CASE REPORT

A rare cause of constrictive pericarditis

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SUMMARY

A 67-year-old man presented with 3 months of exertional dyspnoea and 1 week of oedema. Examination revealed elevated neck veins, pulsus paradoxus, muffled heart sounds, decreased breath sounds and pedal oedema. Transthoracic echocardiogram (TTE) demonstrated cardiac tamponade, and chest X-ray showed pleural effusion. Pericardiocentesis, thoracocentesis, laboratory investigations and CT did not elucidate an underlying aetiology. Three weeks later, he presented with recurrent cardiac tamponade and pleural effusion. Pericardial window histology was benign. Pleural and pericardial fluids were again unrevealing. Three months later, he presented with worsening congestive heart failure. TTE, cardiac catheterisation and cardiac MRI were consistent with constrictive pericarditis. Preoperative workup did not identify an underlying cause. The patient underwent subtotal pericardiectomy. Intraoperative frozen section indicated malignancy. Pathology confirmed metastatic poorly differentiated signet ring adenocarcinoma of intestinal origin. He died 4 days postoperatively from multiorgan failure.

BACKGROUND

Constrictive pericarditis (CP) is characterised by encasement of the heart by a rigid non-pliable pericardium, resulting in symptoms and signs of heart failure. It most commonly occurs as a late sequela of pericardial inflammation caused by prior infections, radiation or cardiothoracic surgery. We present a case of recurrent cardiac tamponade with serially negative investigations that developed into CP, found to be secondary to occult gastrointestinal malignancy at pericardiectomy. This case highlights the challenges in diagnosing occult pericardial malignancy and the importance of clinical suspicion in recurrent pericardial disease of undetermined aetiology.

CASE PRESENTATION

A 67-year-old Caucasian man presented with 3 months of exertional dyspnoea and 1 week of pedal oedema. Medical history included gastro-oesophageal reflux disease, colonic tubular adenoma diagnosed 2 weeks prior to presentation and childhood tuberculosis. Examination was significant for elevated neck veins, muffled heart sounds, pulsus paradoxus, decreased breath sounds and pedal oedema. ECG showed normal sinus rhythm with decreased voltages, and chest X-ray (CXR) showed a small right pleural effusion. Transthoracic echocardiogram (TTE) revealed a large anterior pericardial effusion, with diastolic chamber collapse suggestive of tamponade (figure 1). Pericardiocentesis yielded exudative

pericardial fluid, negative for acid-fast bacilli (AFB), bacteria and malignant cells. A purified protein derivative (PPD) test was negative. CT chest, abdomen and pelvis following pericardiocentesis showed a 5 mm left apical calcified granuloma, scattered mediastinal and bilateral hilar calcifications and an anterior mediastinal soft tissue density thought likely to be postprocedural blood (figure 2). There were no CT findings of gastrointestinal malignancy.

Three weeks later, he presented with recurrent tamponade and right pleural effusion. Pericardial window and biopsy yielded bloody pericardial fluid with negative cultures and cytology. Histology showed benign fibroconnective and adipose tissue with negative AFB stain. A right thoracocentesis revealed transudative effusion with negative cytology and cultures. He was treated with colchicine for recurrent idiopathic pericardial effusion.

Three months later, he presented with 4.5 kg weight gain, dyspnoea, orthopnoea, chest pain on exertion, elevated JVP, bibasilar rales and 2+ pitting oedema. TTE revealed abnormal septal motion during diastole without significant pericardial effusion (figure 1). Cardiac catheterisation showed diastolic equalisation of pressures, decreased cardiac output and normal ejection fraction consistent with CP. Cardiac MRI showed diffuse pericardial thickening (figure 3), abnormal pericardial enhancement and impingement of the intraventricular septum into the left ventricle on inspiration, consistent with CP. There was interval decrease in conspicuity of the previously noted anterior mediastinal soft tissue density. A repeat right thoracocentesis was negative for infectious and malignant aetiologies.

TREATMENT

The patient underwent off-pump subtotal pericardiectomy. Intraoperatively, the mediastinum was frozen with a fibrotic process. Frozen section

Figure 1 (A) Initial TTE showing right ventricular diastolic collapse consistent with cardiac tamponade (arrows). (B) Subsequent TTE showing abnormal septal diastolic movement suggestive of CP (line arrows). Ao, Aorta; CP, constrictive pericarditis; LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle; TTE, transthoracic echocardiogram.

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Figure 2 CT chest. (A) Mediastinal soft tissue density (arrow). (B) Pericardial effusion (line arrow) and large right pleural effusion (**).

Figure 3 (A, B) Cardiac MRI. Pericardial thickening (arrows). (B) Pleural effusion (#).

indicated malignancy. Histopathology (figure 4) and immunohistochemistry showed a metastatic poorly differentiated adenocarcinoma with signet ring features consistent with intestinal origin.

OUTCOME AND FOLLOW-UP

Postoperatively, the patient became haemodynamically unstable, requiring invasive mechanical ventilation and vasopressors. He requested a transition to hospice care and died 4 days postoperatively from multiorgan failure.

DISCUSSION

Metastases reach the heart by direct, transvenous, haematogenous or lymphatic routes, the latter often in pericardial disease.¹ When symptomatic, they manifest as pericardial effusion or rarely CP. Autopsy studies show secondary cardiac tumours in 0.7–3.5% of the general population, 9.1% where a primary tumour is found and 14.2% with multiple metastases. This overestimates clinically significant disease, most cardiac metastases being asymptomatic.¹ Two-thirds of cardiac metastases involve the pericardium,² with aetiology: lung 40%; breast 22%; lymphoma and leukaemia 15%; gastric and colon 3%.³ Symptomatic pericardial effusion may be the initial presentation of malignancy in one-fifth of patients with negative clinical findings and simple laboratory tests.⁴ Malignancy rarely causes CP,⁵ with a 2–5% risk following acute neoplastic pericarditis.⁶ A 2011 review detailed only three cases of signet ring gastric adenocarcinoma with initial presentation as cardiac tamponade.⁷ We found no similar cases of colorectal adenocarcinoma, or any cases of CP as the primary presentation of GI malignancy in the English medical literature. These data highlight that although rare there should be a low index of suspicion for malignancy when faced with a negative work-up.

Clinically, malignant pericardial effusion may range from asymptomatic to tamponade. Beck's triad (hypotension, elevated veins and muffled heart sounds) is not as common as with non-malignant disease.⁵ ECG is non-specific, but large effusion can cause decreased voltages, and tamponade electrical alternans.⁶

Figure 4 (A) Low and (B) high magnification, showing signet cells with clear cytoplasm and peripherally displaced nuclei (arrows).

TTE is the initial investigation of choice and highly sensitive for diagnosing effusion. Tamponade, although a clinical diagnosis, has characteristic TTE findings including chamber collapse and respiratory variation in mitral valve inflow velocity.⁶ Detecting malignant aetiology by TTE is limited by the ability to distinguish tumours from other pericardial echodensities. Effusions may result in cardiomegaly on CXR; mediastinal widening, hilar masses or pleural effusion may suggest a malignant cause.⁶ CT or MRI should be considered when TTE is inconclusive, or when loculation, haemorrhage or pericardial thickening are suspected.⁶ Pericardial masses or irregularity, associated lung or mediastinal changes or CT attenuation of effusion greater than that of water suggest malignancy. Most tumours have low signal intensity on T-1 and high signal intensity of T-2 weighted MRI.⁸

CP is characterised by the encasement of the heart, with resultant diastolic dysfunction. Typical signs are those of congestive heart failure; elevated neck veins, oedema and hepatic congestion. More specific signs, Kussmaul's sign and pericardial knock are less frequent.⁹ CXR findings include pericardial calcification and pleural effusion.⁹ TTE may show suggestive findings including restrictive ventricular filling,^{6,9} however diagnosis is usually not possible by TTE alone. Cardiac haemodynamics include increased atrial pressure with sharp x and y descents, end-diastolic pressure equalisation and a dip and plateau morphology of ventricular diastolic pressure,^{6,9} which may be difficult to distinguish from restrictive cardiomyopathy. CT and MRI show characteristic morphological changes and pericardial thickening with greater sensitivity than echocardiography. CT is sensitive for pericardial calcification. MRI may depict anatomy, inflammation and functional changes^{8,9} and may be the best diagnostic test.

Table 1 Frequency, clinical features, diagnosis, treatment and outcomes

	Neoplastic pericardial effusion	Neoplastic CP
Frequency	<i>Autopsy</i> ⁵ <ul style="list-style-type: none"> ▶ 0.2–6%, death from all causes ▶ Up to 20%, patients with malignancy <i>Patients undergoing pericardiocentesis</i> <ul style="list-style-type: none"> ▶ Neoplastic aetiology in 9–39%⁶ ▶ Presentation of unknown cancer in 7.5%⁴ <i>Invasive procedure, known malignancy</i> ¹⁰ <ul style="list-style-type: none"> ▶ Tamponade in 46% 	<i>Incidence</i> 2–5% risk of CP following acute neoplastic pericarditis ⁶
Symptoms	<i>Autopsy proven pericardial malignancy</i> ¹⁰ <ul style="list-style-type: none"> ▶ Asymptomatic in up to 64% <i>Small symptomatic pericardial effusion</i> ¹⁰ <ul style="list-style-type: none"> ▶ Dyspnoea 73–93% ▶ Chest pain 61% ▶ Cough 30% <i>Invasive procedure, known malignancy</i> ¹⁰ <ul style="list-style-type: none"> ▶ Dyspnoea 81% ▶ Chest pain 20% 	<i>Symptoms include (not malignancy specific)</i> ⁹ <ul style="list-style-type: none"> ▶ Oedema ▶ Abdominal swelling/discomfort ▶ Dyspnoea ▶ Cough
Signs	<i>Invasive procedure, known malignancy</i> ¹⁰ <ul style="list-style-type: none"> ▶ Pulsus paradoxus 32% ▶ Reduced breath sounds 26% ▶ Tachycardia 22% ▶ Peripheral oedema 21% ▶ Elevated JVP 21% ▶ Hypotension 21% ▶ Pericardial rub 15% 	<i>Signs include (not malignancy specific)</i> ⁹ <ul style="list-style-type: none"> ▶ Elevated JVP 93% ▶ Peripheral oedema 76% ▶ Hepatomegaly 53% ▶ Pericardial knock/S3 47% ▶ Ascites 37% ▶ Pleural effusion 35% ▶ Kussmaul's sign 21% ▶ Pulsus paradoxus 19%
Pathological diagnosis	<i>Cytology</i> <ul style="list-style-type: none"> ▶ Sensitivity: 44–100%^{4 10–12} ▶ Specificity: 93.3–100%^{11 12} <i>Pericardial biopsy</i> <ul style="list-style-type: none"> ▶ Pericardiectomy has limited benefit over pericardiocentesis and extended drainage¹³ <i>Thoracotomy and open biopsy</i> <ul style="list-style-type: none"> ▶ Diagnosis in 90% with adequate sampling¹ 	
Treatment and outcomes	<i>Pericardiocentesis for malignancy-related pericardial effusion, all cancers</i> <ul style="list-style-type: none"> ▶ Mean survival 4 months⁴ <i>Poor prognostic factors</i> ¹⁰ <ul style="list-style-type: none"> ▶ Older ▶ Tumour burden/advanced stage ▶ Delayed diagnosis ▶ Recurrent effusion <i>Improved prognostic factors</i> ^{5 10} <ul style="list-style-type: none"> ▶ Breast, lymphoma ▶ Chemo-sensitive/radio-sensitive 	<i>Pericardiectomy</i> <ul style="list-style-type: none"> ▶ Data confounded by concomitant radiation therapy ▶ 10-year survival, neoplastic CP with history of radiation=30%±13%¹⁵

CP, constrictive pericarditis.

Definitive diagnosis of malignancy requires cytology or histology. Pericardiocentesis should be performed when there is suspicion for neoplastic effusion.⁶ Up to two-third of pericardial effusions in patients with malignancy are non-malignant.^{5 6} Bloody pericardial effusion is suggestive.⁶ Sensitivity of cytology is between 44% and 100%,^{4 10–12} due to variation in gold standard (biopsy, clinical follow-up or autopsy) and technical factors (fluid volume, number of pericardiocenteses and operator experience).⁴ Specificity of pericardial fluid cytology is between 93.3% and 100%.^{11 12} Pericardial fluid tumour markers including CEA and CA 19-9 lack sufficient accuracy for diagnosis.⁶ With negative fluid analysis, pericardial biopsy may be considered; pericardioscopy may improve diagnostic yield.⁶ Surgical pericardiectomy may not improve diagnostic accuracy over pericardiocentesis with extended drainage.¹³ When minimally invasive techniques are non-diagnostic, thoracotomy and open biopsy may be necessary; histological diagnosis is possible in 90% with adequate tissue sampling.¹ Diagnosis in our case was hampered by the frequency of non-malignant effusion and the broad range of sensitivities of pathological tests.

Tamponade requires emergent pericardiocentesis or surgical drainage. Treatment of large neoplastic pericardial effusions without tamponade should comprise when possible: systemic chemotherapy; pericardiocentesis to confirm aetiology and improve symptoms; prolonged pericardial drainage with tailored intrapericardial sclerosing or cytostatic agents to help prevent recurrence.⁶ Surgical pericardiectomy does not improve outcomes over pericardiocentesis with extended drainage and has more complications.¹³ Percutaneous balloon-pericardiectomy and pericardial window have a role in recurrent disease.¹³ Prognosis of malignancy-related pericardial effusion depends on age, disease burden, cancer type, chemo-sensitivity and radio-sensitivity.^{5 10} The mean survival in neoplastic pericarditis secondary to gastric carcinoma may be only 4.5 months.¹⁴

Definitive treatment of CP is pericardiectomy; however, palliative treatment of CP is often appropriate.⁶ Outcomes of pericardiectomy for neoplastic CP are confounded by grouping with post-radiotherapy patients in clinical studies.¹⁵ Predictors of overall survival postpericardiectomy include age, left ventricle function, prior radiotherapy, pulmonary artery pressure, serum sodium and creatinine.¹⁵

In summary, occult gastrointestinal malignancy may very rarely present as pericardial disease, its diagnosis may be challenging and outcomes are poor. One should maintain a high index of suspicion for pericardial malignancy when faced with a negative work-up. Frequencies, clinical features, diagnosis, treatment and outcomes are summarised in [table 1](#).

Learning points

- ▶ Occult GI malignancy may rarely present as pericardial disease.
- ▶ Diagnosis of malignancy which initially presents as pericardial disease is challenging due to its rarity, obscuration by more common diagnoses and diagnostic accuracy of available investigations.
- ▶ Tumour markers may be considered to help distinguish benign from malignant pericardial effusions; however, they lack sufficient accuracy to reliably do so.
- ▶ Malignant pericardial disease is associated with a poor prognosis.

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