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CASE REPORT

INTERMEDIATE

CLINICAL CASE

A Rare Case of Carcinoid Constrictive Pericarditis

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ABSTRACT

We describe a case of atypical carcinoid heart disease. A 62-year-old woman with well-differentiated neuroendocrine tumor metastatic to the liver and lymph nodes presented with recurrent unilateral pleural effusions and lower extremity edema. Multimodality imaging and workup resulted in the diagnosis of carcinoid-related constrictive pericarditis, a rare form of carcinoid heart disease. (**Level of Difficulty: Intermediate.**) (J Am Coll Cardiol Case Rep 2020;2:1–5)

HISTORY OF PRESENTATION

A 62-year-old woman presented with a 1-year history of recurrent right-sided pleural effusions, chest tightness, and progressive lower extremity edema. She was hospitalized multiple times in the recent past for marked dyspnea on exertion requiring escalating doses of diuretics and repeated thoracenteses (Supplemental Figure 1). Physical examination revealed a chronically ill-appearing thin woman with blood pressure of 102/69 mm Hg and pulse rate of 58 beats/min and regular. Pertinent physical findings included moderate jugular venous distension with Kussmaul sign, and dullness to percussion with decreased breath sounds over the right posterior lung base. Cardiac examination was otherwise unremarkable, with no murmurs, rubs, or knocks. Extremities showed trace bilateral pitting edema while on moderate doses of diuretics.

LEARNING OBJECTIVES

- Understand the typical and atypical symptoms in presentations of carcinoid heart disease.
- Describe the broad spectrum of cardiac manifestations in carcinoid syndrome.

PAST MEDICAL HISTORY

Past medical history included well-differentiated neuroendocrine tumor (NET) arising in the ileum and metastatic to the liver and lymph nodes, for which she had undergone resection of the primary tumor and a synchronous liver metastasis. She had resultant carcinoid syndrome so therapy with a somatostatin analogue was started, but diarrhea persisted. Interestingly, the patient also carried a germline BRCA1 mutation and was status post bilateral salpingo-oophorectomy and prophylactic bilateral skin-sparing mastectomy. She had a history of 30 pack-years of tobacco smoking and a family history of coronary artery disease in her father and maternal grandfather.

DIFFERENTIAL DIAGNOSIS

Initial differential diagnosis was appropriately broad. Given her NET metastases, carcinoid heart disease

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Informed consent was obtained for this case.

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ABBREVIATIONS AND ACRONYMS

NET = neuroendocrine tumor

and obstruction of the vena cava due to large metastases were strong considerations. Her right-sided heart failure symptoms and Kussmaul sign were suggestive of constriction or restrictive cardiomyopathy. A second primary tumor due to her BRCA1 mutation also was considered. Other less likely considerations included coronary artery disease in the setting of her smoking history and family history, pulmonary hypertension, and dilated cardiomyopathy.

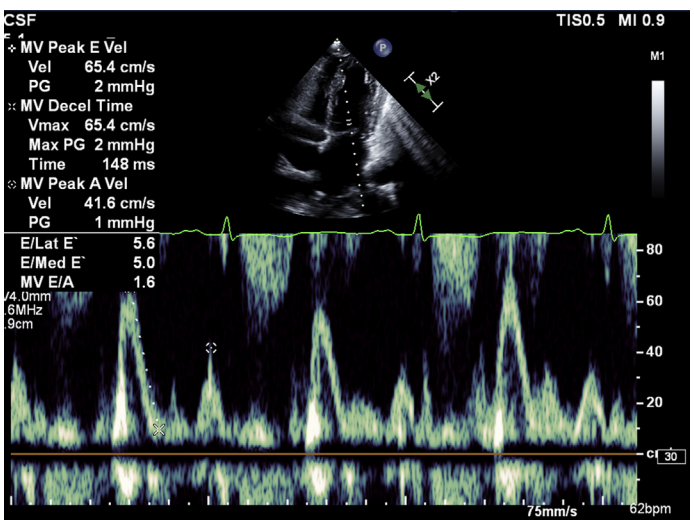
INVESTIGATIONS

To address the extent of her NET metastases, blood tests and initial imaging were performed first. Laboratory test results demonstrated an elevated but stable chromogranin A level of 23.0 ng/ml and urinary 5-hydroxyindoleacetic acid level of 20.7 mg per 24 h suggestive of stable disease. Computed tomography of the chest and abdomen showed extensive metastatic disease in the liver but no obstruction of the vena cava. Results from thoracocentesis performed at a local hospital interestingly demonstrated a borderline exudative process.

Cardiac tests were run concurrently. Electrocardiogram showed sinus rhythm with reduced anterior forces and nonspecific ST-T wave changes. Pharmacological stress testing showed no ischemia. Transthoracic echocardiography demonstrated preserved ejection fraction of 66% (left ventricular internal dimension at end-diastole 3.0 cm), normal pulmonary artery pressures, and no pericardial effusion. Importantly, there was an absence of valvular involvement (no classic "stubby" appearance of the tricuspid or pulmonic valves), making the hallmark type of carcinoid heart disease less likely. However, transthoracic echocardiography demonstrated plethoric inferior vena cava with diastolic dysfunction (mitral valve E/A ratio 1.6; deceleration time 148 ms) (Figure 1) and mitral annulus reversus (Figure 2). In conjunction with a thickened appearance of the pericardium on computed tomography (Figure 3) and only mild biatrial enlargement (left atrial volume index 35 ml/m^2) on transthoracic echocardiography, constriction seemed more likely than restrictive cardiomyopathy.

Subsequently, the patient underwent cardiac catheterization. Simultaneous right and left heart tracings showed elevated right-sided (right atrial pressure 15 mm Hg) and left-sided (pulmonary capillary wedge pressure 15 mm Hg) filling pressures, equalization of right and left ventricular end-diastolic pressures within 5 mm Hg, and discordance during the respiratory cycle consistent with constriction.

FIGURE 1 Pulsed Wave Doppler of the MV



E/A ratio of 1.6 and shortened deceleration time of 148 ms are suggestive of grade II diastolic dysfunction. MV = mitral valve.

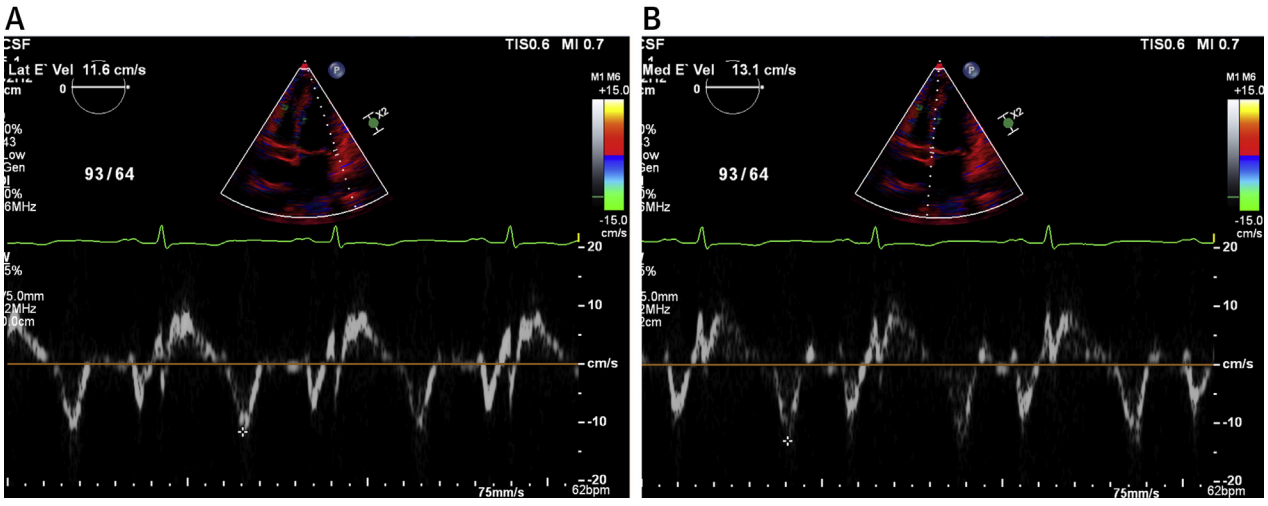
MANAGEMENT

A phrenic-to-phrenic pericardiectomy was performed via median sternotomy. Intraoperatively, extensive adhesions were encountered near the right atrium and taken down to reveal a 5- to 10-mm thickened pericardium. Gentle stripping of the pericardium allowed freeing of the anterior wall of the right and left ventricles, with resultant immediate improvement in systolic and diastolic function noted by echocardiography. Right-sided pleural empyema was also found and required decortication. Histology of the pericardium revealed dense thickened fibroconnective tissue with scattered lymphoplasmacytic chronic inflammatory infiltrate consistent with constrictive pericarditis. One focus of neoplastic cells was embedded within the adipose tissue (Figure 4A) and stained positive for synaptophysin (Figure 4B) and chromogranin A (Figure 4C), consistent with metastatic NET.

DISCUSSION

Well-differentiated NETs arising outside of the pancreas (carcinoid tumors) are rare and thought to originate most commonly from chromaffin cells in the intestinal tract or lungs (1,2). Symptoms of carcinoid syndrome are related to the release of peptides, which produce flushing, hypotension, bronchospasm, edema, and gastrointestinal hypermotility with

FIGURE 2 **Tissue Doppler Imaging**

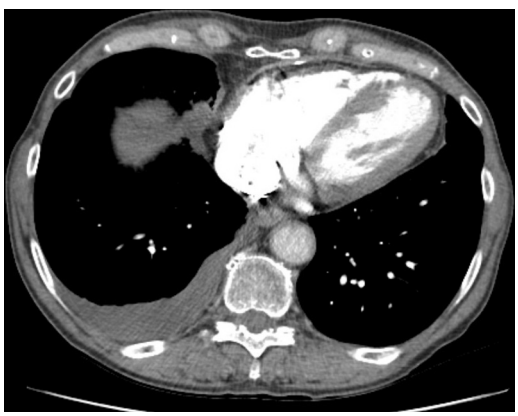


Mitral annulus reversus (lateral E′ velocity 11.6 cm/s **[left]** < medial E′ velocity 13.1 cm/s) **[right]**) is suggestive of constriction.

secretory diarrhea. Serotonin, one of the most common neuropeptides produced, is normally metabolized by monoamine oxidase in the liver and lung. However, high concentrations of serotonin can reach the heart if the serotonin bypasses the liver or is produced by the liver (i.e., hepatic metastases).

Carcinoid heart disease comprises a broad spectrum of cardiac manifestations in patients with carcinoid syndrome and may include valvular dysfunction, direct myocardial involvement, and less frequently, pericardial involvement (3). In the largest case series to date of 74 patients with carcinoid heart disease, 97% had the hallmark tricuspid valve thickening and dysfunction, 14% had pericardial effusion, and 4% had myocardial metastases (4). A smaller case series described 11 patients with pathological confirmation of metastatic carcinoid tumor involving the heart, but all of these tumors were well-circumscribed intramyocardial metastases (5).

FIGURE 3 **Computed Tomography Axial Slice**

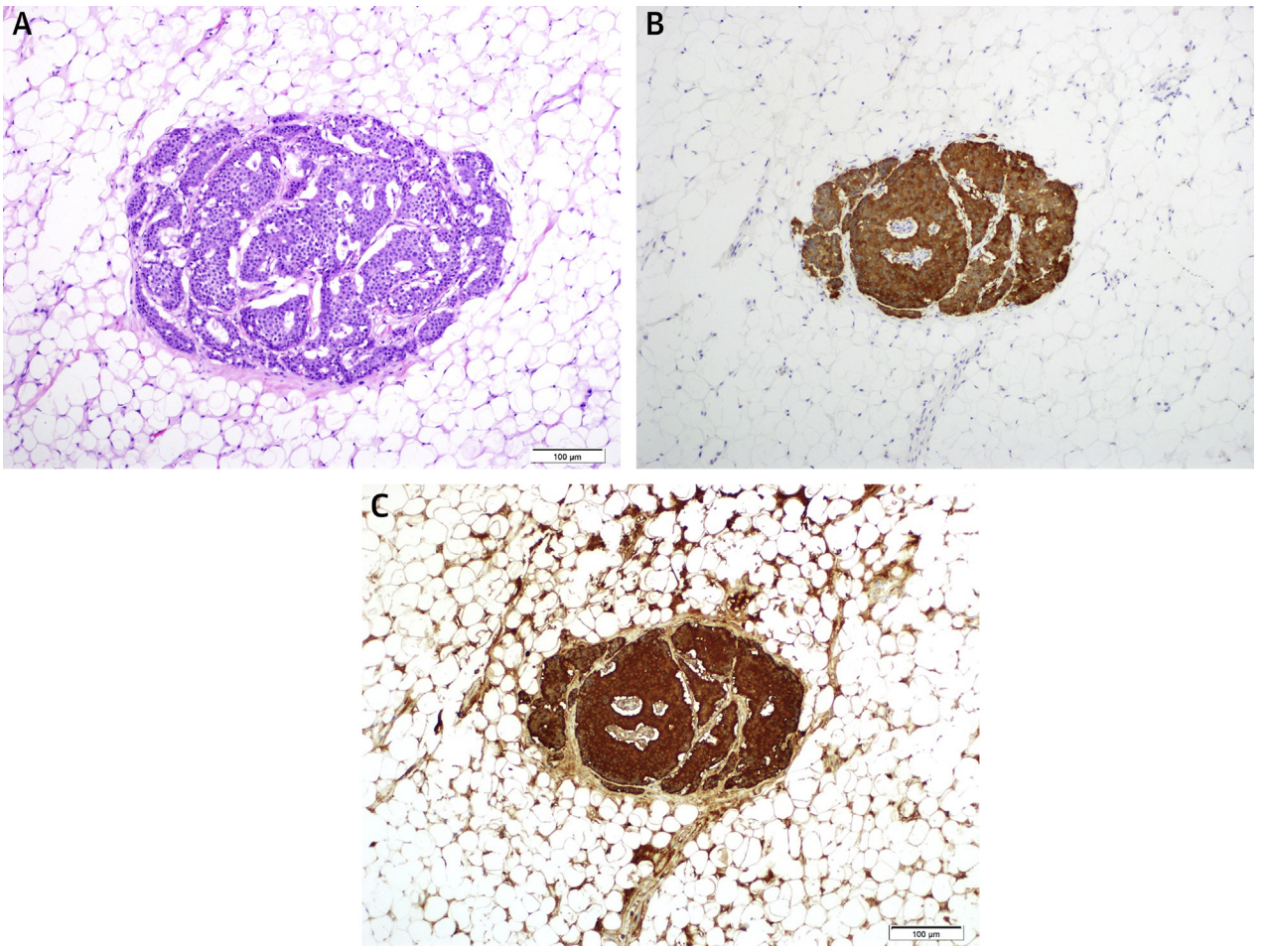


Thickened pericardium with calcifications in addition to right-sided pleural effusion.

Metastatic disease extending to the pericardium is uncommon. To our knowledge, only a handful of case reports in the literature have described direct pericardial invasion: a metastatic carcinoid tumor producing focal chronic pericarditis and fibrosis (6); a carcinoid tumor of the thymus leading to acute pericarditis (7); and a metastatic carcinoid mass entirely within the pericardial space without myocardial involvement (8).

Only 1 case of carcinoid constrictive pericarditis has been previously reported (9). We describe the second case of a unique presentation of constrictive pericarditis due to metastatic carcinoid disease in the absence of valvular involvement. Recurrent pleural effusions are an uncommon presentation of carcinoid heart disease, which classically presents with signs and symptoms of right heart failure. Interestingly, the presentation of right pleural effusion was unique to both case reports of constrictive pericarditis and possibly were the result of severe diastolic dysfunction leading to elevated pressures and subsequent

FIGURE 4 Histology of Pericardium



(A) Hematoxylin and eosin–stained section of pericardium showing a focus of neoplastic cells within adipose tissue. **(B)** Immunohistochemical stain showing neoplastic cells positive for synaptophysin. **(C)** Immunohistochemical stain showing neoplastic cells positive for chromogranin A.

unilateral pleural effusion. Alternatively, empyema in our patient may have resulted in chronic inflammation of the pericardium by extension that, combined with her carcinoid metastasis, contributed to a 2-hit hypothesis and led to her symptoms. Nevertheless, the use of multimodality imaging and invasive hemodynamic evaluation helped to clarify this atypical presentation and diagnostic dilemma.

FOLLOW-UP

The patient's post-operative course was unremarkable, and she had steady clinical improvement after the operation. By 2 months postoperatively, she was able to drive and perform activities of daily living without recurrent hospitalizations.

CONCLUSIONS

We report a rare case of constrictive pericarditis caused by metastatic carcinoid disease in the absence of valvular involvement and otherwise nonprogressive metastatic carcinoid tumor. This case provides useful insights into the spectrum of carcinoid pericardial disease and highlights the importance of pericardial stripping in the treatment of constrictive pericarditis.

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KEY WORDS cancer, constriction, diastolic heart failure, pleural effusion

APPENDIX For a supplemental figure, please see the online version of this paper.