

A Malignant Case of Constrictive Pericarditis



Jorge Betancor, MD, Bo Xu, MD, Arnav Kumar, MD, Carmela D. Tan, MD, E. Rene Rodriguez, MD, Scott D. Flamm, MD, MBA, Craig R. Asher, MD, and Allan L. Klein, MD, *Cleveland, Ohio*

INTRODUCTION

Primary pericardial tumors are rare conditions that can mimic classic constrictive pericarditis. Multimodality imaging can provide enhanced tissue characterization of the pericardium, which improves noninvasive diagnostic performance, particularly in rare cases, such as primary pericardial tumors, presenting with constrictive pathophysiology.

CASE PRESENTATION

A 74-year-old man presented to the emergency department with a 3-month history of progressive dyspnea, fatigue, and pedal edema. His past medical history is pertinent for smoking, Hodgkin's lymphoma treated with radiation therapy, and prostate cancer treated with radical prostatectomy. Cardiopulmonary examination revealed jugular venous distension with positive Kussmaul's sign, decreased breath sounds at the right lung base, an irregular cardiac rhythm, an early peaking 2/6 systolic ejection murmur over the right upper sternal border, and an absent pericardial knock. There was peripheral pitting edema, along with hepatomegaly.

An initial electrocardiogram demonstrated atrial fibrillation with a ventricular response rate of 120 beats per minute. Chest x-ray revealed a right-sided pleural effusion and cardiomegaly without pericardial calcification. Chest computed tomography (CT) with contrast demonstrated a circumferential organized pericardial collection (Figure 1). On CT, the mean density of the right-sided simple pleural effusion was ~ 7 Hounsfield units. In contrast, the density of the pericardial collection was higher, with a mean value of ~ 30 – 45 Hounsfield units, suggesting the presence of a highly proteinaceous fluid collection. A limited transthoracic echocardiogram confirmed the circumferential pericardial effusion, as shown in Figure 2A-D and Video 1. Respiratory variation in transmitral and transtricuspid flow is demonstrated in Figure 3, while annulus reversus on tissue Doppler imaging is demonstrated in Figure 4. Subxiphoid pericardiocentesis (Video 2) yielded 1 L of bloody fluid, with scant reactive mesothelial cells but no malignant cells.

From the Department of Cardiovascular Medicine (J.B., B.X., A.K., C.R.A., A.L.K.) and Department of Anatomic Pathology (C.D.T., E.R.R.), Heart and Vascular Institute, and Department of Cardiovascular Imaging (S.D.F.), Imaging Institute, Cleveland Clinic, Cleveland, Ohio.

Keywords: Pericardial tumor, Pericardial mesothelioma, Constrictive pericarditis, Tissue characterization, Multimodality imaging

Conflicts of Interest: The authors reported no actual or potential conflicts of interest relative to this document.

Copyright 2017 by the American Society of Echocardiography. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>)

2468-6441

<http://dx.doi.org/10.1016/j.case.2016.11.005>

Subsequently, the patient was discharged on beta-blockers, diuretics, nonsteroidal anti-inflammatory analgesia, and colchicine. Over the next few months, he was readmitted to the hospital on several occasions with debilitating shortness of breath and signs of volume overload. A subsequent transthoracic echocardiogram, 6 months after the initial echocardiogram, revealed a circumferential pericardial effusion, diastolic septal bounce, and mild aortic stenosis with calcification of the aortomitral continuity. Myocardial strain imaging revealed reduced peak systolic strain in the anterolateral left ventricular (LV) segments (-13% to -17%), with preserved peak systolic strain in anteroseptum (-24% ; Figure 5). Transesophageal echocardiogram performed prior to cardioversion during an episode of atrial fibrillation was again notable for a circumferential pericardial collection (Video 3A-C).

Cardiac magnetic resonance imaging (CMR) was performed to further investigate the pericardial collection. It demonstrated decreased signal intensity in the pericardial collection, compared with pleural effusions on steady-state free-precession (SSFP) sequences before gadolinium administration (Figure 6A, Videos 4A and 5A). After gadolinium administration, the signal intensity within the pericardial collection increased (Figure 6B, Videos 4B and 5B), suggesting hypervascularity. Further tissue characterization achieved with fat saturation T2-weighted imaging revealed a hyperintense signal throughout the pericardial collection, supporting the diagnosis of a pericardial tumor (Figure 7). Furthermore, delayed gadolinium enhancement

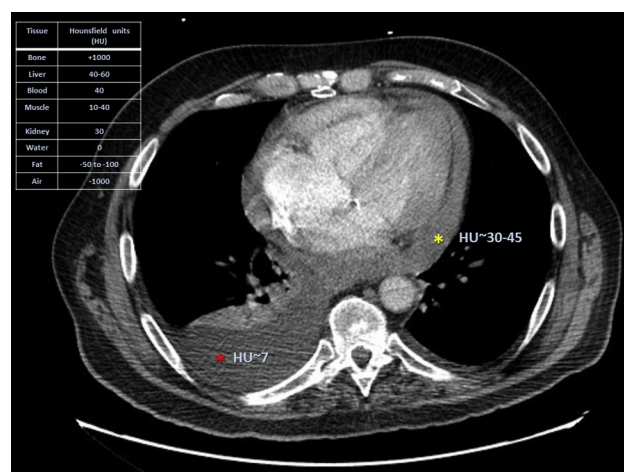


Figure 1 Chest CT with contrast showing a circumferential organized pericardial collection. The density of the right-sided simple pleural effusion had a mean value of ~ 7 Hounsfield units (*red asterisk*). In contrast, the density of the pericardial collection was higher, with a mean value of ~ 30 – 45 Hounsfield units (*yellow asterisk*), suggesting the presence of highly proteinaceous fluid collection.

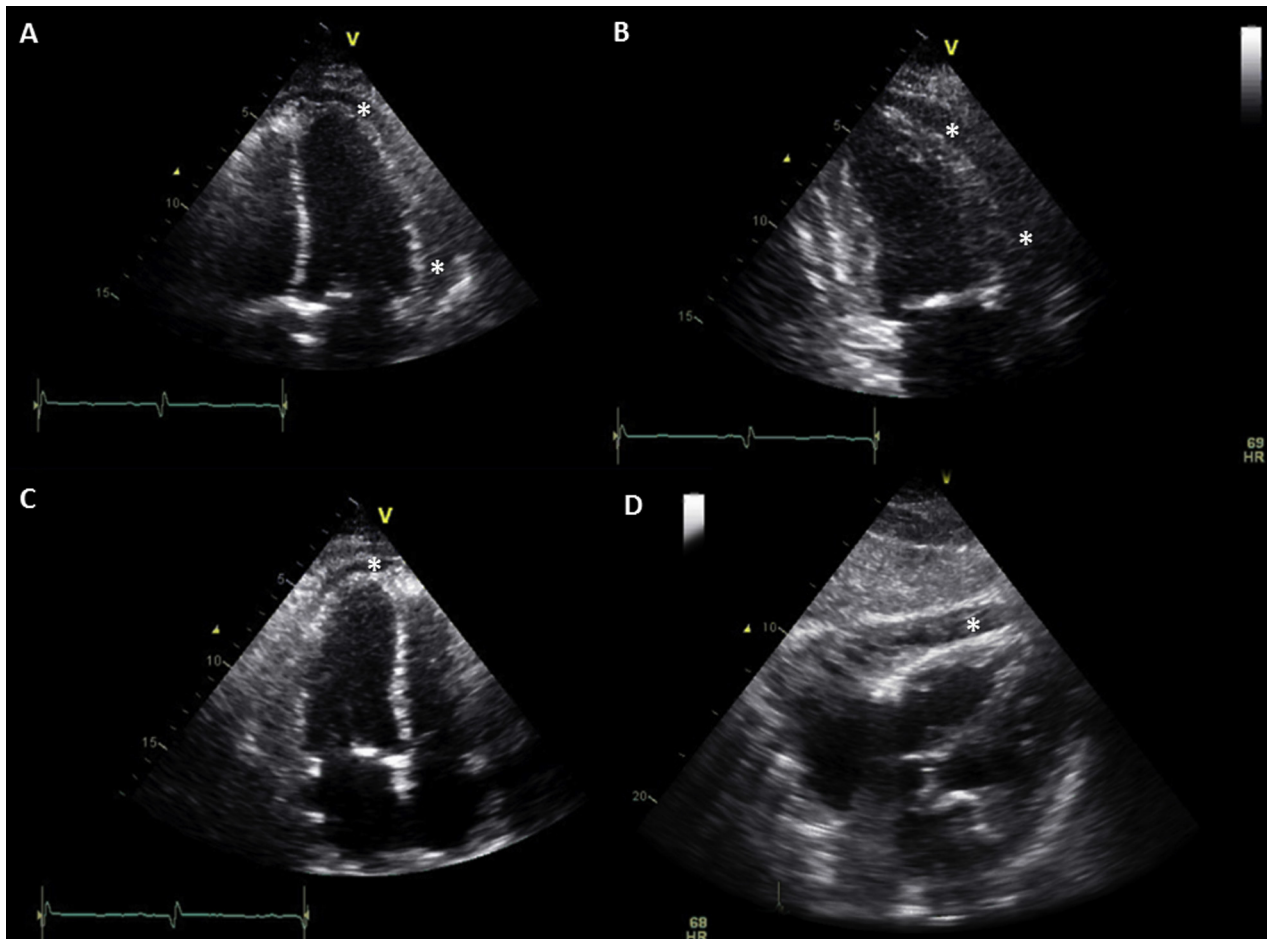


Figure 2 Transthoracic echocardiogram showing a circumferential organized pericardial effusion (asterisk) in the four-chamber (A), two-chamber (B), three-chamber (C), and subcostal views (D).

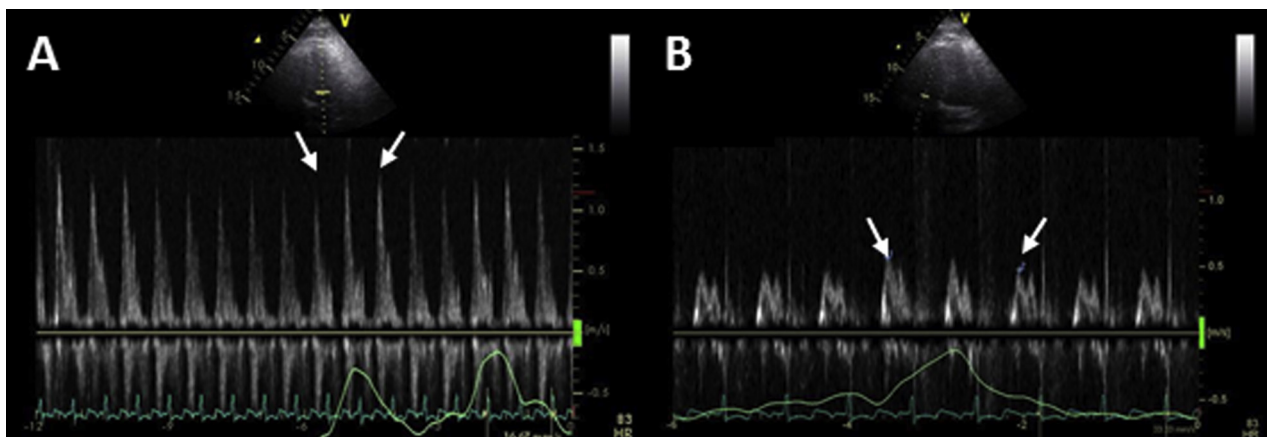


Figure 3 (A) Transmitral pulsed wave Doppler at the level of the mitral leaflet tips with respirometry tracing seen in the second half of the clip, demonstrating significant respiratory variation of more than 25% when comparing the first beat of inspiration with the first beat of expiration (arrows). (B) Transtricuspid pulse wave Doppler at low speed with sample volume at the level of the tricuspid leaflet tips with suboptimal respirometry tracing seen, attempting to demonstrate a significant respiratory variation of more than 40% when comparing the first beat of inspiration with the first beat of expiration (arrows).

images revealed increased though heterogeneous signal intensity, further supporting the diagnosis of a soft-tissue tumor (Figure 8). Additionally, there were classic features of constrictive patho-

physiology as demonstrated by the free-breathing SSFP sequence (Video 6), where the circumferential pericardial tissue results in significant respirophasic septal shift.

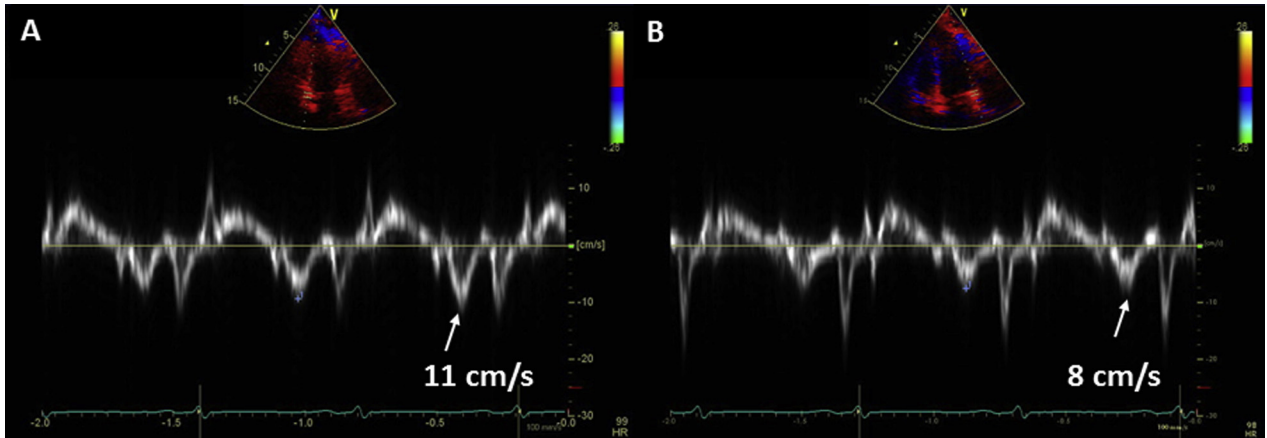


Figure 4 (A) Tissue Doppler tracing at the septal mitral annulus, demonstrating a peak e' velocity of 11 cm/sec. (B) Sample volume is located at the lateral mitral annulus, reaching an e' velocity of 8 cm/sec. Overall, findings are consistent with annulus reversus, where tethering of the lateral annulus/wall prevents normal longitudinal motion, resulting in slight overcompensation of the septal annulus/wall and reversed ratio.

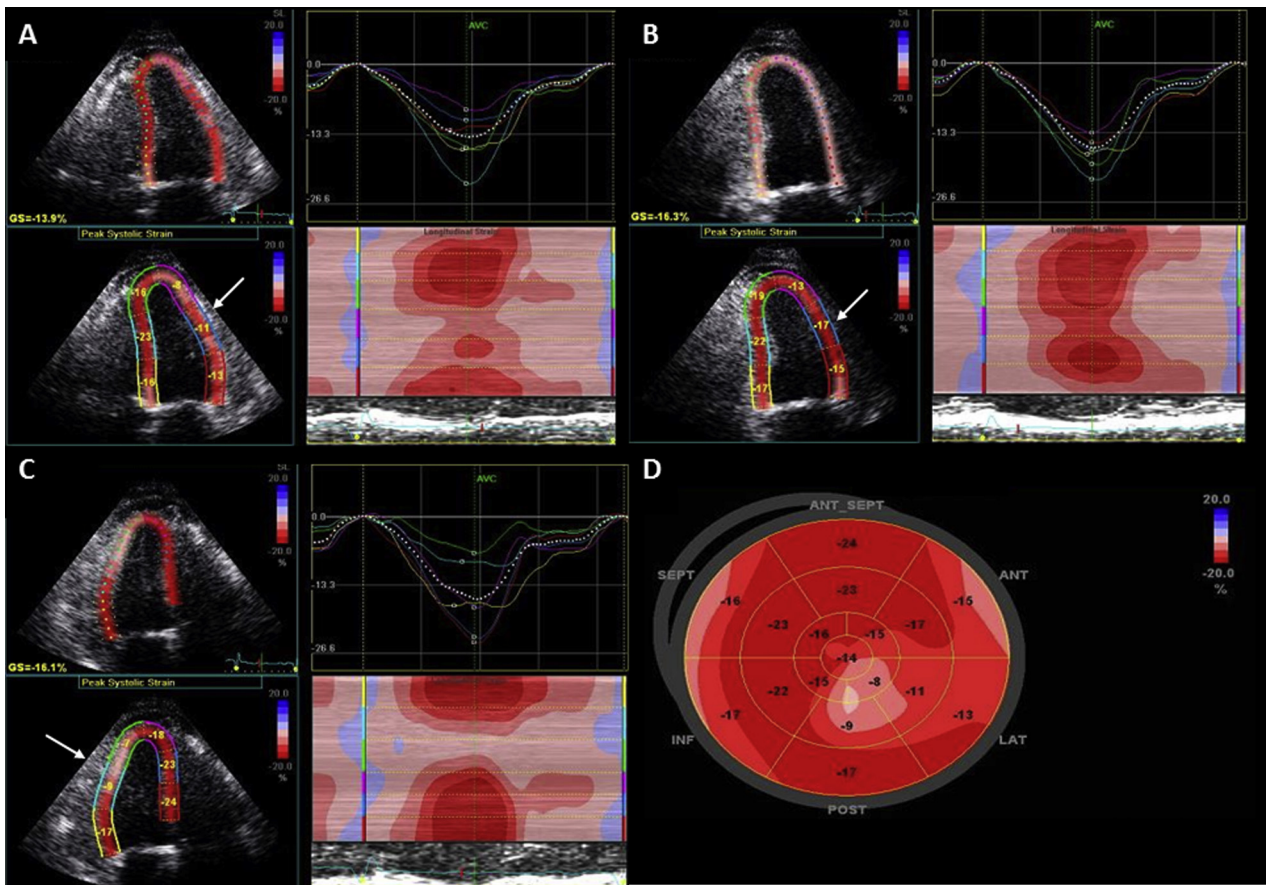


Figure 5 Two-dimensional myocardial longitudinal strain imaging showing reduced segmental peak systolic strain in the anterolateral (A, arrow), anterior (B, arrow), and inferolateral (C, arrow) walls. (D) Bull's-eye plot demonstrates overall reduction in segmental longitudinal strain, with relative preservation of the septal segments.

On the basis of these findings the patient was referred for pericardiectomy with a clinical diagnosis of constrictive pericarditis due to pericardial tumor. Additionally, it was postulated that there could have been an element of restrictive cardiomyopathy,

in the context of prior thoracic radiation. During pericardiectomy, the heart was found to be encapsulated in markedly thickened soft tissue (Figure 9). A pericardial tumor was resected, and pathologic examination demonstrated a malignant mesothelioma

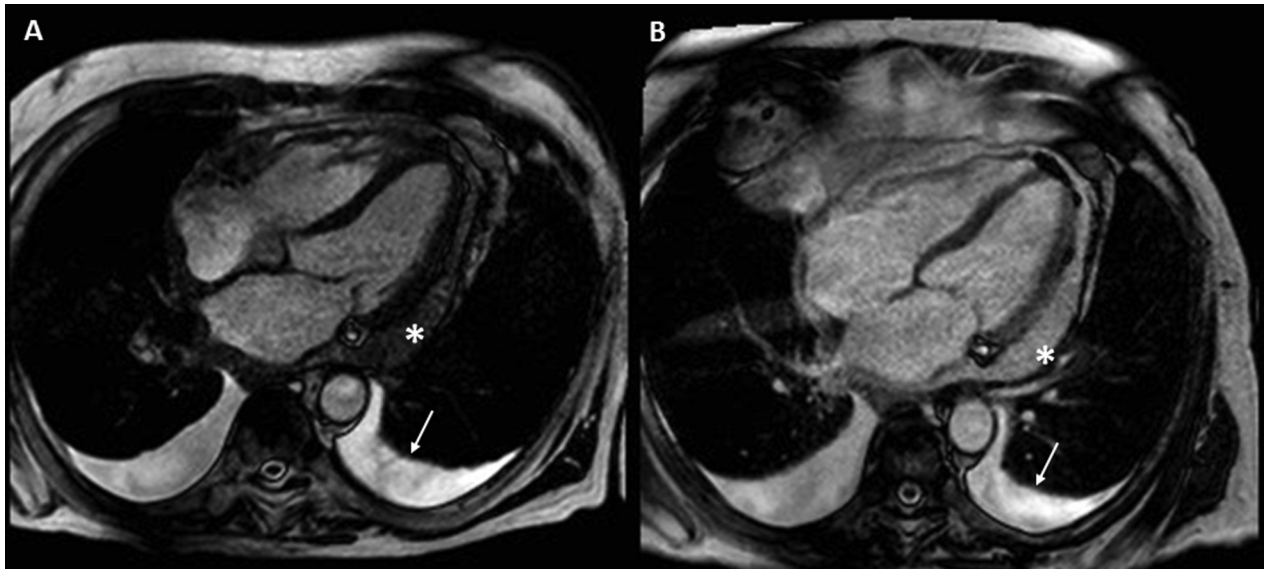


Figure 6 (A) CMR SSFP sequence, horizontal long-axis view, demonstrating decreased signal intensity in the pericardial collection (*asterisk*), compared with the simple pleural effusions (*arrow*), prior to gadolinium injection. (B) After gadolinium administration, the signal intensity within the pericardial collection increased.

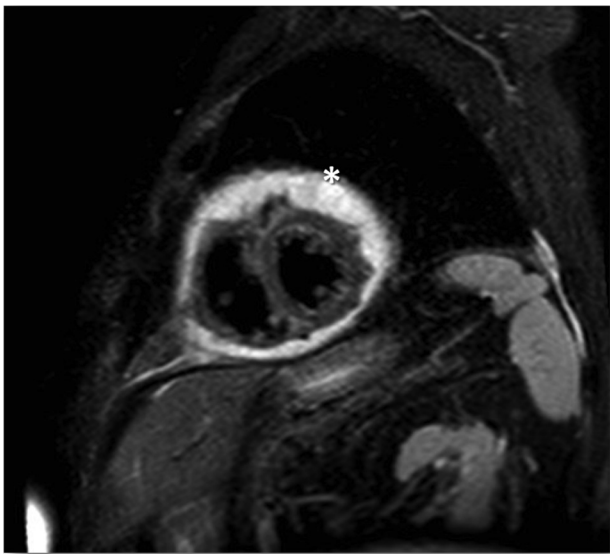


Figure 7 Fat saturation T2-weighted imaging showing hyperintense signal throughout the pericardial collection (*asterisk*), suggesting the presence of vascularity and edema, which are characteristic of soft-tissue tumors.

(Figure 10). Over the next few days, the patient progressively developed worsening multiorgan failure and eventually expired on post-operative day eight.

DISCUSSION

Primary pericardial tumors are rare conditions and may include benign tumors, such as fibroma and lipoma, and malignant tumors, such as mesothelioma and sarcoma.¹ Pericardial mesothe-

lioma is an exceedingly rare tumor, accounting for approximately 1% of all mesotheliomas.¹ The etiology of primary malignant mesothelioma of the pericardium remains unclear, although asbestos exposure has been reported in some cases.² The median survival of unresectable pericardial mesothelioma is dismal: usually in the order of 6 months.³ Radical surgery remains the cornerstone of treatment in an attempt to resect the localized disease.⁴ However, the long-term prognosis often remains poor, despite surgical treatment. This may be related to the malignant nature of the condition but also may partially reflect the difficulties often associated with the diagnosis of this condition. Only several hundred cases of pericardial mesothelioma have been reported in the literature, and it has been reported that the correct antemortem diagnosis was made in only around one quarter of these patients.⁵

This case describes a rare case of a primary malignant pericardial mesothelioma presenting as constrictive pericarditis. However, on echocardiography initially, the impression was that the patient's symptoms were a result of a circumferential pericardial effusion. This led to an initial pericardiocentesis. However, this intervention was not successful, and our patient presented to the hospital again on multiple occasions with worsening dyspnea and signs of volume overload. Subsequently, on detailed assessment involving multimodality cardiac imaging with echocardiography, multidetector cardiac CT, and CMR, we were able to demonstrate that the circumferential echo-lucent "pericardial effusion" indeed represented a malignant circumferential pericardial soft-tissue tumor. Advanced echocardiographic assessment with strain imaging was used for the assessment of constrictive physiology. Regional myocardial mechanics have been studied in patients with constrictive pericarditis.^{5,6} It has been shown that patients with constrictive pericarditis have selectively depressed LV anterolateral wall strain and right ventricular free wall longitudinal strain but preserved LV septal wall systolic strain.^{6,7} Our patient underwent pericardiectomy, and the final

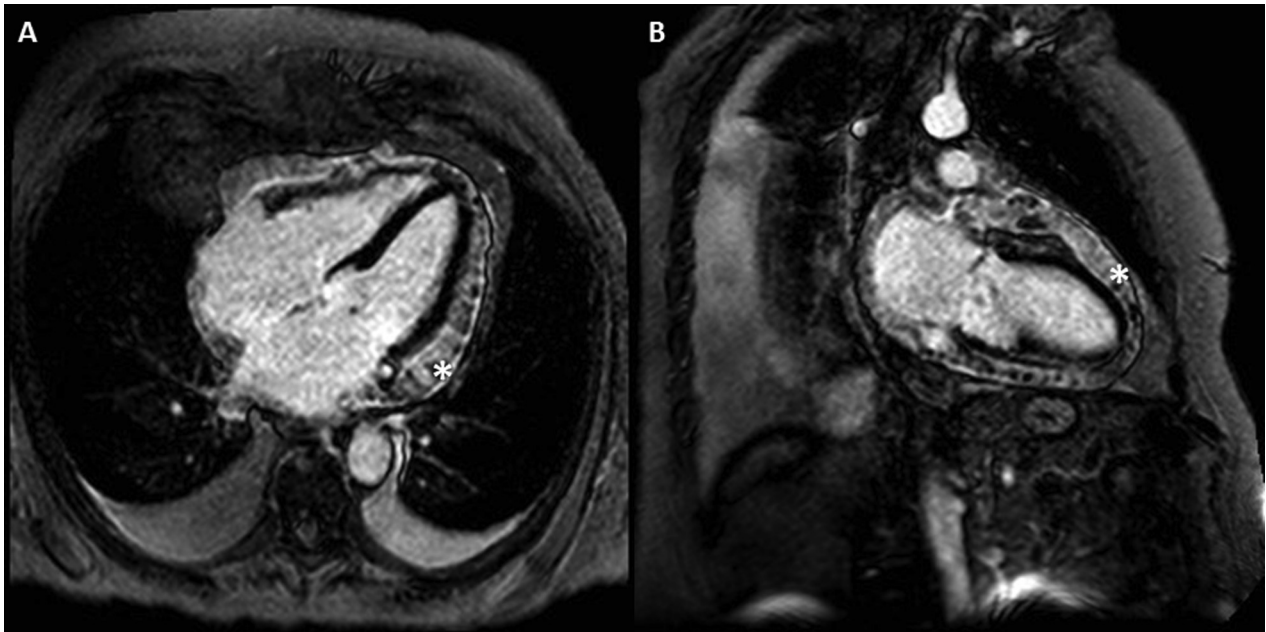


Figure 8 Delayed gadolinium enhancement (A) four-chamber and (B) two-chamber views showing heterogeneous hyperenhancement throughout the pericardium (asterisk), suggesting a soft-tissue mass with increased interstitial space.

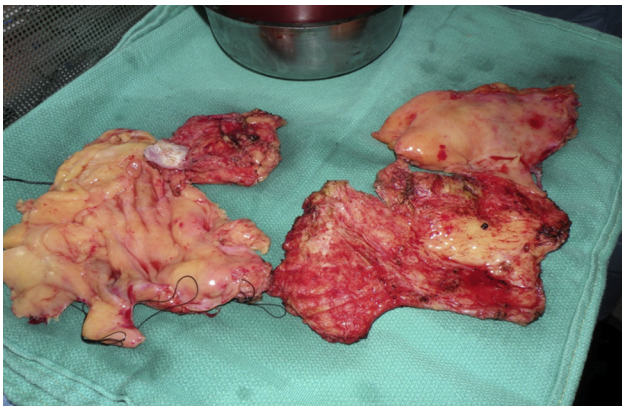


Figure 9 Postoperative image of resected pericardial mass with an indurated and retracted appearance.

histological examination confirmed the multimodality cardiovascular imaging findings.

This case highlights the importance of incorporating multimodality cardiovascular imaging in the assessment of selected cases of constrictive pericarditis, in order to ensure that rare pericardial conditions, such as a primary malignant pericardial mesothelioma, are appropriately diagnosed.

SUPPLEMENTARY DATA

Supplementary data related to this article can be found at <http://dx.doi.org/10.1016/j.case.2016.11.005>.

REFERENCES

1. Patel J, Sheppard MN. Primary malignant mesothelioma of the pericardium. *Cardiovasc Pathol* 2011;20:107-9.
2. Thomason R, Schlegel W, Lucca M, Cummings S, Lee S. Primary malignant mesothelioma of the pericardium. Case report and literature review. *Tex Heart Inst J* 1994;21:170-4.
3. Nilsson A, Rasmuson T. Primary pericardial mesothelioma: report of a patient and literature review. *Case Rep Oncol* 2009;2:125-32.
4. Eren NT, Akar AR. Primary pericardial mesothelioma. *Curr Treat Options Oncol* 2002;3:369-73.
5. Suman S, Schofield P, Large S. Primary pericardial mesothelioma presenting as pericardial constriction: a case report. *Heart* 2004;90:e4.
6. Klein AL, Abbara S, Agler DA, Appleton CP, Asher CR, et al. American Society of Echocardiography Clinical Recommendations for Multimodality Cardiovascular Imaging of Patients with Pericardial Disease. *J Am Soc Echocardiogr* 2013;26:965-1012.
7. Kusunose K, Dahiya A, Popovic ZB, Motoki H, Alraies C, Zurick AO, et al. Biventricular mechanics in constrictive pericarditis comparison with restrictive cardiomyopathy and impact of pericardiectomy. *Circ Cardiovasc Imaging* 2013;6:399-406.

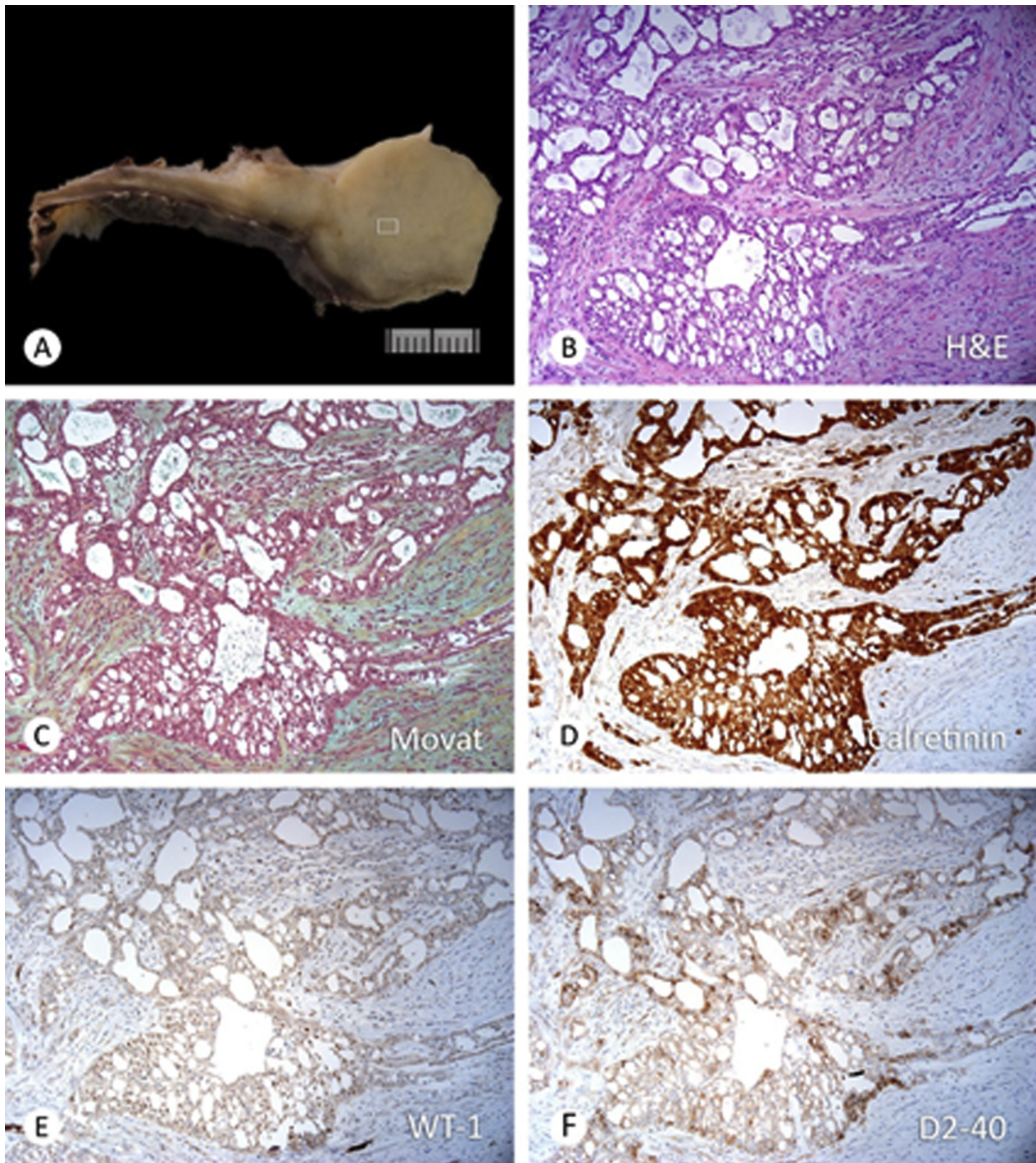


Figure 10 Malignant mesothelioma of the pericardium. **(A)** Gross specimen showing the parietal pericardium transitioning from mild to moderate thickening and formation of a bulky 2.5-cm mass (scale bar, 1 cm). The *small white rectangle* indicates the area of the tumor shown in panels **B-F**. **(B)** On microscopic examination, there is clear epithelioid malignant mesothelioma with tumor cells forming gland-like spaces and micropapillae ($\times 400$, hematoxylin and eosin). **(C)** The same area of the tumor (*red cells*) shows active fibrosis (*green yellow*) with spindle cells in the stroma, which imparts a white color to the gross specimen ($\times 400$, Movat pentachrome). **(D)** Immunohistochemistry for detection of calretinin shows strong immunoreactivity both in the cytoplasm and in the nuclei of the tumor cells ($\times 400$, calretinin immunohistochemistry). **(E)** The tumor cells also show nuclear staining for WT-1 ($\times 400$, WT-1 immunohistochemistry). **(F)** The sustentacular cells of the tumor are intensely stained by D2-40 ($\times 400$, D2-40).