
Cardiac sarcomas
Echocardiography
Surgery
Multimodal imaging
Malignancy
Case report

associated with primary cardiac sarcomas, particularly the challenges in achieving accurate diagnoses and formulating effective treatment strategies.

Introduction

Undifferentiated/unclassified cardiac sarcoma is an extremely rare and aggressive tumor that arises from the mesenchymal cells of the heart. It represents about 5% of all cardiac tumors and has a poor prognosis due to its aggressive nature and propensity for metastasis [1–3]. The clinical presentation of cardiac sarcomas can be variable, ranging from asymptomatic incidental findings to symptoms of heart failure, chest pain, and arrhythmias [4]. The diagnosis of cardiac sarcoma is challenging and requires a multimodality imaging approach, including echocardiography, computed tomography (CT), and magnetic resonance imaging (MRI). However, histologic examination with immunohistochemical and ultrastructural confirmation remains the gold standard for definitive diagnosis [5].

Despite advancements in diagnostic imaging techniques and treatment modalities, the prognosis for undifferentiated/unclassified cardiac sarcoma remains poor, with a median survival of approximately 6 months to 2 years after diagnosis [6]. Treatment options are limited due to the rarity of the disease and the lack of randomized clinical trials. Surgical resection with negative margins is considered the gold standard treatment for cardiac sarcoma, but complete resection is often difficult due to the infiltrative nature of the tumor and its location within the heart. Chemotherapy and radiation therapy may be used as palliative treatment, but their efficacy remains unclear [7].

Here, we present a case report of a patient with undifferentiated/unclassified cardiac sarcoma, diagnosed through a multimodality imaging approach and confirmed by histologic examination. We discuss the clinical presentation, diagnostic evaluation, and management of this rare and aggressive cardiac tumor.

Case presentation

A 28-year-old Iranian female patient was admitted to the Respiratory Ward of Rasoul Akram Hospital in Tehran on October 25, 2022, with complaints of pain, muscle weakness, shortness of breath, and hemoptysis (coughing up blood). The pain and weakness in her limbs, fatigue, and morning dryness had started about a year ago and had been gradually progressing. The patient mostly experienced muscle weakness in her upper limbs, especially in the proximal parts. She also reported experiencing difficulty standing up from the ground and discoloration of her fingernails and toenails. The shortness of breath had started about 3 months ago and was at the level of FCII-III. The patient did not report any fever, chills, cough, sputum, orthopnea, or paroxysmal nocturnal dyspnea (PND). According to the patient, she had lost about 12 kilograms of weight and had night sweats over the past 5 months. The patient also mentioned that she had been suffering from migraines, blurred vision, and paresthesia in her hands and feet for about a year and had been examined by a neurologist and an ophthalmologist, but no problems were found. Polycystic ovary syndrome (PCOS) diagnosis was included in the patient's medical history in 2021, and as a familial medical history the patient's mother had rheumatoid arthritis (RA). There was no history of alcohol, cigarette, or opium use or addiction. Due to depression caused by past psychological crises, the patient was under treatment with 25 mg TDS nortriptyline, 25 mg 1/2 quetiapine daily, 75 mg BD venlafaxine, and 500 mg TDS metformin.

Upon admission, the patient's vital signs were as follows: BP: 130/70, PR: 90, RR: 22, T: 37, and O2 sat: 93% without a mask. Lung sounds were clear, and heart sounds were regular without murmurs or extra sounds. There was no evidence of edema or congestion, and the force of all 4 limbs was complete and 5/5. The patient had an echocardiogram done on July 9, 2022, which was normal, and also, she had reports of spirometry test with a restrictive pattern, high C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) level.

Laboratory tests conducted on the patient's first day of admission showed the following results: white blood cells (WBC) at $5.8\times103/mm^3$ (normal: 4-10 $\times$ $103/mm^3$), anemia (hemoglobin = 10 g/dl) (normal: 12-16 g/dl), ferritin at 268 ng/ml (normal: 10-124 ng/ml), uric acid at 6.8 mg/dl (normal: 2.3-6.1 mg/dl), cholesterol at 206 mg/dl (borderline: 200-240 mg/dl), triglyceride (TG) at 262 mg/dl (normal: 60-160 mg/dl), lactate dehydrogenase (LDH) at 556 U/L (normal: 225-500 U/L), ESR at 55 mm/hr (normal: $<$20 mm/h), and CRP at 25.7 mg/L (normal: $<$6 mg/L). The patient exhibited elevated liver function test results, while kidney function tests fell within the normal range, indicating proper kidney function. High levels of LDH, total bilirubin, and CRP, indicating an inflammatory or infectious process. In addition to the above tests, the patient's D-dimer was checked, which was 1361 (ULN: 500).

Further diagnostic procedures were performed for them, including a CT angiography, which showed vague evidence of ground glass lesions throughout the lung field and a 13mm nodule in the lateral Right lower lobe (RLL). Due to suspicion of Interstitial lung disease (ILD) and malignancy and lack of clarity in the CT angiography, a bronchoscopy was performed,

which was normal, and no lesion was observed in the bronchi. due to the patient's presentation of Raynaud's phenomenon and the vague ground glass lesions on CT angiography, clinical suspicion of a rheumatological disease was raised, and therefore, BAL and TBLB (blind tissue sampling during bronchoscopy) were performed.

The patient was discharged with good general condition and stable vital signs after consulting with the rheumatology service and receiving diagnostic tests and recommendations to visit the clinic upon receiving pathology results.

Upon the readiness of the pathology results (about 10 days later), the patient's mother returned to the hospital with complaints of her daughter's worsening condition. The pathology was reviewed by the lung service, but no significant findings were observed. On the same night, the patient was referred to this center under EMS supervision with complaints of severe shortness of breath at FC IV level. In this session, the patient also presented with a history of mild hemoptysis in the form of a small streak of blood. The patient's vital signs in the emergency department were BP: 110/80 PR: 127 T: 36.9 O2 sat: 89% without mask.

Laboratory tests in this time of admission showed the following results: WBC 8.7 × 103/ mm^3 (normal: 4-10 × 103/mm^3), anemia (hemoglobin = 8.4 g/dl) (normal: 12-16 g/dl), LDH 825 U/L (normal: 225-500 U/L), calcium 7.4 mg/dl (normal:8.6-10.6 mg/dl), sodium 139 mEq/L (normal: 136-145 mEq/L), potassium 3.6 mEq/L (normal: 3.7-5.5 mEq/L), magnesium 1.7 mg/dl (normal: 1.8-2.6 mg/dl). Liver function tests were normal. Urine and blood cultures were sterile. Venous blood gas (VBG) analysis showed PH=7.43 (normal: 7:31-7:41), PCO2=23.8mm Hg (normal: 41-51 mm Hg), PO2=34.5 mm Hg (normal: 35-40 mm Hg), HCO3=15.6 mm Hg (22-26 mm Hg). Additional laboratory investigations were done. TB, covid19, INF A, INF B PCR were negative.

In an emergency situation, with a clinical diagnosis of a flare-up of Granulomatosis with polyangiitis (GPA), the patient received cortisone pulse, which proved to be effective and improved the patient's general condition. Due to shortness of breath and suspicion of pulmonary thromboembolism (PTE), CT angiography (Figs. 1A and B) was performed for the patient. The results were examined by the pulmonary service, revealing a large filling defect in the left atrium and left atrial appendage veins. The filling defect was suspected to be a thrombus or a tumor. After consulting with the radiology department and considering the absence of previous information about the tumor and the presence of rheumatological diseases in the patient, such as lupus and antiphospholipid syndrome and also elevated levels of D-dimer anticoagulant therapy was started due to the likelihood of thrombosis associated with rheumatological diseases.

One hour later, the patient was referred to a cardiologist for a specialized echocardiography (Figs. 2 and 3), which revealed a large fixed mass (5.3 cm x 3. 2 cm) with moving particles on it in the left atrium, and intermittent protrusion to the mitral valve inflow (length: 1 cm) resulting in compression of pulmonary veins entrance to left atrium. The echocardiography report suggested that the mass was tumoral and was affecting the heart valves.

As a result, the patient was a candidate for heart surgery, and a sample was taken for further examination by the pathology team. After surgery, the patient's general condition improved significantly, and their spo2 levels reached 99%. They had no complaints of pain, shortness of breath, or hemoptysis, and were discharged from the hospital after 2-3 days of being hospitalized in the ICU. They were given warfarin tablets (1/4 tablet daily) and were advised to check their PT, PTT, and INR levels daily, as well as to return for dose adjustment and to provide the pathology report to the cardiac and pulmonary clinic.

Pathological examinations were carried out to determine the nature of the tumor. Despite the use of different staining techniques, the pathology group could not reach a definite diagnosis. Finally, after conducting several IHC tests, the pathology (Figs. 4 and 5) report revealed that the patient's tumor was

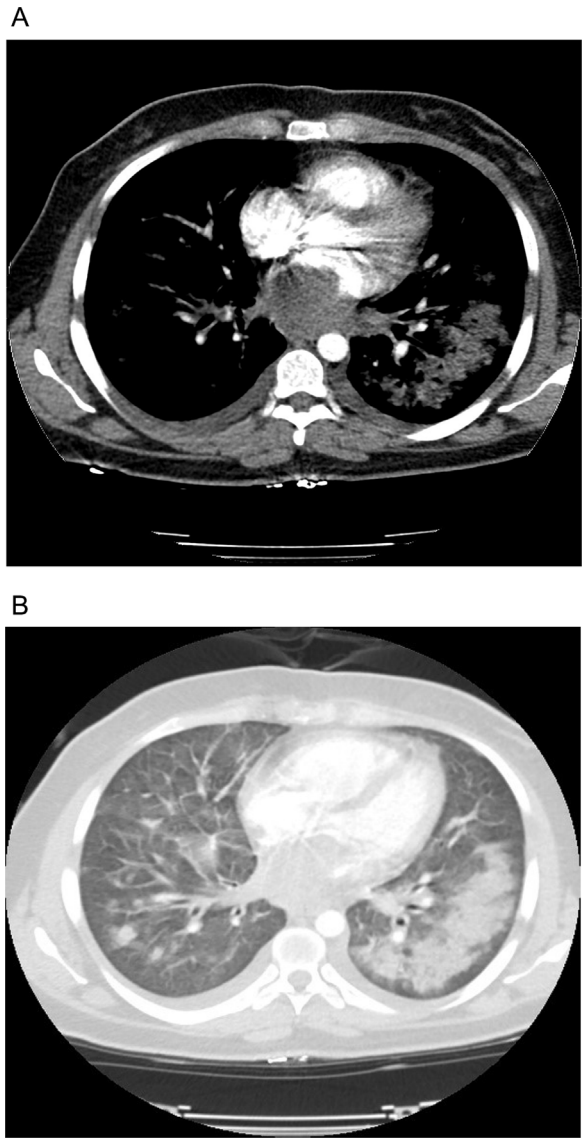


Fig. 1 – Upright Chest X ray (PA) shows fluffy and reticular opacities in both lungs with mild dominancy in middle and lower zones, the cardiac size is normal and costophrenic angles are not blunted yet.

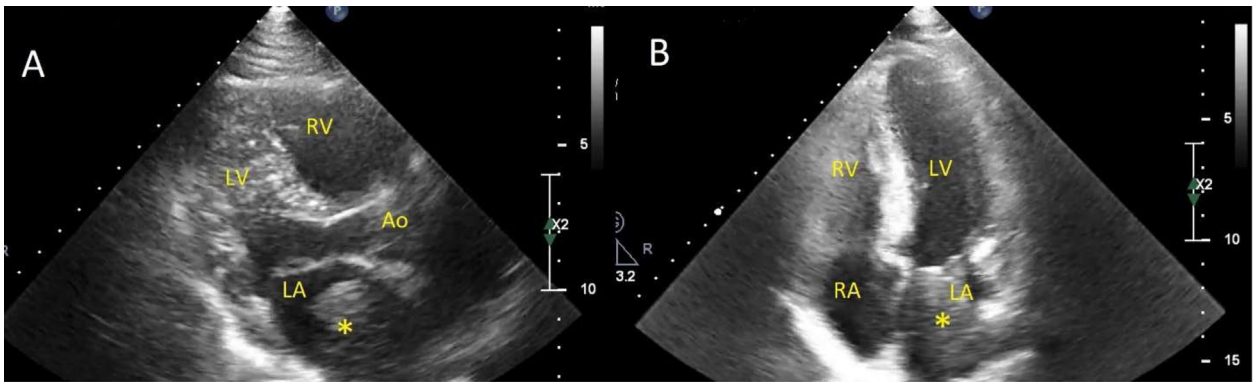


Fig. 2 – (A) A CT pulmonary angiography. (A) mediastinal view shows large mass with lobulated margins in left atrium with extension to lower pulmonary veins, mild pleural effusion is seen in both sides, left heart and aortic enhancement is not desired in standard CT pulmonary angiography which was due to prolongation of the study. (B) Lung window shows alveolar pattern consolidation in left lower lobe and a few nodules in left lower and left middle lobe suggesting alveolar filling due to either pulmonary edema or alveolar hemorrhage.

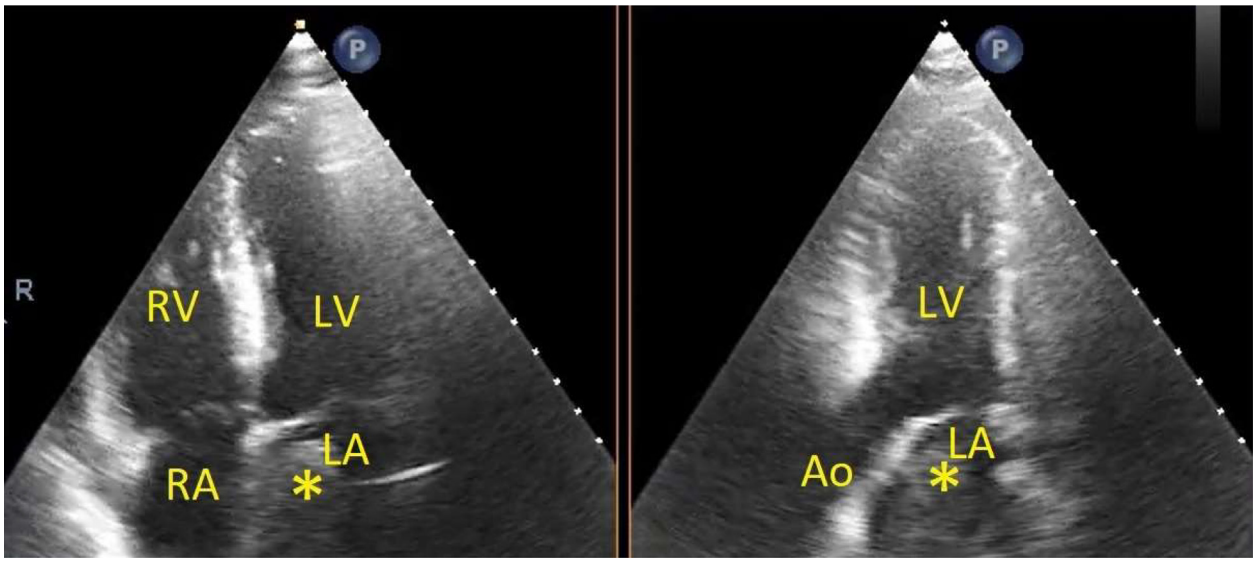


Fig. 3 – Left atrial mass; transthoracic echocardiography (A) PLAX-view showing LA mass (yellow asterisk). (B) four chamberview showing LA mass (yellow asterisk). LA, left atrium; LV, left ventricle; RV, right ventricle; Ao, ascending aorta.

a high-grade spindle cell sarcoma, presenting features that did not fit into a specific subtype classification. the patient's tumor appeared to be a high-grade spindle cell sarcoma that could not be classified into a specific subtype. The tumor cells had moderately pleomorphic nuclei that were oval to cigar-shaped and showed a clumped chromatin pattern. Some tumor cells had prominent nucleoli and exhibit cytoplasmic clearing with vesicular nuclei. The presence of at least 15 mitoses per 10 high-power fields and large areas of necrosis suggested a high proliferation rate and aggressive behavior. Immunostaining revealed that the tumor cells were positive for vimentin and showed scattered positivity for TLE-1 and CD31, but negative for PANCK, SMA, CD34, S100, Desmin, LC, CD3, CD20, CD23, STAT6, MDM2, EMA, CD99, and BCL2. The Ki67 staining indicated that up to 50% of the tumor cells were actively dividing. Overall, the diagnosis was a high-grade spindle cell sarcoma that cannot be further classified based on the available information.

The medical team carried out the necessary examinations to determine the next steps of treatment.

During this time, the patient underwent a whole-body positron emission tomography (PET) scan, which was performed to investigate involvement of the pleura, mediastinum, and chest muscles. Eventually, with the discharge of exudative secretions and improvement in the patient's general condition, they became a candidate for receiving chemotherapy concurrently with broad-spectrum antibiotics. However, due to unstable vital signs, the patient was intubated during the decision-making process of the medical team to determine the timing of chemotherapy initiation, and resuscitation measures were performed, which unfortunately were unsuccessful and the patient expired.

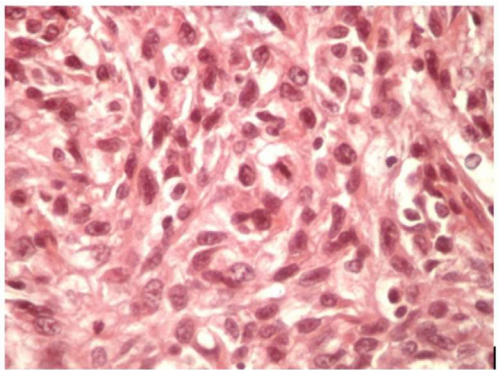
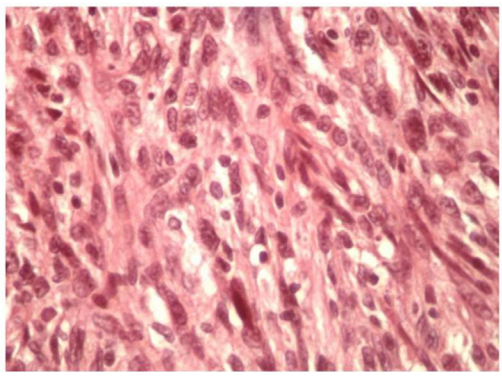


Fig. 4 – Left atrial mass; transthoracic echocardiography X plane-view showing LA mass (yellow asterisk). LA, left atrium; LV, left ventricle; RV, right ventricle; Ao, ascending aorta.



Figs. 5 – Sections show tumoral cell with pleomorphic nuclei and spindle cell cytoplasm. Frequent mitotic activities are evident. (x40).

Discussion

Primary tumors of the heart are not common, with a frequency of 0.001%-0.030% observed during autopsy [8]. Analyzing data from 22 large autopsy studies published between 1934 and 1993, Reynen found 157 cases of cardiac tumors in 731,309 autopsies (0.021%), which translates to an incidence of 2 cardiac tumors per 10,000 autopsies [9]. The majority of primary cardiac tumors are benign, with myxoma being the most prevalent type [10]. Approximately 25% of primary cardiac tumors are malignant, with sarcomas being responsible for 95% of cases and lymphomas accounting for the remaining 5% [8]. The median age at diagnosis of malignant tumors is typically 40-50 years [11].

Liposarcoma, rhabdomyosarcoma, fibrosarcoma, leiomyosarcomas, angiosarcomas, synovial sarcomas, and undifferentiated sarcomas are the most common types of cardiac sarcomas [4]. These tumors usually affect only one chamber of the heart, often the left or right atria [8]. Among them, angiosarcoma is the most frequent type (37%), and it typically occurs in the right atrium with pulmonary and distant metastases. Another tumor that affects the left atrium in an advanced stage is an undifferentiated sarcoma [4,8]. Undifferentiated pleomorphic sarcomas (UPSs) originating from the heart can grow invasively through the atrial and ventricular walls, which can lead to left-sided heart failure caused by mitral valve dysfunction [12]. UPSs account for about 10% of all primary cardiac tumors and are the most common primary cardiac malignancy. They mainly affect adults and are not gender-specific [13,14]. In the case of our patient, the tumor (a high-grade undifferentiated/unclassified sarcoma) was located in the left atrium with mobile particles and intermittent protrusion into the mitral valve inflow. Other possible diagnoses for masses in the left atrium include myxoma (in the fossa ovalis), lipoma, thrombus (in the left atrial appendage), and sarcoma (in the posterior wall) [14]. Primary malignant tumors of the heart are extremely rare, and as a result, most medical oncologists have had little experience treating them [9]. The initial clinical and radiographic evaluation of undifferentiated pleomorphic cardiac sarcoma can be difficult because it presents similarly to benign cardiac tumors and other more common cardiac sarcomas [15]. Symptoms of cardiac tumors typically depend on the location of the mass. Although many cardiac tumors are asymptomatic, they are often diagnosed at an advanced stage of the disease [16]. Dyspnea is the most common symptom, followed by chest pain, congestive heart failure, and palpitations [17]. Other symptoms include cough, hemoptysis, syncope, and generalized fatigue [18,19]. Cardiac sarcomas tend to spread to other parts of the body, such as the lungs, bones, soft tissue, and brain, at an early stage [8]. Symptoms of cardiac tumors vary and can be caused by obstruction of intracardiac blood flow, interference with valve function, local invasion, arrhythmias, or pericardial effusions [20,21]. In addition, right-sided tumors can cause pulmonary embolisms, while left-sided tumors can lead to embolisms in the systemic circulation, resulting in stroke or damage to other organs [22].

Anemia, hypergammaglobulinemia, and an elevated ESR are common laboratory abnormalities seen in patients with cardiac sarcomas [10]. Increased levels of LDH and schistocytes in the blood may suggest mechanical destruction, which can occur due to friction and shearing stress caused by the tumor. In the case mentioned, high LDH levels were detected, indicating the presence of mechanical destruction [23].

Assessing undifferentiated pleomorphic cardiac sarcoma during the initial clinical and radiographic evaluation can be difficult because its presentation is similar to that of benign cardiac tumors and other more prevalent cardiac sarcomas [24]. Different imaging techniques can be utilized for the assessment of individuals with primary cardiac tumors. Although a chest x-ray can be beneficial as an initial diagnostic image for patients with general symptoms, cardiac sarcomas are usually indistinguishable via the cardiac outline, and more sophisticated imaging methods are required. Transthoracic (TTE) and transesophageal (TEE) echocardiogram, CT, and MRI are advanced imaging modalities that have significantly enhanced the detection and diagnosis of primary cardiac tumors. These imaging techniques have proven to be helpful in making therapeutic decisions Echocardiography is often the initial diagnostic imaging tool used for suspected cardiac tumors due to its noninvasive nature and widespread avail-

ability. It can provide valuable information about the tumor's size, location, and impact on cardiac function. However, it has its limitations, and more advanced imaging modalities may be necessary for a definitive diagnosis [25].

The view of the heart during echocardiography may be restricted due to the patient's body shape, and this method may not provide complete tissue characterization [26]. Cardiac MRI is increasingly being used as a secondary diagnostic tool for cardiac masses, and specific features observed on MRI can help to determine the likelihood of malignancy and differentiate between a tumor, a thrombus, and myocardial invasion [27,28]. In addition, the density of T1 and T2 images can allow for the identification of the tumor cell type [22].

CT imaging plays an important role in the management of primary cardiac sarcoma (PCS), as modern CT protocols can provide detailed imaging of structures, aiding in the characterization of tumor extent [29]. Additionally, CT can provide some evaluation of surrounding lung tissue, the presence of pulmonary metastases, and the tumor's coronary supply. While MRI has higher temporal resolution and can provide additional tissue characterization, CT remains a valuable imaging tool in the diagnosis and management of cardiac tumors.

However, distinguishing between malignant and benign cardiac lesions can be difficult, with the majority of cardiac tumors being benign [25].

Fluorodeoxyglucose (FDG) PET can be helpful in distinguishing malignant from benign cardiac lesions. Rahbar et al. conducted a study to compare the efficacy of PET with contrast-enhanced CT criteria of malignancy and histology in detecting malignancy in cardiac lesions [15]. They found PET to have a sensitivity of 100% and specificity of 86%, with an overall accuracy of 96% for malignancy detection. Thus, PET may provide a noninvasive means of determining malignancy, although biopsy is necessary for definitive diagnosis and histologic subtype determination using percutaneous or open biopsy methods. While advanced imaging techniques have improved the understanding of the imaging characteristics and anatomical extent of cardiac masses, a pathologic diagnosis is essential for the diagnosis of cardiac sarcoma. This diagnosis is often made during surgical extirpation, which usually does not provide an opportunity for neoadjuvant strategies [25].

Metastasis is commonly found in Primary cardiac sarcomas (PCSs) patients during diagnosis, ranging from 20% to 46%. Sarcomas spread through the blood, and the most frequent site of dissemination is the lungs in both PCS and bone/soft tissue sarcomas [30–32]. Other areas of metastasis include bones, mediastinum, and the brain. Notably, PCS has a higher incidence of brain metastases than other soft tissue sarcomas, especially in left-sided cardiac sarcomas. Previous reports have shown an incidence of 31% of brain metastases in PCS, compared to 1-8% in other soft tissue sarcomas [30,33,34]. The higher incidence of brain metastasis in PCS is probably due to the location of these tumors in the heart, and periodic brain imaging is necessary. Left-sided tumors have a higher incidence of brain metastases due to the anatomic location of the brain downstream of the left ventricular outflow tract [25]. To diagnose cardiac masses, it is important to use multiple imaging techniques, but sometimes a histologic examination is necessary, which is considered the standard for diagnosis [35]. Histopathological examination is essential for determining whether a cardiac mass is benign or malignant and the exact type of mass [5]. Undifferentiated sarcomas can be detected on CT as large, irregular, intracavitary masses with low attenuation, appearing isointense on T1-weighted images and hyperintense on T2-weighted images. They show a heterogeneous, delayed enhancement pattern [13,26,35]. A definitive diagnosis can be made through immunohistochemical or ultrastructural confirmation, which includes the presence of typical spindle and polygonal cells with abundant eosinophilic cytoplasm and positive desmin and myoglobin immunoreactivity [11]. These cells are CD68 negative [13].

Sarcomas are usually treated with surgical excision, which is associated with better survival rates. However, obtaining negative margins during surgery can be challenging due to delayed diagnosis and the extent of myocardial involvement. Partial resection may provide some relief from symptoms but is associated with poor prognosis [11,25].

The effectiveness of chemotherapy and radiation in undifferentiated pleomorphic sarcoma (UPS) is not well-defined, and treatment is extrapolated from extra-cardiac sarcomas [36–38]. Combining neo-adjuvant chemotherapy and radiation with surgical resection may improve outcomes and reduce the risk of recurrence [30,31]. Studies have shown that neo-adjuvant chemotherapy can significantly improve the rate of negative margins and overall survival [39,40]. In this case, surgical resection with negative margins was not possible, and chemotherapy and radiation were used for palliative purposes due to the presence of metastases at the time of diagnosis.

Conclusion

In conclusion, the diagnosis of cardiac tumors remains a challenge due to their rarity and non-specific symptoms. Imaging modalities play a crucial role in the diagnosis and characterization of cardiac masses, but histopathological examination is necessary in challenging scenarios to establish the precise diagnosis. High-grade spindle cell sarcomas, unclassified, are rare and aggressive cardiac tumors that are associated with poor prognosis. Surgical excision with negative margins is the gold standard treatment, but achieving negative margins is difficult due to the infiltrative pattern of the tumor and delayed diagnosis. The utility of chemotherapy and radiation in these tumors remains undefined, but several studies have shown that neo-adjuvant chemotherapy and radiation may improve the results of surgical resection and reduce the risk of mass recurrence. Multidisciplinary management involving cardiologists, cardiac surgeons, radiologists, pathologists, and oncologists is necessary to achieve the best possible outcome in patients with cardiac tumors.

Patient consent

We hereby confirm that written, informed consent has been obtained from the patient's parents, for the publication of her

case and related information. The purpose of obtaining this consent is to ensure the patient's involvement in contributing valuable medical knowledge and to promote advancements in healthcare practices. It is understood that all personal identifying information will be kept confidential, and the case will be presented in an anonymous manner.

REFERENCES

[1] Centofanti P, Di Rosa E, Deorsola L, Dato GMA, Patane F, La Torre M, et al. Primary cardiac tumors: early and late results of surgical treatment in 91 patients. Ann Thorac Surg 1999;68(4):1236–41.
[2] Shapiro LM. Cardiac tumours: diagnosis and management. Heart 2001;85(2):218–22.
[3] Burke A, Virmani R. Tumors of the heart and great vessels. American Registry of Pathology; 1996.
[4] Shanmugam G. Primary cardiac sarcoma. Eur J Cardiothorac Surg 2006;29(6):925–32.
[5] Tamin SS, Maleszewski JJ, Scott CG, Khan S, Edwards WD, Bruce CJ, et al. Prognostic and bioepidemiologic implications of papillary fibroelastomas. J Am Coll Cardiol 2015;65(22):2420–9.
[6] Truong PT, Jones SO, Martens B, Alexander C, Paquette M, Joe H, et al. Treatment and outcomes in adult patients with primary cardiac sarcoma: the British Columbia Cancer Agency experience. Ann Surg Oncol 2009;16:3358–65.
[7] Kim MP, Correa AM, Blackmon S, Quiroga-Garza G, Weilbaecher D, Bruckner B, et al. Outcomes after right-side heart sarcoma resection. Ann Thorac Surg 2011;91(3):770–6.
[8] Butany J, Nair V, Naseemuddin A, Nair GM, Catton C, Yau T. Cardiac tumours: diagnosis and management. Lancet Oncol 2005;6(4):219–28.
[9] Reynen K. Frequency of primary tumors of the heart. Am J Cardiol 1996;77(1):107.
[10] Basso C, Rizzo S, Valente M, Thiene G. Cardiac masses and tumours. Heart 2016;102(15):1230–45.
[11] Ramlawi B, Leja MJ, Saleh WKA, Al Jabbari O, Benjamin R, Ravi V, et al. Surgical treatment of primary cardiac sarcomas: review of a single-institution experience. Ann Thorac Surg 2016;101(2):698–702.
[12] Watson R, Frye J, Trieu M, Yang MX. Primary undifferentiated pleomorphic cardiac sarcoma with MDM2 amplification presenting as acute left-sided heart failure. Case Rep 2018;2018 bcr-2018-226073.
[13] Neuville A, Collin F, Bruneval P, Parrens 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(4):461–9.
[14] 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.
[15] Rahbar K, Seifarth H, Schäfers M, Stegger L, Hoffmeier A, Spieker T, et al. Differentiation of malignant and benign cardiac tumors using 18F-FDG PET/CT. J Nucl Med 2012;53(6):856–63.
[16] Andrei V, Scheggi V, Stefàno PL, Marchionni N. Primary cardiac sarcoma: a case report of a therapeutic challenge. Europ Heart J 2020;4(6):1.
[17] Devbhandari MP, Meraj S, Jones MT, Kadir I, Bridgewater B. Primary cardiac sarcoma: reports of two cases and a review of current literature. J Cardiothorac Surg 2007;2(1):1–5.
[18] Meng Q, Lai H, Lima J, Tong W, Qian Y, Lai S. Echocardiographic and pathologic characteristics of primary cardiac tumors: a study of 149 cases. Int J Cardiol 2002;84(1):69–75.
[19] Shapira OM, Korach A, Izhar U, Koler T, Wald O, Ayman M, et al. Radical multidisciplinary approach to primary cardiac sarcomas. Eur J Cardiothorac Surg 2013;44(2):330–336.
[20] Zhang G, Gao Q, Chen S, Chen Y. Primary cardiac synovial sarcoma that was continuous with the mitral valve caused severe thrombocytopenia: a case report. J Cardiothorac Surg 2019;14:1–6.
[21] Shah D, Gupta K, Naik D, Bhavsar N. Right atrial synovial sarcoma with thrombocytopenia: a deceptive presentation. J Card Surg 2021;36(8):2992–5.
[22] Vander Salm TJ. Unusual primary tumors of the heart. Seminars in thoracic and cardiovascular surgery. Worcester: Elsevier; 2000.
[23] Mishra R, Shemmeri E, Pani S, Tribble M. Primary cardiac sarcoma presenting with easy bruising: a case report. Eur Heart J-Case Rep 2022;6(9):ytac331.
[24] Kerbl D, Exposito J, Carabello J, Hale A. An undifferentiated, pleomorphic cardiac sarcoma masquerading as myxoma. J Cardiol Cases 2023;27(1):41–5.
[25] Siontis BL, Leja M, Chugh R. Current clinical management of primary cardiac sarcoma. Expert Rev Anticancer Ther 2020;20(1):45–51.
[26] Motwani M, Kidambi A, Herzog BA, Uddin A, Greenwood JP, Plein S. MR imaging of cardiac tumors and masses: a review of methods and clinical applications. Radiology 2013;268(1):26–43.
[27] Hoffmann U, Globits S, Schima W, Loewe C, Puig S, Oberhuber G, et al. Usefulness of magnetic resonance imaging of cardiac and paracardiac masses. Am J Cardiol 2003;92(7):890–5.
[28] Fussen S, De Boeck BW, Zellweger MJ, Bremerich J, Goetschalckx K, Zuber M, et al. Cardiovascular magnetic resonance imaging for diagnosis and clinical management of suspected cardiac masses and tumours. Eur Heart J 2011;32(12):1551–60.
[29] Achenbach S, Kondo T. Technical advances in cardiac CT. Cardiol Clin 2012;30(1):1–8.
[30] Siontis BL, Zhao L, Leja M, McHugh JB, Shango MM, Baker LH, et al. Primary cardiac sarcoma: a rare, aggressive malignancy with a high propensity for brain metastases. Sarcoma 2019;2019.
[31] 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(1):128–36.
[32] Simpson L, Kumar SK, Okuno SH, Schaff HV, Porrata LF, Buckner JC, et al. Malignant primary cardiac tumors: review of a single institution experience. Cancer 2008;112(11):2440–6.
[33] Espat NJ, Bilsky M, Lewis JJ, Leung D, Brennan MF. Soft tissue sarcoma brain metastases: prevalence in a cohort of 3829 patients. Cancer 2002;94(10):2706–11.
[34] Yoshida S, Morii K, Watanabe M, Saito T. Brain metastasis in patients with sarcoma: an analysis of histological subtypes, clinical characteristics, and outcomes. Surg Neurol 2000;54(2):160–4.
[35] Maleszewski JJ, Anavekar NS, Moynihan TJ, Klarich KW. Pathology, imaging, and treatment of cardiac tumours. Nat Rev Cardiol 2017;14(9):536–49.
[36] Woll PJ, Reichardt P, Le Cesne A, Bonvalot S, Azzarelli A, Hoekstra HJ, et al. Adjuvant chemotherapy with doxorubicin, ifosfamide, and lenograstim for resected soft-tissue sarcoma (EORTC 62931): a multicentre randomised controlled trial. Lancet Oncol 2012;13(10):1045–54.
[37] Patel SR, Gandhi V, Jenkins J, Papadopolous N, Burgess MA, Plager C, et al. Phase II clinical investigation of gemcitabine

in advanced soft tissue sarcomas and window evaluation of dose rate on gemcitabine triphosphate accumulation. J Clin Oncol 2001;19(15):3483–9.
[38] Hensley ML, Maki R, Venkatraman E, Geller G, Lovegren M, Aghajanian C, et al. Gemcitabine and docetaxel in patients with unresectable leiomyosarcoma: results of a phase II trial. J Clin Oncol 2002;20(12):2824–31.
[39] Iwamoto Y, Tanaka K, Isu K, Kawai A, Tatezaki S-I, Ishii T, et al. Multiinstitutional phase II study of neoadjuvant chemotherapy for osteosarcoma (NECO study) in Japan: NECO-93J and NECO-95J. J Orthop Sci 2009;14:397–404.
[40] Larrier NA, Czito BG, Kirsch DG. Radiation therapy for soft tissue sarcoma: indications and controversies for neoadjuvant therapy, adjuvant therapy, intraoperative radiation therapy, and brachytherapy. Surg Oncol Clin 2016;25(4):841–60.