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Multimodality Imaging of Intimal Sarcoma Causing Both Severe Mitral Stenosis and Mitral Regurgitation

Ciddi Mitral Darlığı ve Yetersizliğine Neden Olan İntimal Sarkomun Multimodalite Görüntülemesi

ABSTRACT

Intimal sarcomas (IS) are rare, malignant, rapidly progressive mesenchymal tumors that typically occur in the tunica intima of larger vessels, and they rarely involve the heart. IS are frequently misdiagnosed during the initial clinical presentation. This case report describes an uncommonly located IS, highlighting specific findings obtained through multimodality imaging.

Keywords: Intimal sarcoma, multimodality imaging, rare location

ÖZET

İntimal sarkomlar (İS) nadir görülen, malign, hızlı ilerleyen, mezenkimal tümörler olup genellikle büyük damarların tunika intimasında ortaya çıkar ve nadiren kalbi de tutar. İS ilk klinik başvuruda sıklıkla yanlış teşhis edilir. Nadir görülen bir yerleşime sahip olan bu İS olgusunda, multimodalite görüntülemedeki spesifik bulgular tanımlanmıştır.

Anahtar Kelimeler: İntimal sarkom, multimodalite görüntüleme, nadir yerleşim

CASE REPORT
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Primary cardiac sarcomas are extremely rare tumors.[1] However, they constitute the majority of primary malignant heart tumors.[1,2] Intimal sarcomas (IS) are uncommon and relatively aggressive malignant mesenchymal tumors that originate from the tunica intima of larger vessels, and they rarely involve the heart.[2] To our knowledge, only nine cases of primary cardiac origin have been reported in the literature to date. This case illustrates the importance of multimodality imaging in the diagnosis of the intimal sarcoma of the left heart.

Case Report

A 67-year-old female presented to our outpatient clinic with exertional dyspnea. She had also reported experiencing additional symptoms, such as weight loss and nocturnal sweats, for eight months. Her past medical history was notable for well-controlled type 2 diabetes mellitus, managed with oral hypoglycemic medications. She denied any history of tobacco or alcohol use. At the time of admission, her vital signs were within normal limits. Physical examination revealed a 3/6 grade mild systolic murmur upon auscultation, and her peripheral oxygen saturation was above 95% in room air. Electrocardiography showed a sinus rhythm. She exhibited mild anemia with a hemoglobin level of 10.1 g/dL, and an elevated N-terminal pro-B-type natriuretic peptide (NT-proBNP) level of 810 pg/mL. Transesophageal echocardiography (TEE) revealed a segmented, slightly hypoechoic, heterogeneous mass in the left atrium, extending from the interatrial septum to the anterolateral commissure. This mass covered the anterior and posterior mitral leaflets, with another similar mass filling the entire left upper pulmonary vein (Figure 1 A-B, Video 1). These masses also invaded the posteromedial muscle, especially the anterolateral papillary muscle. Moreover, they prolapsed from the mitral valve during diastole, causing an increase in mean and peak

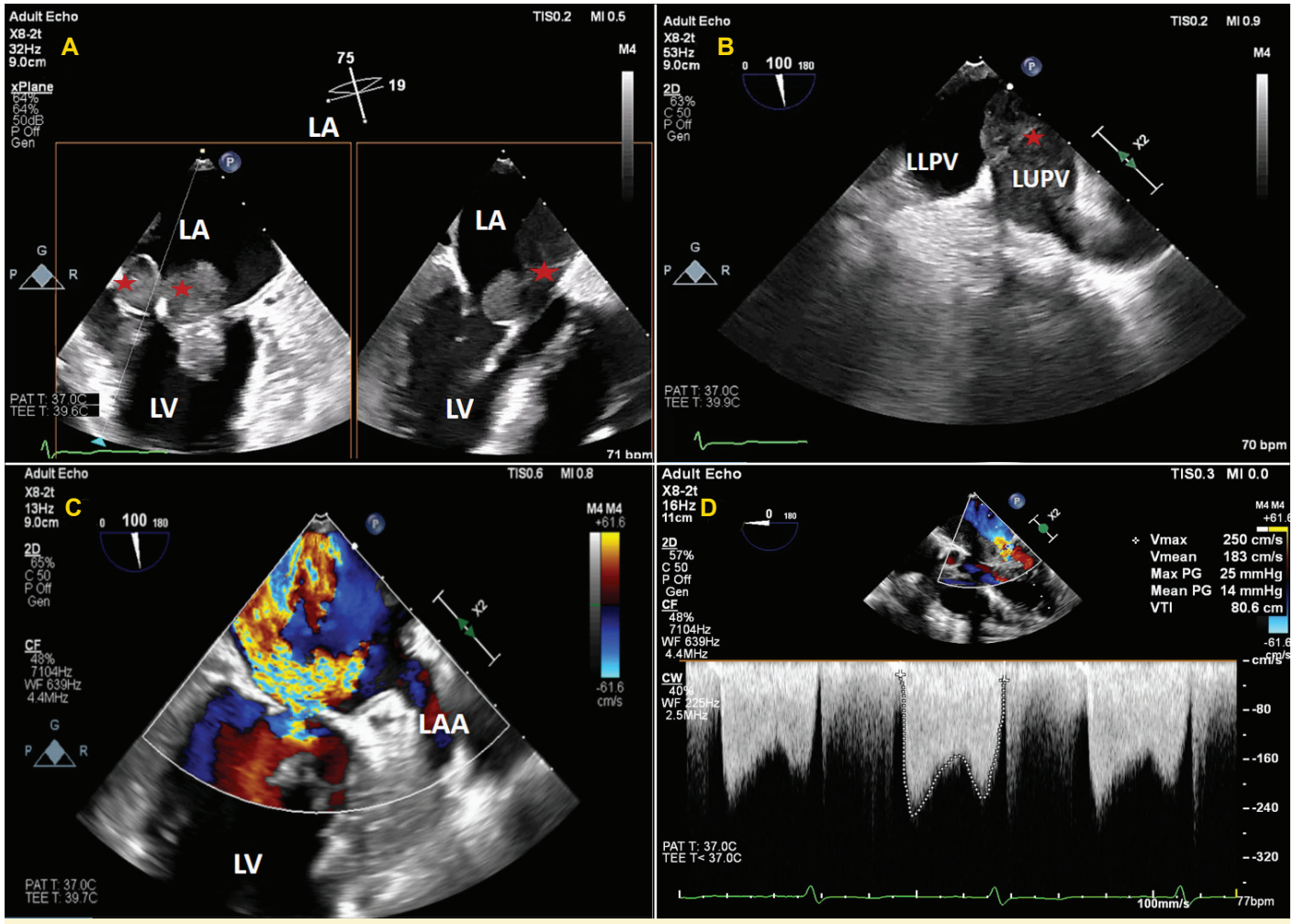

Figure 1. Transesophageal echocardiography. (A-B): X-plane imaging and a 100° view demonstrate multilobed heterogeneous masses that extend from the interatrial septum to the anterolateral commissure, cover the anterior and posterior mitral leaflets, and fill the entire left upper pulmonary vein. (C-D): Color and continuous wave Doppler imaging demonstrate both moderate to severe mitral regurgitation and stenosis, with increased mean and peak transmitral gradients (14 mmHg and 25 mmHg, respectively).

ABBREVIATIONS

CD31	Cluster of Differentiation 31
CD34	Cluster of Differentiation 34
CDK-4	Cyclin-Dependent Kinase 4
CK8/18	Cytokeratin
CMR	Cardiac Magnetic Resonance Imaging
CT	Computed Tomography
FVIII	Factor VIII
FDG	Fluorodeoxyglucose
HMB45	Human Melanoma Black 45
H&E	Hematoxylin and Eosin
IS	Intimal Sarcoma
MDM-2	Mouse Double Minute 2
NT-proBNP	N-Terminal Pro B-Type Natriuretic Peptide
PET-CT	Positron Emission Tomography - Computed Tomography
S100	Saturated 100 Protein
SMA	Smooth Muscle Actin
STIR	Short Tau Inversion Recovery
TEE	Transesophageal Echocardiography

transmitral gradients (14 mmHg and 25 mmHg, respectively) and moderate to severe mitral regurgitation (Figure 1 C-D, Video 2). Cardiac magnetic resonance imaging (CMR) revealed a mass approximately 42 x 20 mm in diameter originating from the left atrial septal wall. This mass extended through the mitral valve into the left ventricle via subvalvular structures, with another mass of similar tissue characteristics filling the entire left upper pulmonary vein. The tissue characteristics of these masses were isointense on T1-weighted images, slightly hyperintense on T2-weighted images, and hyperintense on Short Tau Inversion Recovery (STIR) imaging (Figure 2 a-b-c). No significant contrast enhancement was observed at 4, 7, and 11 minutes post-image acquisition. Positron Emission Tomography - Computed Tomography (PET-CT) illustrated increased Fluorodeoxyglucose (FDG) uptake starting from the left interatrial septum, passing through the mitral valve level, extending to the left ventricle, and in the left upper pulmonary vein region (Figure 2 D-F). No FDG uptake was detected in any other body parts. The patient underwent surgery for the resection of these masses (Figure

3A). Histopathology revealed a predominantly undifferentiated, myxoid, chondroid, and pleomorphic, high cellularity malignant neoplasm that had progressed into the papillary muscle and myocardium (Figure 3B). Moreover, areas of necrosis, a high mitotic index, and nuclear multifocal Mouse Double Minute 2 (MDM2) expression were detected, while no Cyclin-Dependent Kinase 4 (CDK4) amplification was observed (Figure 3C). These pathologic findings were considered compatible with

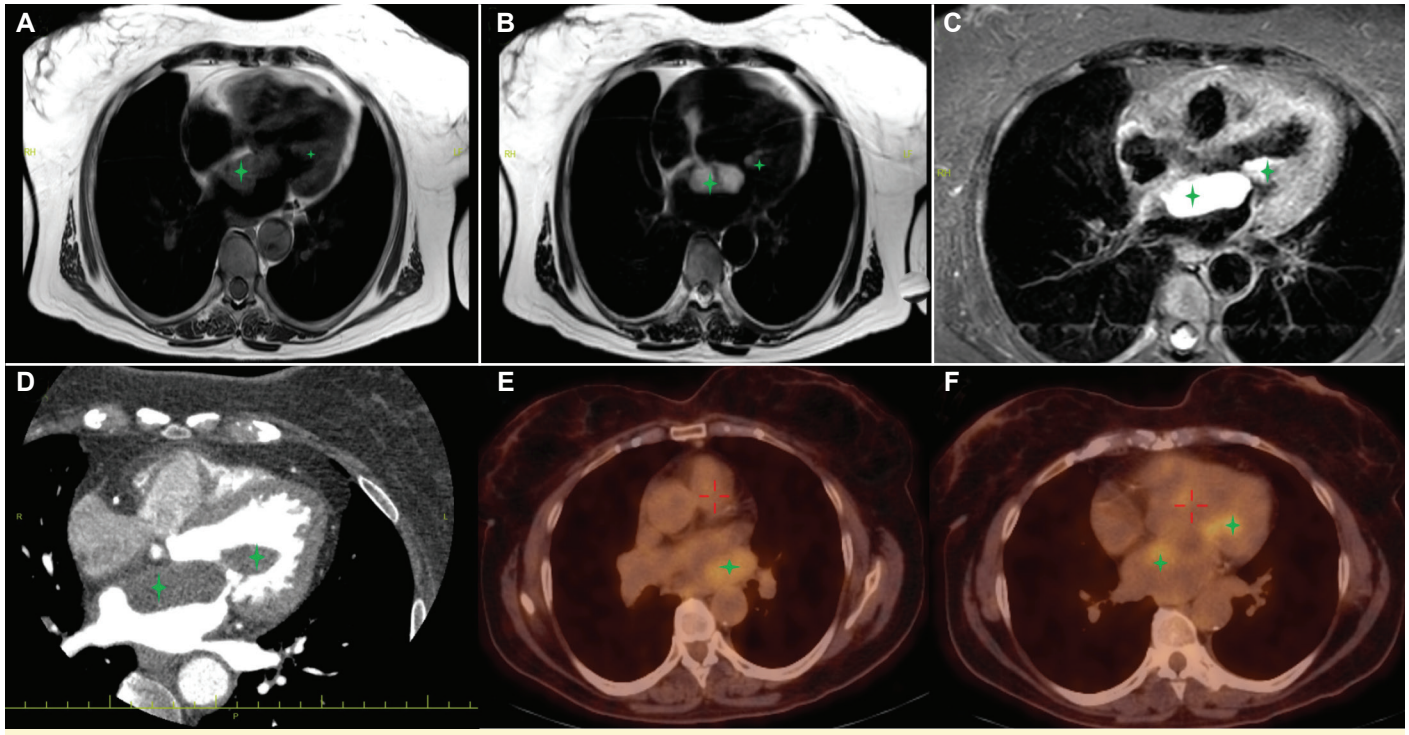

Figure 2. (A-C): Four-chamber cardiac magnetic resonance imaging T1 and T2-weighted, and STIR images illustrate the mass which appears isointense, mild hyperintense and hyperintense, respectively. (D-F): A large hypoattenuated mass extends from the interatrial septum to the papillary muscles in PET-CT/CT. Axial fused FDG PET-CT images show radiotracer uptake in these areas.

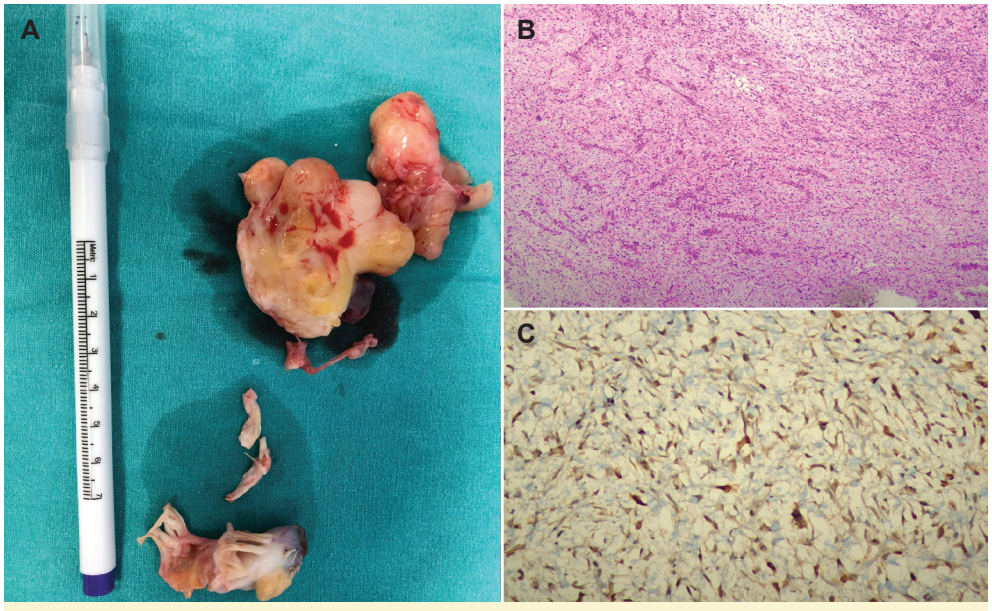

Figure 3. (A). Macroscopic view of the excised masses. (B). Histopathology: (H&E, ×40) A highly cellular malignant neoplasm predominantly composed of undifferentiated, myxoid, chondroid, and pleomorphic epithelioid cells. (C). Immunohistochemistry: (MDM2, ×200) Nuclear multifocal MDM2 expression observed, with no amplification of CDK4 or other markers (CD31, CD34, S100, SMA, Desmin, FVIII, CK8/18, HMB45).

IS. Oncology evaluation determined that the patient's general condition was not suitable for chemotherapy. Unfortunately, the patient died due to sepsis within a month.

Discussion

IS are rapidly progressing malignant and locally aggressive tumors. The most widely accepted hypothesis is that these tumors are likely to originate from primitive mesenchymal cells of the intima of the great arteries and heart.[2] The overall prognosis is poor, and the recurrence rate is high. However, successful surgical resection can increase median survival and symptom palliation for up to five years.[3] The most common symptoms are usually nonspecific and include dyspnea, chest or back pain, coughing, and hemoptysis. Additional symptoms such as weight loss, fever, or anemia further increase the suspicion of malignancy.[4,5] In this case, IS were detected during an examination for exercise-induced dyspnea. However, weight loss, night sweats, and anemia, which started eight months before presentation, raised suspicion for malignancy. In fact, the patient had been evaluated for these symptoms approximately five months prior to admission. Gastrointestinal endoscopy and abdominal ultrasound were performed to determine the etiology, but no pathology was detected. In these patients, all symptoms should be considered collectively and evaluated for alternative malignant foci with the aid of a multi-system physical examination.

IS are often misdiagnosed due to similar hemodynamic changes, clinical signs, and morphological features as those of a thrombus. A multimodal approach using various imaging modalities such as echocardiography, Computed Tomography (CT), PET-CT, and CMR to visualize the heart, thorax, and vascular structures, is the best method for for rapid diagnosis of IS diagnosis of IS.[3-5]

Transthoracic echocardiography and TEE are primarily used to determine the location of the mass, its relationship with surrounding tissues, and the presence of invasion. IS typically exhibit an irregular internal echo and specific blood flow signals, usually localized in the great arteries, left heart, and pulmonary veins.[2,5]

On CT imaging, IS are characterized by mass-filling shadows within the great arteries, often in the left heart and pulmonary veins, displaying irregular density, irregular borders, and lobulated, nodular, or septal appearances. CT is more sensitive in assessing the size and extent of the mass, especially in identifying IS located in large arteries.[3,4]

CMR enables accurate positioning of the tumor, assessment of the extent of involvement, evaluation of the functional impact, and tissue characterization of the lesion. CMR is helpful in distinguishing neoplastic masses from thrombi and provides appropriate visualization of vasculature and tissue edema. IS show diffusion restriction and increased heterogeneity compared to thrombi.[4,5]

FDG uptake on PET-CT is positive for malignant tumors such as IS and negative for thrombi. Additionally, PET-CT can clearly evaluate close and distant metastases of tumors.[5]

The definitive diagnosis is made through pathology, with MDM2 expression observed in the majority of the patients.[2,5] In this case, the location of the mass and its relationship with symptoms were determined by multi-staged imaging, leading to a preliminary diagnosis. There is no standard treatment for the management of patients with IS; it usually involves a multidisciplinary approach including surgery, radiation, chemotherapy, and targeted therapy. In this case, the mass was primarily surgically excised due to the presence of compression symptoms, its focal location, and the absence of a suitable site for conducting a preliminary diagnostic biopsy.

Conclusion

IS are usually misdiagnosed at the initial clinical presentation, which delays diagnosis and worsens the prognosis of a neoplastic disease with an already low survival rate. These challenging manifestations often lead to discrepancies between imaging interpretation and subsequent pathologic findings of unsuspected IS. Recognizing the distinctive features of anatomical and microscopic pathology and combining them with imaging findings should improve timely diagnosis and intervention.

Informed Consent: Written informed consent was obtained from the patient's first-degree relatives for the publication of the case report and the accompanying images.

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Video 1. Two-dimensional TEE at the mid-esophageal level, zoomed x-plane image, demonstrates a multilobed heterogeneous mass extending from the interatrial septum to the anterolateral commissure and covering the anterior and posterior mitral leaflets.

Video 2. Two-dimensional TEE at the mid-esophageal level, zoomed 100° view with color flow Doppler, indicates moderate to severe mitral regurgitation with flow convergence.

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