Fleshing Out the Invisible: A Pericardial Paraganglioma

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INTRODUCTION

Pericardial paragangliomas are rare neuroendocrine tumors of chromaffin cells. We present a patient with of a pericardial paraganglioma presenting as a non-ST-segment elevation myocardial infarction (NSTEMI) initially diagnosed by coronary angiography. We illustrate the challenge of identification by echocardiography and the use of multimodality cardiovascular imaging in the diagnosis, surgical planning, and intraoperative management of this patient.

CASE PRESENTATION

A 71-year-old woman presented to the hospital with acute onset of chest pressure. The patient's medical history was notable for hypertension, hyperlipidemia, and prior transient ischemic attack. The patient was previously evaluated for chest pain a year prior and underwent an exercise stress echocardiogram that showed no evidence of ischemia and a normal blood pressure response. No baseline imaging abnormalities were appreciated at the time. Initial vital signs were notable for a blood pressure of 151/83 mm Hg, a heart rate of 70 beats per minute with regular rhythm, and a respiratory rate of 16 breaths per minute with an oxygen saturation of 95% on room air. The physical exam was unremarkable, with normal cardiac sounds and clear lung fields bilaterally.

Initial laboratory testing was pertinent for an elevated troponin-T, which peaked at 0.30 (upper limit of normal <0.01). Electrocardiogram showed normal sinus rhythm with no ischemic changes, and a chest x-ray showed no cardiopulmonary abnormalities. The patient was administered loading doses of aspirin and clopidogrel and started on a heparin infusion. They were admitted to the cardiology service and underwent coronary angiography, which showed mild coronary artery disease and a cardiac mass near the left atrium (LA) with vascular supply from both the right coronary artery (Figure 1A, Video 1) and the left circumflex coronary artery (Figure 1B, Video 2). A complete transthoracic echocardiogram (TTE) performed prior to the coronary angiogram showed normal biventricular systolic function with a calculated left ventricular ejection fraction of 60%. On review of the stress echocardiogram from 1 year prior, a faint echodensity was noted posterior to the LA on the parasternal long-axis view (Figure 2A, Video 3). This was not visualized on the precatheterization TTE (Figure 2B, Video 4). The patient's chest pain improved, and a cardiovascular magnetic resonance imaging

VIDEO HIGHLIGHTS

Video 1: Selective coronary angiogram of the right coronary artery (RCA), right anterior oblique (RAO) projection, demonstrates an apical branch of the RCA supplying a retroatrial mass.
Video 2: Selective coronary angiogram of the left coronary system in RAO projection demonstrates the left circumflex in the atrioventricular groove with atrial branches supplying a retroatrial mass.
Video 3: Two-dimensional TTE, parasternal long-axis view performed 1 year earlier, demonstrates a subtle, ill-defined retroatrial mass.
Video 4: Two-dimensional TTE, parasternal long-axis view performed at admission without evidence of the previously noted ill-defined retroatrial mass.
Video 5: Intraoperative two-dimensional TEE, lower-esophageal, zoomed 4-chamber (0°) view at the level of the posterior atrioventricular groove, demonstrates the coronary sinus compressed by the intrapericardial paraganglioma.
Video 6: Intraoperative two-dimensional TEE, lower esophageal, 4-chamber (0°) view, demonstrates the cannulation of the coronary sinus for retrograde cardioplegia.
Video 7: Intraoperative three-dimensional TEE full-volume acquisition with 3 multiplanar two-dimensional displays (*left panel*) and volume-rendered display (*right panel*) at the level of the posterior atrioventricular groove demonstrates the pericardial paraganglioma posterior to the atrioventricular groove near the LA.
Video 8: Cardiovascular magnetic resonance imaging sagittal orientation, basal short-axis view at the level of the atrioventricular groove, first-pass contrast perfusion sequence, demonstrates sequential perfusion of the right atrium, the pulmonary artery and branches, the LA, the aorta, and the retroatrial mass and then the kidneys, the inferior vena cava, and the liver. The extracardiac, intrapericardial mass has rapid homogenous perfusion aside from a small central region.

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Keywords: Pericardial paraganglioma, Cardiac mass, TTE, TEE

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2468-6441
https://doi.org/10.1016/j.case.2023.06.005

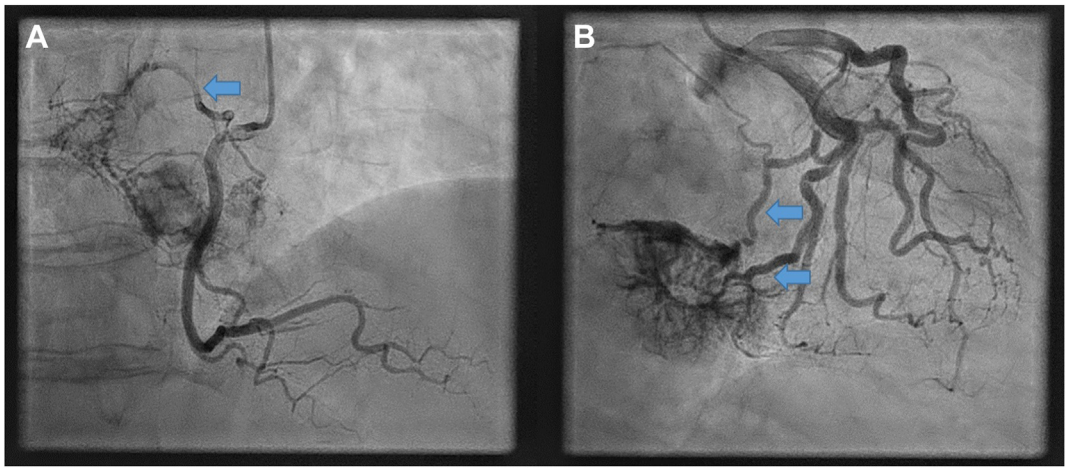

Figure 1 **(A)** Coronary angiogram of the right coronary artery (RCA) in right anterior oblique (RAO)/cranial projection showing an atrial branch of the RCA supplying a retroatrial mass (*arrow*). **(B)** Coronary angiogram of the left coronary system in RAO/caudal projection showing the left circumflex supplying a retroatrial mass (*arrows*).

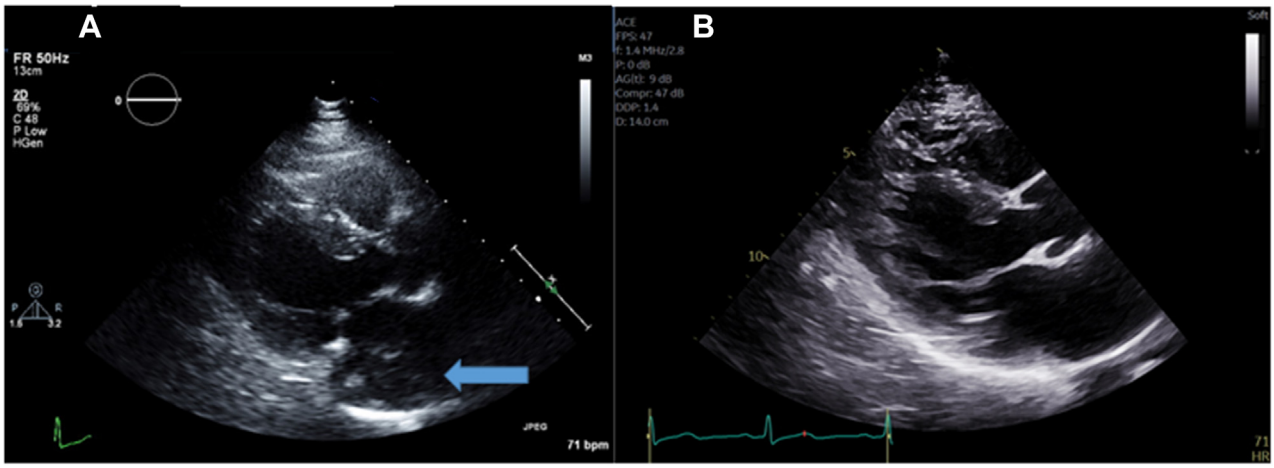

Figure 2 **(A)** Parasternal long-axis view with a noted subtle ill-defined echodensity located near the LA (*blue arrow*) performed as resting imaging at the time of exercise stress echocardiogram. **(B)** Similar parasternal long-axis view performed 1 year later as part of a comprehensive resting echocardiogram without evidence of the ill-defined echodensity.

(CMR) scan was performed and revealed an extracardiac, intrapericardial, 42 × 24 × 37 mm mass posterior to the LA. During first-pass perfusion, there was rapid homogenous enhancement with rapid washout, suggesting a paraganglioma and less likely a pseudotumor or hemangioma (Figure 3A and B). After evaluation by cardiac surgery, cardiac computed tomography (CCT) was obtained for surgical planning, which showed a 48 × 43 × 23 mm mass with vascular supply from the right coronary artery and left circumflex artery and compression of the coronary sinus without invasive or infiltrative features (Figure 4A and B). Further lab work showed an elevated chromogranin A (269 ng/mL, normal <93 mg/mL) and serum-free normetanepherines (5.5 nm/L, normal <0.9 nm/L), suggesting a paraganglioma. A fluorodeoxyglucose positron emission tomography (FDG-PET) scan showed that this mass was FDG avid without metastases (Figure 5). Family history was reviewed with no noted history of malignancy or neuroendocrine tumors in any known relatives.

The patient was discharged home and, after outpatient follow-up, returned for surgical excision of the pericardial mass with transesophageal echocardiographic (TEE) guidance (Figure 6, Videos 5-7). With coronary sinus cannulation and initiation of retrograde cardioplegia, acute onset of severe hypertension was noted. After similar acute episodic hypertension was noted with antegrade cardioplegia administration, catecholamine washout via the coronary vasculature was suspected. This was subsequently controlled with coordinated administration of nicardipine boluses prior to cardioplegia dosing, facilitating successful tumor excision (Figure 7).

At 6-month follow-up, the patient has done well with no recurrence of angina and no surgical complications. Pathology confirmed the presence of a homogenous appearing vascular tumor with epithelioid cells and positive chromogranin A and S100 stains consistent with a paraganglioma (Figure 8). Repeat CCT was performed showing complete resection of the pericardial mass (Figure 4C).

DISCUSSION

We present a patient with a pericardial paraganglioma in the posterior atrioventricular groove presenting with angina and subsequent NSTEMI. With this case, we highlight the importance of

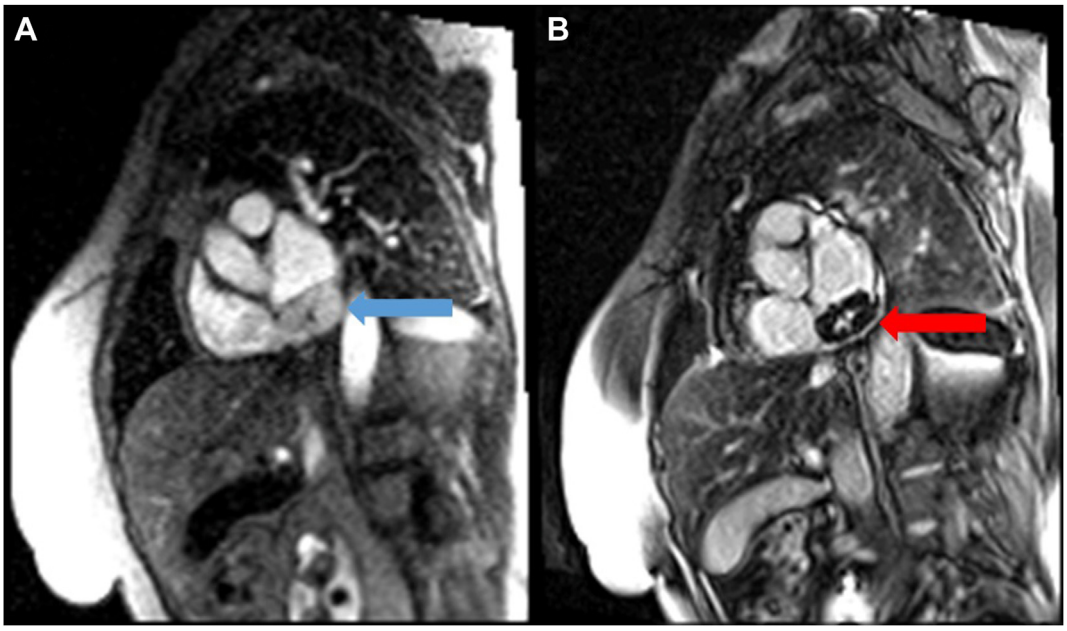

Figure 3 Cardiovascular magnetic resonance imaging sagittal display, basal short-axis view, first-pass perfusion **(A)** and phase-sensitive inversion-recovery **(B)** demonstrates an extracardiac, intrapericardial mass with homogenous perfusion sparing a central stellate region (*blue arrow*) and late gadolinium enhancement in the central stellate region (*red arrow*).

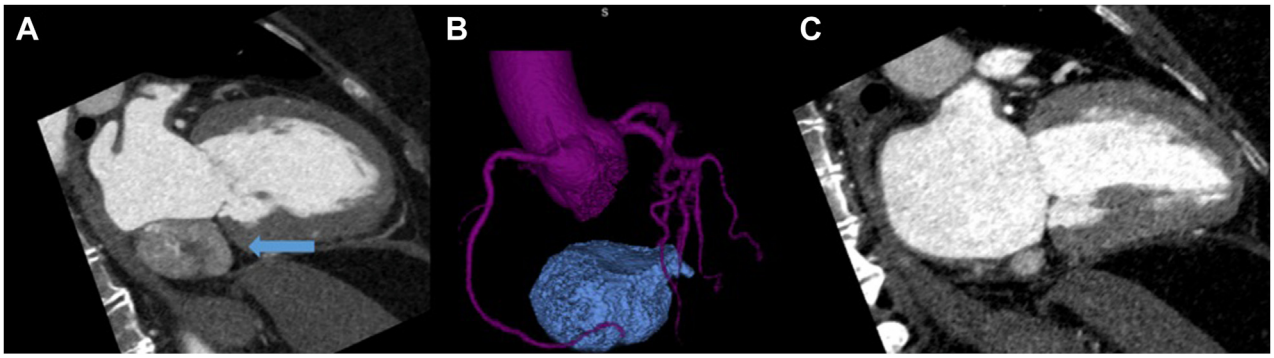

Figure 4 **(A)** Cardiac computed tomography scan, 2-chamber display, demonstrates the retroatrial, intrapericardial mass (*arrow*) with compression of a poorly visualized coronary sinus. **(B)** Volume-rendered three-dimensional reconstruction of the coronary supply to the retroatrial mass. **(C)** Two-chamber display after surgical resection demonstrates normal retroatrial anatomy.

multimodality imaging (Figure 9) in the evaluation and treatment of this rare finding. We start with the limitations of TTE with subtle findings, which, in this case, were initially missed and led to a delay in diagnosis. We then exemplify the use of CCT and CMR for better tissue definition to narrow the differential diagnosis of a pericardial mass and evaluate for the feasibility of and planning for surgical resection. We then highlight the increased imaging resolution for TEE in this posterior mass, as well as its importance for real-time intraoperative imaging during surgical resection.

The exact incidence of pericardial tumors and specifically paragangliomas is unknown. In one large database evaluating surgical and autopsy studies, the incidence of primary pericardial tumors was rare, with a prevalence of <0.03%[1]; paragangliomas were among the least common and represented <1% of primary tumors.[2] These tumors most commonly are attached to the LA in the aortopulmonary groove, with rare cases associated with the right atrium. Most commonly, paragangliomas are sporadic but can occur as part of a familial syndrome and present with multiple catecholamine-secreting tumors. These tumors can further be classified as benign or malignant, based on the presence of tissue invasion in malignant tumors. Further, these tumors can be defined as inactive or functionally active. In patients with functionally active tumors, known as pheochromocytomas or extra-adrenal catecholamine-secreting tumors, the presentation can include catecholaminergic effects including the classic triad of episodic tachycardia, headache, and diaphoresis.[3] Over 50% of these patients will have hypertension. In inactive cardiac paragangliomas, symptoms most commonly occur due to local compressive effects and include chest pain, dyspnea, and syncope. It is hypothesized that coronary steal due to a large mass as well as coronary vasospasm may also play a role in the setting of patients with chest pain and NSTEMI, which is likely the mechanism in this case as the mass was located above the major epicardial vessels in the atrioventricular groove. A subset of patients may also be diagnosed following an incidental finding on imaging. The only curative treatment is complete surgical resection.[4]

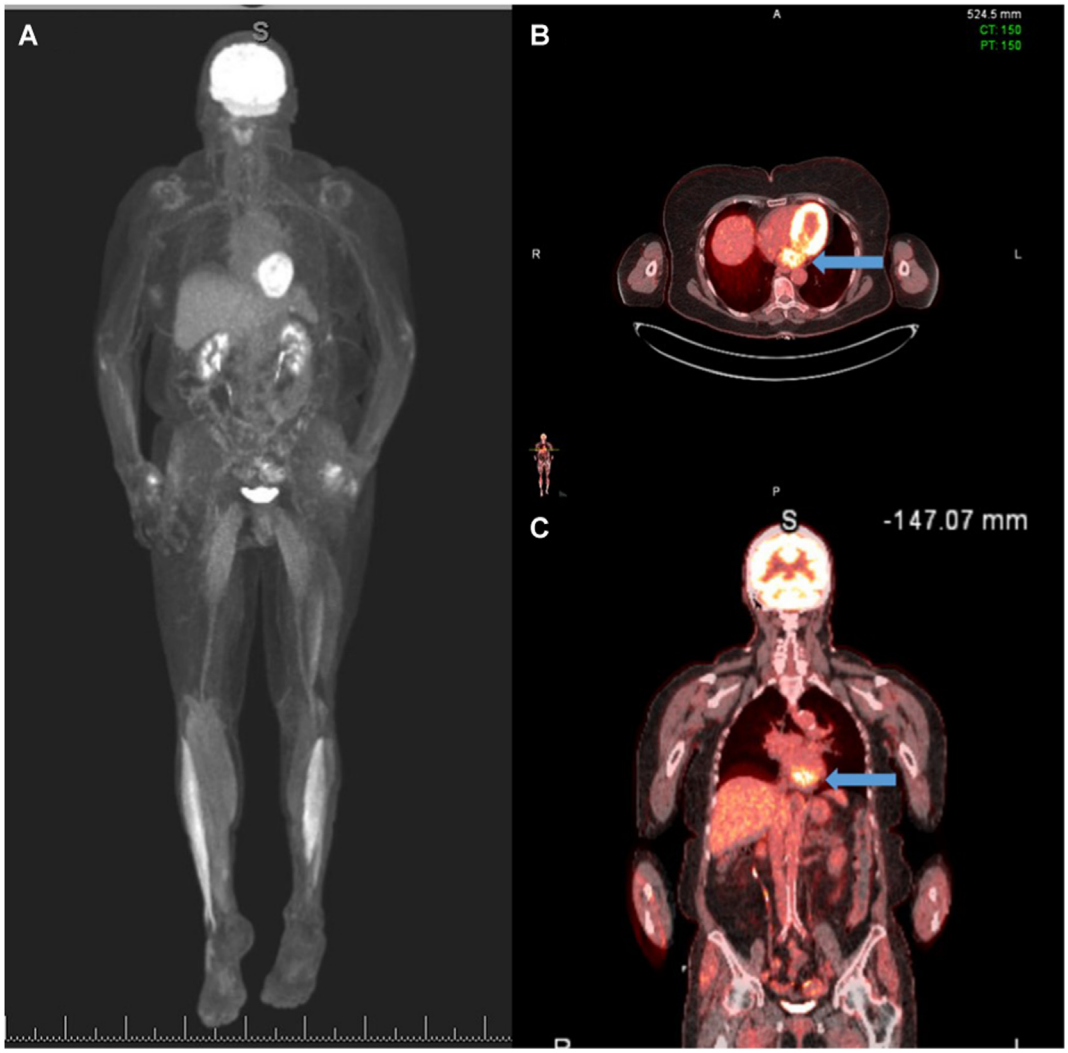

Figure 5 A FDG-PET scan with computed tomography overlay three-dimensional reconstruction, full-body display **(A)**, demonstrates normal activity in the brain, kidneys, and bladder as well as lower and upper extremity soft tissues with abnormal increased FDG activity at the level of the heart. Axial display **(B)** demonstrates the FDG-avid tumor in the posterior pericardial space (*arrow*). Coronal display through the posterior pericardium **(C)** demonstrates the FDG-avid lesion in the posterior pericardium at the level of the AV groove (*arrow*).

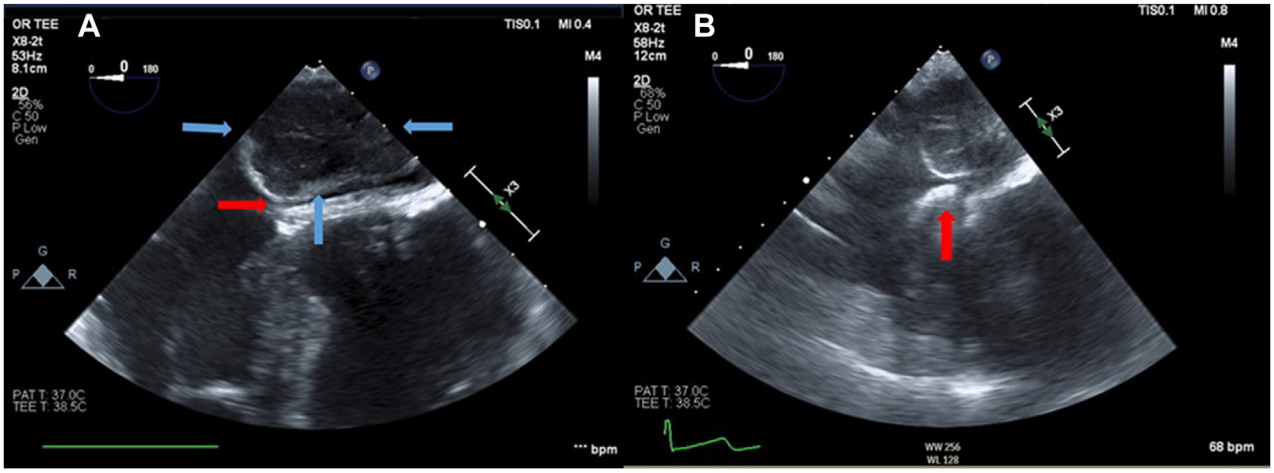

Figure 6 **(A)** Intraoperative two-dimensional TEE, lower-esophageal window, zoomed 4-chamber view (0°), demonstrates a mass (*blue arrows*) lying in the atrioventricular groove with compression of the coronary sinus with visualization for cardioplegia in the coronary sinus ostium (*red arrow*) and **(B)** cannulation of the coronary sinus for retrograde cardioplegia (*red arrow*).

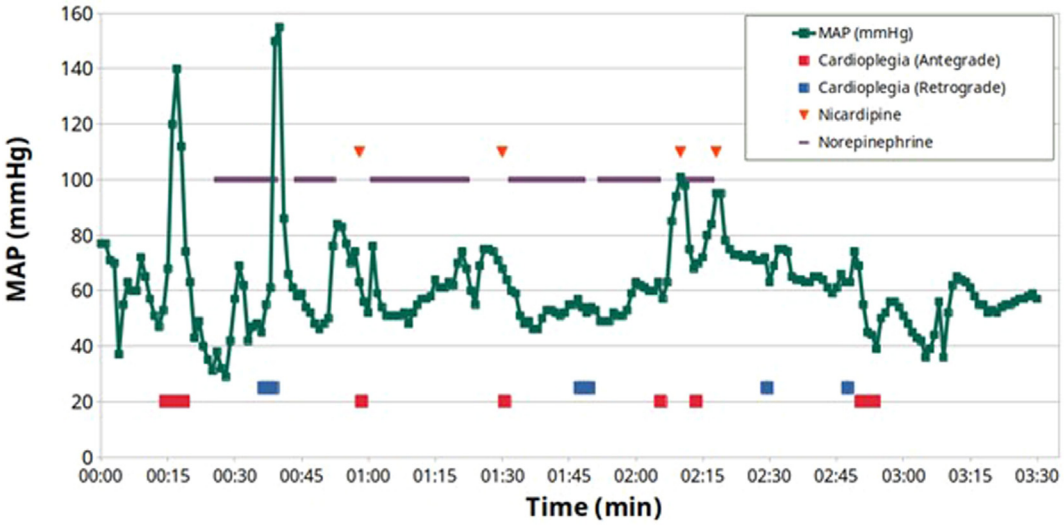

Figure 7 Intraoperative hemodynamics showing catecholaminergic surges with cardioplegia (*red and blue squares*) and response to intravenous antihypertensives (*orange triangles*).

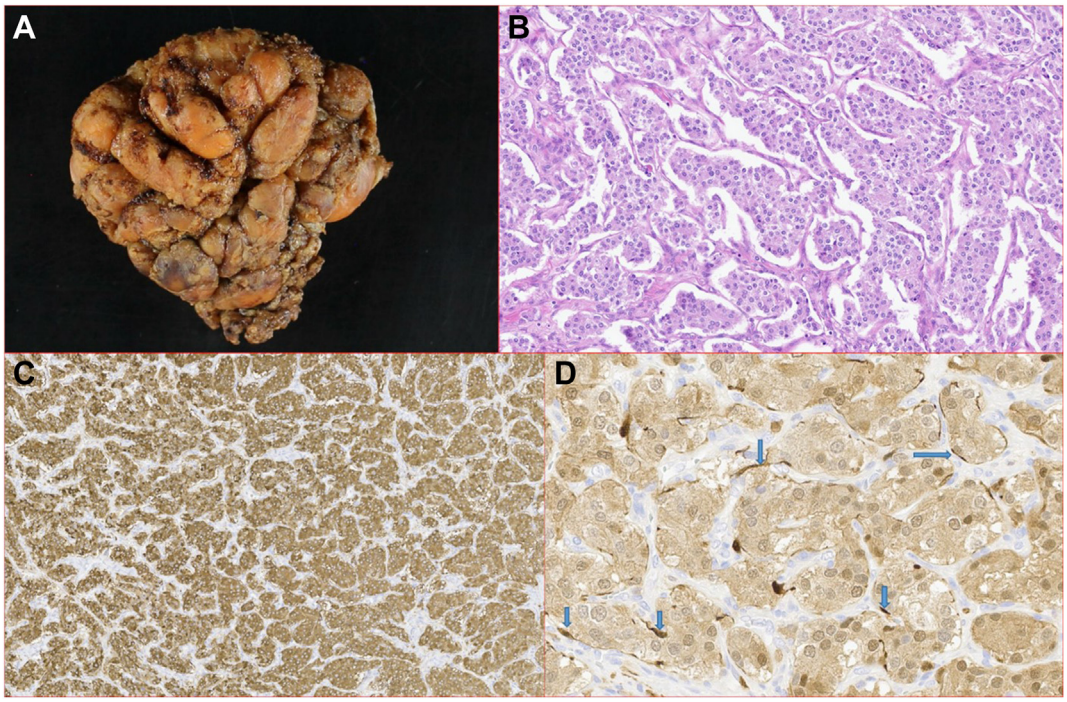

Figure 8 **(A)** Gross pathology of the excised retrocardiac tumor showing lobulated appearance with smooth exterior. **(B)** Hematoxylin and eosin stain demonstrating epithelioid chief cells arranged in distinctive clusters/nests (zellballen pattern) with inconspicuous sustentacular cells and fibrovascular stroma at periphery. Chief cells show round to oval nuclei, discernible nucleoli, and eosinophilic and finely granular cytoplasm. **(C)** Epithelioid cells with positive chromogranin A stain. **(D)** S100-positive sustentacular cells (*blue arrows*) suggestive of peripheral neural cell origin.

The diagnostic evaluation for pericardial paraganglioma depends on the clinical presentation of the patient. In patients presenting with known extracardiac, catecholamine-secreting tumors or symptoms of catecholamine excess with laboratory evaluation positive for urine or serum elevation of catecholamines, the diagnosis is usually made with the use of full-body nuclear imaging such as I-131 meta-iodobenzylguanidine scan or FDG-PET. The overall sensitivity and specificity of these studies nears 100% with current techniques.[5-7] In patients such as ours who are diagnosed by other modalities and are found to have chemically active tumors, full-body nuclear scanning is appropriate to determine metastatic disease, assess for surgical resectability, and assist surgical planning.

For functionally inactive tumors presenting with symptoms of angina and/or heart failure, the workup usually begins with a TTE. While TTE is often able to suggest the diagnosis, in many cases, it is nondiagnostic and further imaging is needed including TEE, CMR,

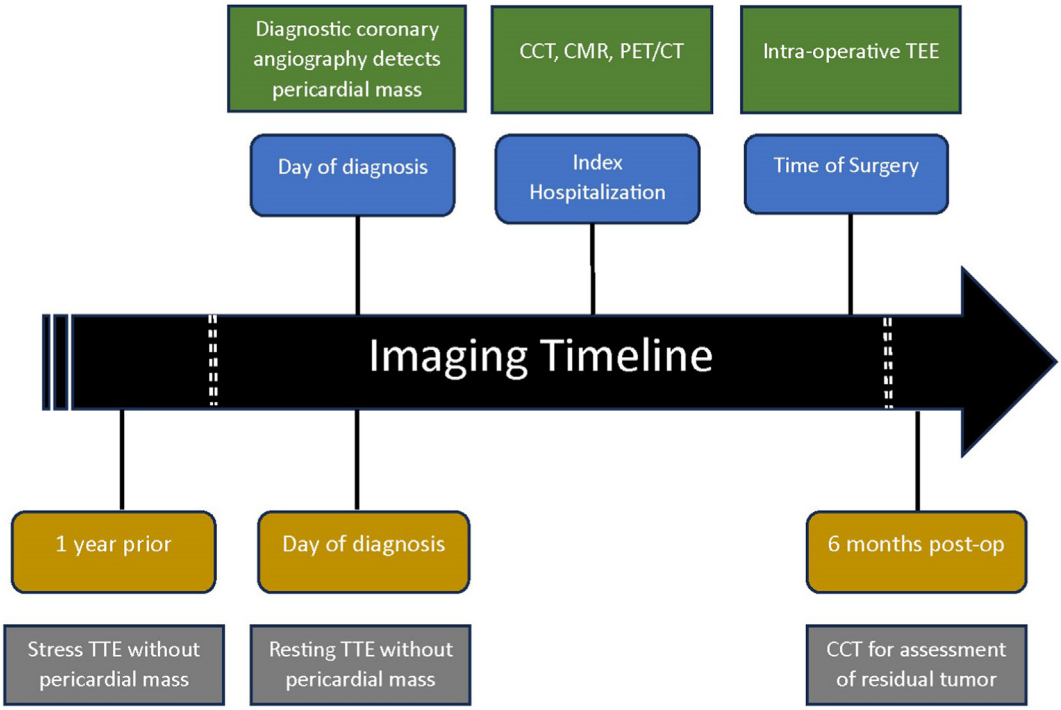

Figure 9 A timeline of imaging studies performed in the evaluation and treatment of this patient.

or CCT.[8-10] Some of the limitations of TTE include limited acoustic windows, limited imaging plane, and decreased spatial resolution, as well as lack of recognition of subtle findings by the sonographer and echo reader. The use of second harmonic imaging can be beneficial by increasing the signal-to-noise ratio, highlighting the tumor borders, but also detrimental as the axial resolution decreases in these far-field structures, making identification more difficult. The findings on TTE can be subtle and require further assessment with Doppler interrogation or contrast enhancement, both of which can identify blood flow in a suspicious structure. This can help to differentiate a true mass from artifact and in the differentiation of masses by assessing the vascularity, as some masses (e.g., hemangioma, paraganglioma) will have increased vascularity, while other mimics (i.e., thrombus) will have no perfusion seen with Doppler or after the administration of an ultrasound-enhancing agent.[11,12] In our case, the appreciation of the echodensity in the parasternal long-axis view in one study, with no evidence in a subsequent study with a slightly different plane, highlights the importance of using sweeps, which can help to mitigate the limitations of acoustic windows and the limited imaging plane that TTE has in comparison to cross-sectional imaging.

As our case demonstrates, advanced cardiac imaging with CMR and CCT can play a vital role in differentiation and treatment of cardiac masses. Evaluation with CMR provides better soft tissue characterization of masses, which can differentiate tumor from thrombus and suggest a differential for cardiac masses. CMR imaging can also assess for malignant features, which are achieved with the use of perfusion imaging and assessment for late gadolinium enhancement (LGE). Homogenous perfusion and extensive LGE are suggestive of malignancy, with size of tumor and pericardial effusion also suggestive of malignant tumors.[13] In our case, the findings of early and rapid perfusion sparing a central stellate region with early clearance of contrast aside from central stellate LGE suggested a paraganglioma without malignant features. CMR is also used in surgical planning to determine tissue planes for resection.

Cardiac computed tomography provides higher spatial resolution than CMR, which allows for evaluation of smaller tumors, although with more limited soft tissue characterization. In the case of a pericardial paraganglioma, CCT can provide another assessment of malignancy, of which tissue invasion is the most sensitive marker of malignant potential. In cases where invasive angiography has not been performed, CCT can provide additional information, including the vascular supply of the tumor for surgical planning, and may be obtained even in the setting of coronary angiography. This was done in our case and suggested compression of the coronary sinus, which was important in planning for initiation of bypass with retrograde cardioplegia.[14]

Transesophageal echocardiography can play a role in both the initial diagnosis as well as in the intraoperative management of patients with pericardial paragangliomas. As these tumors are usually found in the posterior heart, often in the atrioventricular groove, TEE has an increased sensitivity in comparison to TTE in initial diagnosis of pericardial paragangliomas. This is because TEE uses a higher-frequency probe; due to the lack of intervening structures between the probe and the heart (i.e., ribs and muscle), posterior structures are in the near field of the TEE probe, which increases the image quality and spatial resolution, in comparison to TTE, where these posterior structures are in the far field. These advantages of TEE are readily apparent on review of the TTE versus TEE images in our case. As with TTE, the use of ultrasound-enhancing agents can help to delineate vascularity and narrow the differential diagnosis. The role of TEE in the initial diagnosis has declined with the increasing prevalence of advanced cross-sectional imaging with CCT and CMR. However, it still is useful when these advanced imaging modalities are contraindicated or unavailable. Transesophageal echocardiography remains crucial in the intraoperative setting for the delineation of resection planes as well as for providing real-time guidance for cannulation for retrograde cardioplegia. This is particularly important with posterior masses, which can be difficult to directly visualize. Transesophageal echocardiography can provide high-quality imaging

for definitive resection and evaluation for complications including myocardial or coronary perforation, which can rarely be associated with these tumors.[15]

As artificial intelligence becomes more developed for the identification of pathologic cardiac masses by TTE, it may one day be possible for artificial intelligence to assist in making an earlier diagnosis.

CONCLUSION

This case highlights the utility and limitations of cardiac imaging modalities in the assessment and treatment of pericardial tumors. Multimodality imaging is crucial for the successful management of this rare diagnosis.

ETHICS STATEMENT

The authors declare that the work described has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans. The authors declare that the work described has been carried out in accordance with the ARRIVE guidelines and with the U.K. Animals (Scientific Procedures) Act, 1986 and associated guidelines, EU Directive 2010/63/EU for animal experiments, or the National Research Council's Guide for the Care and Use of Laboratory Animals.

CONSENT STATEMENT

Complete written informed consent was obtained from the patient (or appropriate parent, guardian, or power of attorney) for the publication of this study and accompanying images.

FUNDING STATEMENT

The authors declare that this report did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

DISCLOSURE STATEMENT

The authors report no conflict of interest.

ACKNOWLEDGMENTS

We thank Philip Adams and Justin Ornatkowski for the acquisition of echocardiographic images.

SUPPLEMENTARY DATA

Supplementary data to this article can be found online at https://doi.org/10.1016/j.case.2023.06.005.

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