JACC: CASE REPORTS VOL. 18, 2023

CASE REPORT

INTERMEDIATE

CLINICAL CASE

A Rare Case of Constrictive Pericarditis

Inflammatory Myofibroblastic Tumor

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ABSTRACT

A previously healthy 15-year-old adolescent female presented with dependent edema, ascites, and dyspnea on exertion. The result of her initial evaluation was consistent with constrictive pericarditis in the setting of local low-grade spindle cell sarcoma. She was unresponsive to traditional medical management and required concurrent mass resection and radical pericardiectomy for definitive treatment. (**Level of Difficulty: Intermediate.**)
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A 15-year-old adolescent female presented with a 3-week history of lower extremity edema, abdominal distension, fatigue, and dyspnea on exertion. She described having a viral upper respiratory infection that preceded her current symptoms. She did not endorse chest pain, orthopnea, or paroxysmal nocturnal dyspnea. The result of her examination was notable for an elevated jugular venous pressure to the angle of the jaw, abdominal distension with hepatomegaly, and 2+ pitting edema in the bilateral lower extremities.

LEARNING OBJECTIVES

- To understand the clinical presentation of constrictive pericarditis and associated diagnosis and management.
- To understand the role of multimodality imaging in diagnosing and managing constrictive pericarditis.
- To understand the role of histopathology in the diagnosis and management of IMT and appreciate IMT as a very rare cause of constrictive pericarditis.

MEDICAL HISTORY

The patient had no pertinent medical history. A previous work-up for her symptoms at another institution had included abdominal ultrasound, which revealed ascites and hepatomegaly. Subsequent evaluation included unremarkable viral hepatitis serologies, ceruloplasmin levels, and anti-smooth muscle antibodies. Computed tomography (CT) of the chest showed a 6.2- × 4-cm mass in the prevascular space, diffuse necrotic mediastinal lymphadenopathy, pericardial thickening with biatrial enlargement, smaller ventricular cavities, reflux of contrast material into the dilated inferior vena cava, and heterogenous appearance of the liver. Right heart catheterization showed elevated filling pressures (Table 1). Constrictive

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

Manuscript received March 16, 2023; revised manuscript received April 27, 2023, accepted May 11, 2023.

ISSN 2666-0849 https://doi.org/10.1016/j.jaccas.2023.101908

ABBREVIATIONS AND ACRONYMS

CMR = cardiac magnetic resonance

CP = constrictive pericarditis

CT = computed tomography

IMT = inflammatory myofibroblastic tumor

PTEN = phosphatase and tensin homolog

pericarditis (CP) was thus considered in the differential diagnosis. Subsequent work-up for infectious causes yielded negative results. The patient was then referred to our clinic for further work-up and management.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis included CP of a viral or neoplastic cause, cirrhosis, and cardiomyopathy.

INVESTIGATIONS

Laboratory investigations included normal inflammatory markers (erythrocyte sedimentation rate of 2 mm/h and ultrasensitive C-reactive protein of 0.6 mg/L) and an elevated N-terminal prohormone brain natriuretic peptide of 287 pg/mL (normal <125 pg/mL). An echocardiogram showed pericardial thickening with a small pericardial effusion, biventricular compression and deformity, respirophasic septal shift, respiratory variation across the mitral and tricuspid valves, annulus reversus, and increased expiratory reversal of hepatic vein flow (**Figure 1**). Cardiac magnetic resonance imaging (CMR) revealed pericardial thickening, pericardial enhancement on T2 short tau inversion recovery imaging with severe circumferential delayed pericardial enhancement on late gadolinium enhancement imaging (**Figure 1**). CT of the chest showed a mediastinal mass (**Figure 2**). She then underwent video-assisted thoracoscopic biopsy of the mass, and histologic analysis showed an inflammatory myofibroblastic tumor (IMT) (**Figure 3**). Next-generation sequencing of the tissue sample revealed a phosphatase and tensin homolog (PTEN) mutation.

TABLE 1 Right Heart Catheterization Tracings Showing Elevated Biventricular Filling Pressures and Equalization of Biventricular Diastolic Pressures

Right atrial pressure, mm Hg	20/18 (16)
Right ventricular systolic pressure, mm Hg	42
Right ventricular end-diastolic pressure, mm Hg	20
Pulmonary artery pressure, mm Hg	38/22 (29)
Pulmonary capillary wedge pressure, mm Hg	20
Left ventricular systolic pressure, mm Hg	82
Left ventricular end-diastolic pressure, mm Hg	20

Values in parentheses indicate the mean filling pressure.

MANAGEMENT

The patient was initially treated with ibuprofen 600 mg 3 times daily, colchicine 0.6 mg once daily (reduced dosing interval because of gastrointestinal upset), and prednisone taper (40 mg) for presumed transient CP. After IMT was diagnosed, the patient was started on everolimus and weaned off prednisone. Interval studies over the next year showed stable tumor burden but with persistent evidence of pericardial inflammation and constriction. The patient experienced worsening congestive symptoms and liver function; as a result, she underwent tumor debulking and radical pericardiectomy.

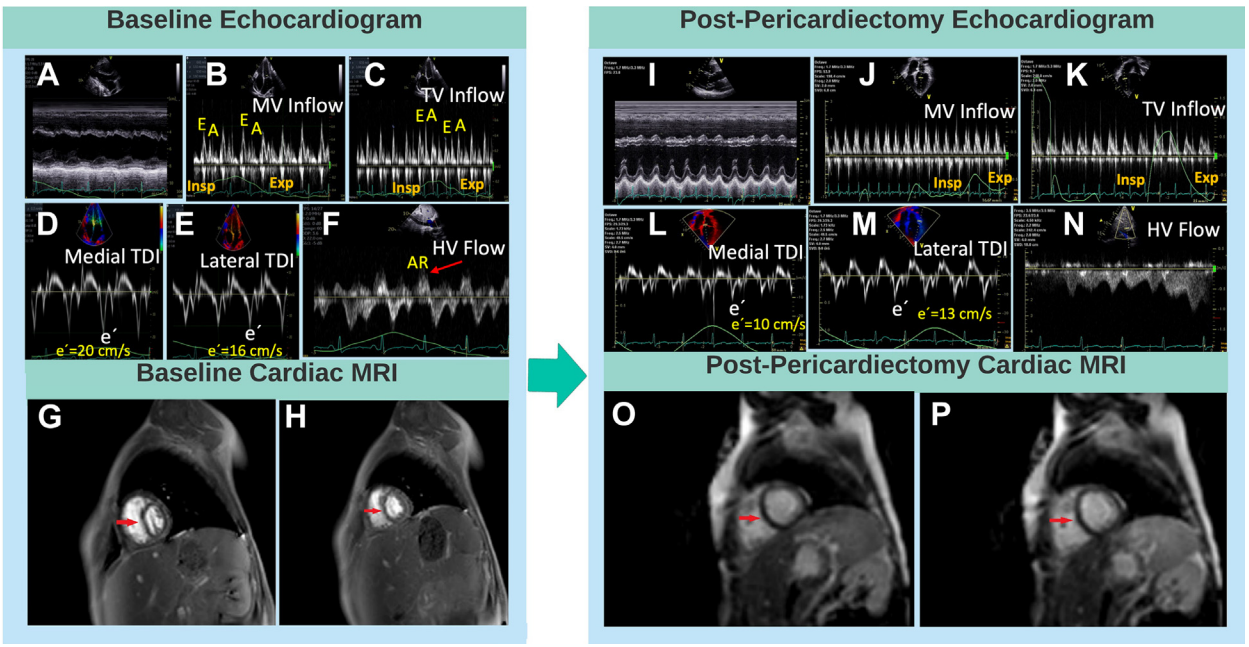
DISCUSSION

IMT is a rare benign tumor composed of spindle cells mixed with infiltrates of varying numbers of inflammatory cells.[1] IMT is regarded as an intermediate biological potential neoplasm, with an estimated 2% risk of metastasis and a 25% recurrence rate.[2] Although IMT can present in any age group, most patients who experience IMT are children, adolescents, or young adults.[3] IMT is incredibly rare, with an estimated 150 to 200 cases diagnosed annually, and its cause remains unclear; immunologic and infectious causes are thought to be potential causes.[4]

IMTs are frequently painless, and clinical presentation typically reflects localized symptoms at the site of tumor growth.[4] IMTs are usually found in the lungs, abdominopelvic region, and mediastinum.[2] Cardiac IMTs are particularly rare, with <60 documented cases in the literature, and most cardiac IMTs are endocardial based.[5] Cardiac IMT involving the pericardium causing CP is a particularly unique presentation.

Multimodality imaging is essential in the diagnosis of CP. Echocardiography can show findings that include bowing of the interventricular septum toward the left ventricle with inspiration and shift of the septum towards the right ventricle (expiration) (respirophasic septal shift) caused by ventricular interdependence in a constricted pericardium; an increase in medial mitral valve annulus tissue velocity relative to lateral (annulus reversus) caused by limited lateral motion of the heart resulting from the constrictive pericardium; respiratory variations in mitral and tricuspid valve inflow velocities; and reversal of hepatic vein flow during expiration caused

FIGURE 1 **Baseline and Post-Pericardiectomy Transthoracic Echocardiogram and Cardiac Magnetic Resonance Imaging**

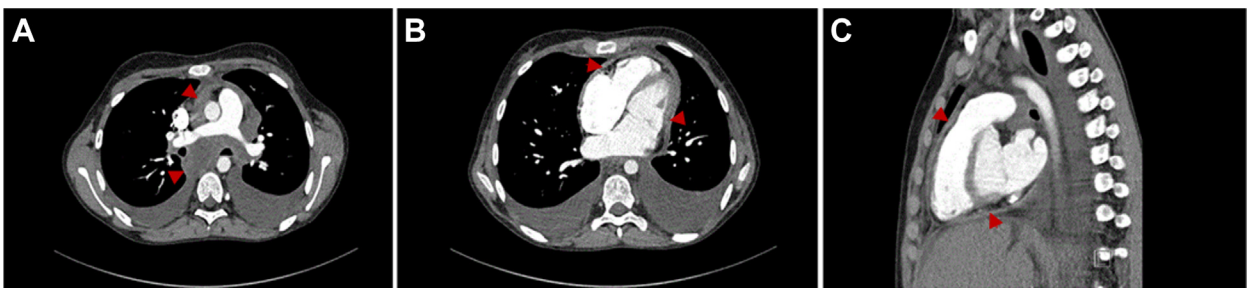


Baseline transthoracic echocardiogram demonstrating septal bounce and respirophasic shift on M-mode **(A)**, respiratory variation across mitral valve **(B)**, tricuspid valve inflows **(C),** Tissue Doppler imaging demonstrating annulus reversus **(D, E)**, and increased hepatic vein expiratory diastolic flow reversal compared to forward diastolic flow **(F)**. Baseline CMR showing respirophasic shift with septal flattening on inspiration **(G)** and normal motion on expiration **(H)**. Postpericardiectomy imaging showing resolution of constrictive findings on echocardiography and CMR **(I to P)**.

by dissociated intrathoracic and intracardiac pressures and enhanced ventricular interdependence.[6] CMR can show conical ventricular deformity, pericardial thickening, interventricular dependence (bowing of the interventricular septum toward the left ventricle during inspiration), and pericardial edema and inflammation with T2 short tau inversion recovery hyperintensity and late gadolinium enhancement imaging.[6] Chest CT demonstrated the presence of a mediastinal mass; however, a tissue biopsy was required to make a diagnosis of IMT.[1]

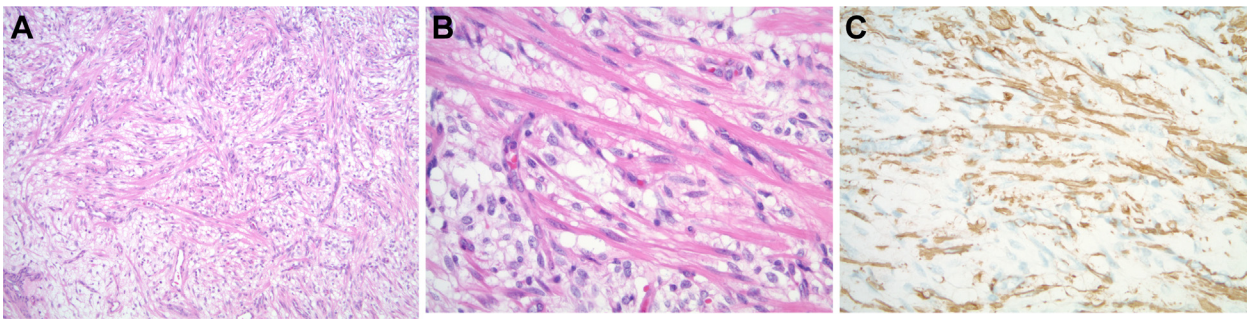
Management of IMTs is challenging because treatment protocols have yet to be clearly established. There are case reports of spontaneous or steroid-induced regression in tumors deemed unresectable.[7] More recently, systemic chemotherapy has been

FIGURE 2 **Baseline Chest Computed Tomography**



Chest CT axial image **(A)** showing mediastinal mass **(arrowhead)**. Chest CT axial **(B)** and sagittal **(C)** images showing pericardial thickening with small pericardial fluid.

FIGURE 3 Post-Pericardiectomy Histopathology of Pericardial Specimen



(A) Low-power examination of morphology demonstrates loose fascicles of bland fibroblasts and myofibroblasts (×20, hematoxylin and eosin). **(B)** On high-power examination, the lesional cells show elongated tapered cytoplasm with bland nuclei and inconspicuous nucleoli without cytologic atypia or increased mitotic activity (×40, hematoxylin and eosin). **(C)** Smooth muscle actin highlights the lesional cells in a tram-track pattern, consistent with myofibroblastic differentiation (×40, smooth muscle actin).

used in an attempt to control unresectable or metastatic IMTs.[7]

Next-generation sequencing of the mass lesion revealed a PTEN mutation, which reduces or eliminates the PTEN gene's suppressive activity on the mammalian target of rapamycin growth-promoting signaling cascade, leading to tumor growth.[8] This test result was not consistent with the typical rearrangements observed in IMT.[5] Given this finding, everolimus was initiated. Everolimus, an inhibitor of mammalian target of rapamycin, has demonstrated efficacy in treating conditions caused by PTEN mutations.[9] Additionally, the use of nonsteroidal anti-inflammatory drugs and corticosteroids have shown efficacy in the treatment of IMTs, likely because of the increased expression of vascular endothelial growth factor and cyclo-oxygenase-2 in the inflammatory infiltrates of IMT.[10] The mainstay of treatment of IMT is tumor resection, and pericardiectomy is often pursued for definitive treatment of CP.

FOLLOW-UP

After surgery, the patient experienced resolution of her symptoms. Echocardiography and CMR performed 5 months after surgery revealed resolution of constrictive physiology and preserved biventricular function (**Figure 1**). Histologic assessment of the surgically resected mass revealed a low-grade spindle cell neoplasm. Given the low-grade nature of the mass, the patient was initially observed in the absence of targeted therapy but experienced local recurrence requiring restarting everolimus.

CONCLUSIONS

IMT is a rare tumor most often seen in childhood that can involve numerous different organs. However, IMT presenting as CP caused by pericardial involvement has not previously been described in the literature. Multimodality imaging was essential in diagnosing this unique presentation of CP. This case emphasizes the importance of maintaining a broad differential diagnosis, especially in children and adolescents.

FUNDING SUPPORT AND AUTHOR DISCLOSURES

Dr Klein has received research funding from Kiniksa Pharmaceuticals, Ltd; and has served on scientific advisory boards for Kiniksa Pharmaceuticals, Ltd, Swedish Orphan Biovitrum AB, Cardiol Therapeutics, and Pfizer, Inc. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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KEY WORDS **cardiac magnetic resonance, cardiomyopathy, constrictive pericarditis, pericardial effusion, peripheral edema**