CLINICAL VIGNETTE

Diagnosis and Management of Constrictive Pericarditis in an Otherwise Healthy 48-Year-Old Man

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Case Report

A 48-year-old male with no prior medical history was referred to cardiology for chronic relapsing dyspnea, decreased exercise tolerance, weight gain, and lower extremity edema. He reported atypical chest discomfort but denied fever, orthopnea, paroxysmal nocturnal dyspnea, palpitations, dizziness, or syncope. He did not smoke or drink alcohol. His family history was unremarkable.

Three months prior, he was diagnosed with a viral pneumonia and continued to have weight gain, decreased exercise tolerance, abdominal discomfort, and bilateral lower extremity edema. His evaluation was significant for elevated D-dimer to 756. Computed tomography angiography of the chest ruled out pulmonary embolism but showed pericardial thickening, right heart enlargement, and inferior vena cava dilatation. He was prescribed a course of anti-inflammatories and referred to cardiology.

Cardiology exam was significant for 17-pound weight gain, jugular venous distension, and 3+ lower extremity pitting edema. His EKG showed normal sinus rhythm with nonspecific ST changes. He underwent transthoracic echo which showed borderline left ventricular ejection fraction of 50%, septal bounce, and an elevated right-sided filling pressure. The patient was continued on non-steroidal anti-inflammatories (NSAIDs), and started on diuretics given fluid retention as well as Colchicine. He underwent cardiac magnetic resonance imaging (CMR), which showed low normal systolic function, restrictive physiology with septal bounce, and concentric pericardial thickening measuring up to 5 mm without myocardial enhancement to suggest scar or infiltrative disease. He was also evaluated by Rheumatology and Infectious Disease and diagnosed with constrictive pericarditis (CP) which may have been precipitated by the viral syndrome 3 months earlier. At follow-up visit, the patient felt better on his medical regimen, and he was less edematous. A referral to Cardiothoracic Surgery was discussed if CP persists.

Background and Etiology

Constrictive pericarditis (CP) is due to inelasticity of the pericardium and is associated with restrictive diastolic filling and diminished cardiac output. It is a complex, but potentially a treatable cause of heart failure.[1-3] The prevalence of CP is unknown, but its epidemiology has changed over the past century as the number of cardiac surgeries has increased.[1] The most common etiologies of CP in developed nations include idiopathic/viral and post-cardiac surgery, whereas the most common etiology in developing nations remains tuberculosis (TB).[1,2,4] The risk of idiopathic/viral pericarditis progressing to CP has been reported to be less than 1%, while the risk from TB pericarditis is 20-30%.[5,6] Other less common causes include, ionizing radiation, connective tissue disease, uremia, neoplasm, and purulent bacterial infection.[5] Transient CP that self-resolves or resolves with medical treatment has also been described and can arise from similar etiologies, but the natural history and incidence remain unclear.[3,7,8] The incidence is estimated to be 9-17% of CP, and symptom resolution is within 3 months.[8,9]

Pathophysiology

The normal pericardium is a thin fluid-filled sac that provides structure to prevent acute distension and optimize diastolic filling of the heart. In CP, inflammation and fibrosis stiffen the pericardium which becomes inelastic, leading to impaired compliance and filling.[1] More than 80% of CP patients have a thickened pericardium, although a normal pericardial thickness (</= 2mm) does not exclude the diagnosis.[10] The precise timing from injury to clinical presentation has not been elucidated, but ranges from days to years.[4] The pathophysiology of transient CP is similar with regards to inflammation and fibrin deposition, though it may represent an early manifestation that does not progress to irreversible fibrosis.[8]

Dissociation between intrathoracic and intracardiac pressures and ventricular interdependence are the hallmark hemodynamic principles of CP. With a non-compliant pericardium, a decrease in intrathoracic pressure during inspiration is transmitted to the pulmonary veins and extrapericardial vena cava, but not to the cardiac chambers. This results in a decrease in left ventricular filling pressures, allowing the interventricular septum to bounce towards the left ventricle during inspiration and towards the right ventricle during expiration. Left ventricular filling impairment leads to diminished stroke volume and cardiac output. Cardiac filling stops prematurely, leading to elevated venous pressure as well as signs and symptoms of congestion.[1,4,11-13]

Physical Exam

Presence of signs and symptoms of right-sided heart failure without valvular dysfunction, myocardial disease, or hypertension should prompt suspicion of CP.[1,4] Symptoms include fatigue, cough, dyspnea, lower extremity swelling, and abdominal discomfort. History may include prior cardiac surgery, TB, pericardial effusion, or antecedent viral illness. Physical exam findings include elevated jugular venous pressure, hepatosplenomegaly, ascites, and lower extremity edema.[12] Pericardial knock, Kussmaul's sign, and pulsus paradoxus are seen in up to 47%, 21%, and 19% of patients with CP respectively.[4]

Diagnosis

The diagnosis of CP can be challenging, particularly because it mimics other forms of heart failure. Lab findings such as transaminitis from hepatic congestion and elevated erythrocyte sedimentation rate secondary to inflammation can be seen.[12,14] Brain natriuretic peptide (BNP) levels are typically lower in idiopathic CP compared to those in restrictive cardiomyopathy or CP secondary to cardiac surgery or radiation therapy.[14]

Electrocardiographic findings are nonspecific, but atrial fibrillation, left-atrial enlargement, and low QRS voltage have been described.[4,12,14] In areas where TB is uncommon, pericardial calcification on chest x-ray has been noted in 27% of surgically-proven cases.[15] Transthoracic echocardiography (TTE), with or without a respirometer, is crucial to evaluate respiratory variation and ventricular interdependence. In one study, TTE was diagnostic in 70% of surgically confirmed cases.[1] The three most important TTE findings based on the Mayo Clinic TTE criteria include respiration-related septal shift, prominent hepatic vein expiration diastolic flow reversal, and preserved or increased medial mitral e' velocity.[8,11,16] Evidence of respiration-related shift in addition to either of the other two findings resulted in 87% sensitivity and 91% specificity for CP.[8,11]

Computed tomography (CT) can detect pericardial thickening and calcification or help with surgical planning, though it is not needed for diagnosis. CMR using gadolinium enhancement is a useful tool to evaluate pericardial inflammation which may be a marker for reversibility or transient CP, and can be used to guide treatment with anti-inflammatory medications.[1,9] CMR delayed enhancement and pericardial thickening > 3mm has been found to be 86% sensitive and 80% specific to identify transient CP.[8] In patients who have non-diagnostic imaging studies or complex hemodynamics, cardiac catheterization is indicated to aid diagnosis.[1,4] Pericardial biopsy and surgical exploration can be performed if the diagnosis is still uncertain.[1,4,13] In our case, both TTE and CMR demonstrated septal respiratory variation and elevated right-sided pressures, suggestive of CP. While CMR did not elucidate areas of active inflammation in the pericardium, it did show concentric pericardial thickening measuring up to 5 mm. Invasive hemodynamics were not required to make the diagnosis of CP.

Management

Pericardiectomy is the only definitive treatment for progressive CP.[4,7,12,17,18] Symptomatic treatment includes diuretics as needed. The typical approach for radical pericardiectomy is via median sternotomy to also excise the diaphragmatic pericardium and the pericardium surrounding the left phrenic nerve. An anterior phrenic-to-phrenic approach is easier, but is not recommended because it is associated with higher rates of repeat pericardiectomy and increased mortality (74% vs 84% survival).[2,4,17] Overall perioperative mortality is similar amongst different studies and ranges between 5-6%.[2] Seven-year survival after pericardiectomy is related to etiology, with idiopathic CP having a 7-year Kaplan-Meir survival rate of 88%, post-surgical with 66%, and post-radiation with 27%.[18] Early intervention is favorable to prevent later complications from congestive heart failure.

In patients with transient CP, pericardiectomy is not required and CP will resolve with an average 3-month course of medical management including NSAIDs, colchicine, or corticosteroids.[3,8] These patients tend to have elevated inflammatory markers and gadolinium enhancement on CMR. It is reasonable to do a trial of medical management prior to referral for pericardiectomy.[1] Further studies are needed to elucidate the appropriate length of medical management prior to pericardiectomy referral, and whether one class of medication is preferred over another. Our patient had elevated inflammatory markers including D-dimer, but did not have gadolinium enhancement on CMR. He experienced symptomatic improvement of his symptoms while taking NSAIDs, colchicine, and diuretics. Given lack of complete resolution of his symptoms, a referral to a cardiothoracic surgeon was offered. The patient was hesitant to consider surgical options, and for now, he elected to continue on medical therapy with close follow-up.

Conclusion

CP can be challenging to diagnose, but is potentially curable by surgical pericardiectomy. CP should be considered for patients who have clinical signs and symptoms of right-sided heart failure and a history of pericardial inflammation, cardiac surgery, radiation, or TB. A thorough examination and TTE that shows dissociation between intrathoracic and intracardiac pressures and ventricular interdependence can establish the diagnosis without the need for invasive hemodynamics. Gadolinium enhancement on CMR and increased inflammatory markers can predict transient CP, which may self-resolve or be medically treated with anti-inflammatory therapy. A trial of medical treatment is reasonable prior to surgical referral, but the only definitive treatment remains pericardiectomy if CP persists.

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