Residents' Clinic

71-Year-Old Man With Syncope and Chronic Leg Edema

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A 71-year-old man was transferred to our institution for evaluation of a syncopal event. He had had light-headedness without dyspnea, palpitations, nausea, vomiting, sweating, or chest pain, which caused him to fall and sustain minor lacerations on the left side of his forehead and upper lip. He was reportedly unconscious for less than 1 minute, and the paramedic crew found him alert and oriented, without complaints of shortness of breath or chest pain. The systolic blood pressure was 60 to 70 mm Hg, the heart rate was about 50 beats/min, and a cardiac rhythm strip showed normal sinus rhythm. Tests done in the local emergency department included roentgenography of the cervical spine and computed tomography (CT) of the abdomen, both of which revealed normal findings. Despite vigorous hydration with intravenously administered fluids (3 L), dopamine (3 µg/kg per min), and atropine (1 mg), hypotension and bradycardia persisted and prompted transfer of the patient to our institution.

The past medical history of the patient disclosed that he had undergone coronary artery bypass grafting because of angina 14 years before the current admission, and he had not experienced angina pectoris subsequently. He had one documented, symptomatic episode of atrial fibrillation with rapid ventricular response that had necessitated electrocardioversion 3 years earlier. No documented history of sick sinus syndrome was noted. The patient had also had a near-syncopal episode of unclear cause approximately half a year before the current admission and bilateral lower extremity edema for several months, which had been unresponsive to oral diuretic therapy and for which the patient had recently increased the dose of his diuretics on his own initiative. His admission medications (all administered orally) were quinidine (324 mg three times daily), spironolactone (50 mg twice daily), furosemide (40 mg twice daily), aspirin (325 mg daily), and potassium chloride (10 mEq twice daily).

On admission, the patient had a blood pressure of 75/47 mm Hg. Because of the already low blood pressure, orthostatic pressure was not assessed. The patient was alert, oriented, and afebrile and had a heart rate of 97 beats/min and a regular cardiac rhythm. The clinical examination revealed no acute distress, plethora of the face in conjunction with distended neck veins, clear lung fields on auscultation, no cardiac murmurs, gallops, rubs, or knocks, warm extremities, and minimal pedal edema bilaterally. The initial laboratory studies (3.5 hours after the event) showed the following: creatine kinase 61 U/L (normal range, 52 to 336), serum sodium 130 mEq/L, potassium 4.1 mEq/L, magnesium 1.8 mg/dL, creatinine 2.1 mg/dL, urea 78 mg/dL, hemoglobin 12.7 g/dL, leukocytes 12.5 X 10^9/L, platelets 153 X 10^9/L, arterial oxygen and carbon dioxide tensions of 76 and 36 mm Hg, respectively, pH 7.36, and oxygen saturation of 93% with the patient breathing room air. A chest roentgenogram showed cardiomegaly, poststemotomy changes, and clear lung fields with no obvious pericardial calcifications, pleural effusions, or left atrial enlargement. An electrocardiogram revealed normal sinus rhythm, prolonged QT interval (528 ms), preterminal T-wave inversions in leads V 3 through V 6, nonspecific ST- and T-wave abnormalities in leads II, III, and aVF, and substantial Q waves in leads V 4 and V 5.

An emergent echocardiogram showed small left and right ventricles and no left ventricular hypertrophy, pericardial effusion, or regional wall motion abnormalities. The patient was maintained on dopamine at 7 µg/kg per min and intravenous infusion of NaCl, and he was admitted to the coronary-care unit. Because of persistent hypotension, a pulmonary artery flotation catheter (Swan-Ganz catheter) was inserted. It showed a prominent x and y descent along with a right atrial pressure of 24 mm Hg, a right pulmonary artery end-diastolic pressure of 22 to 25 mm Hg, and a pulmonary artery wedge pressure of 24 mm Hg.

1. Which one of the following diagnoses is most likely in view of the available information on admission?
   a. Acute pulmonary embolus
   b. Acute myocardial infarction of right side of heart
   c. Cardiac tamponade
   d. Constrictive pericarditis
   e. Congestive heart failure

The initial clinical findings of syncope and treatment-resistant hypotension in our patient make pulmonary embolus a diagnostic possibility. They suggest a massive...
pulmonary embolus (more than 50% obstruction of the pulmonary vascular bed). Because of the absence of severe hypoxemia (age-adjusted oxygen tension predicted to 75 mm Hg versus the measured value of 76 mm Hg) and tachypnea (note that respiratory alkalosis was not present), however, this diagnosis is unlikely.

Right ventricular myocardial infarction can manifest with unexplained hypotension, clear lung fields on the examination as well as on a chest roentgenogram, and increased central venous pressure. Nevertheless, the absence of anginal symptoms and of ST-segment elevation or ST-segment depression in electrocardiographic leads V1 and V2, normal creatine kinase values on two occasions, lack of response to adequate volume loading and pressors (dopamine), and absence of regional wall motion abnormalities on echocardiography oppose the diagnosis of right ventricular infarction.

Cardiac tamponade is classically characterized by the constellation of clinical signs described by Beck1 in 1935—low arterial blood pressure, increased systemic venous pressure, and distant heart sounds. In our patient, this diagnosis was considered early on because of the increased central venous pressure (plethora of the head), hypotension, and chest roentgenographic evidence of cardiomegaly. The absence of pericardial effusion on echocardiography effectively excluded this diagnosis. The patient's history and the equalization of right- and left-sided diastolic filling pressures noted on the readings obtained from the Swan-Ganz catheter, together with the signs of increased systemic venous pressure, strongly suggested the diagnosis of constrictive pericarditis. The patient denied having dyspnea at rest or with exertion or orthopnea that would have suggested congestive heart failure; absence of a third or fourth heart sound was corroborating evidence against this diagnosis.

2. In light of the foregoing diagnostic possibilities, which one of the following physical signs is least likely in this patient?

a. Jugular venous distention
b. Kussmaul's sign
c. Pulsus paradoxus
d. Peripheral edema
e. Pulmonary edema

Limitation of systemic venous inflow into the right cardiac chambers by circumscribed expansion of the pericardium leads to prominent jugular venous distention or even venous plethora of the face and head, as seen in this patient. Absence of an inspiratory decrease in jugular venous pressure (Kussmaul's sign)—due to a nondistensible pericardial sac—is a classic physical finding in constrictive pericarditis and would be expected in this patient with facial plethora, prior cardiac operation, and suspected constrictive pericarditis. Pulsus paradoxus is defined as a decline in systolic blood pressure of at least 10 mm Hg during inspiration with the patient in the supine position. This finding results from the inspiratory decrease in left ventricular filling caused by dominant filling of the right side of the heart (during inspiration) because of increased negative intrathoracic pressure. The space in the pericardial sac is limited by the constrictive process, which causes preferential filling of the right heart chambers at the expense of the left heart chambers and leads to a decreased left-sided cardiac output during inspiration.

Peripheral edema, ascites, and enlargement of the liver are prominent findings in constrictive pericarditis attributed to substantially increased systemic venous pressure. Peripheral edema was one of our patient's complaints and therefore an expected finding. Pulmonary edema is not a common finding in pure constrictive pericarditis and, if present, should direct investigations toward another diagnosis. Pulmonary edema was not noted on the chest roentgenogram, and the increased pulmonary capillary wedge pressure was probably related to high filling pressures and redistribution of pulmonary flow without frank pulmonary edema.

3. Which one of the following tests is least likely to help in confirming the clinically suspected diagnosis?

a. Chest roentgenography
b. Echocardiography
c. Computed tomography of chest
d. Magnetic resonance imaging (MRI) of chest
e. Electrocardiography

Chest roentgenography can be helpful in diagnosing constrictive pericarditis if pericardial calcification is present in a setting of a hemodynamically documented constrictive or restrictive physiologic process. Conversely, the presence of pericardial calcifications on chest roentgenography does not alone prove the diagnosis of constrictive pericarditis.2 Echocardiography has emerged as a useful procedure in the diagnosis of suspected constrictive pericarditis. The respiratory variations on Doppler velocimetry and two-dimensional echocardiography associated with the characteristic anatomic and physiologic abnormalities in constrictive pericarditis help distinguish this condition from the clinically and oftentimes hemodynamically indistinguishable restrictive cardiomyopathy.3 Reperformance of transthoracic echocardiography and respirometry with Doppler flow analysis in our patient confirmed the previous echocardiographic findings. Because of prior cardiac surgical intervention and resultant postoperative mediastinal changes, Doppler flow analysis was possible only from the mitral inflow. It did, however, demonstrate an inspiratory decrease and expiratory increase in flow across the mitral valve, findings that supported a diagnosis of constrictive pericarditis. These reciprocal changes (so-called ventricular interdependence) do not occur in restrictive cardiomyopathy. In a
setting of appropriate hemodynamic documentation of constrictive or restrictive physiologic findings, evidence of a thickened pericardium on chest CT or MRI is confirmatory of constrictive pericarditis. No specific electrocardiographic changes are suggestive of constrictive pericarditis or restrictive cardiomyopathy. In our patient, CT of the chest (Fig. 1) showed thickening and calcification of the pericardium, most prominently over the inferior surface of the heart, on the left side, and at the apex.

4. Which one of the following is the most likely cause of our patient’s condition?
   a. Viral infection
   b. Bacterial infection
   c. Tuberculosis
   d. Neoplasm
   e. Previous cardiac surgical procedure

Viral and bacterial infections may cause pericarditis and constriction; however, because of our patient’s history and the absence of a prior severe systemic illness or fever, infectious causes seem highly unlikely. The availability of antituberculous drugs and effective public health surveillance have decreased the incidence of tuberculous pericarditis in industrialized nations. Complications of tuberculous pericarditis include constrictive pericarditis. The chest roentgenogram and chest CT failed to show a pneumonic process, and our patient denied having any previous exposure to tuberculosis or episodes of night sweats, sputum production, hemoptysis, and weight loss; hence, the diagnosis of tuberculosis is unlikely. A neoplasm is also unlikely in our patient, who had no associated weight loss or cachexia, no history of tobacco use, and no endobronchial lesions on CT. The most likely cause of constrictive pericarditis in our patient was a previous cardiac surgical procedure. Postoperative constrictive pericarditis reportedly occurs in 0.2% of patients and can be seen immediately or after a delay of weeks, months, or years.

The patient was stabilized by fluid resuscitation and discontinuation of all diuretic therapy. His blood pressure increased, and administration of dopamine was subsequently stopped. He continued to do well, and after stabilization in the coronary-care unit, he was transferred to a regular ward. The diagnosis of constrictive pericarditis was confirmed, and therapeutic options were discussed with the patient.

5. Which one of the following therapeutic measures is most appropriate in our patient?
   a. Pericardiectomy
   b. Nonsteroidal anti-inflammatory drugs
   c. Antibiotics
   d. Corticosteroids
   e. No treatment

Patients with constrictive pericarditis usually require thoracotomy and pericardiectomy to relieve their symptoms. Nonsteroidal anti-inflammatory drugs, antibiotics, and corticosteroids are inappropriate therapy in this patient because he had no evidence of infectious, autoimmune, or inflammatory conditions and had an extremely thickened and substantially calcified pericardium. Providing no treatment would be inappropriate; the noncompliant pericardium would not resolve spontaneously, and chronic debilitating symptoms due to increased venous pressures would be highly likely.

A surgical opinion was sought for our patient; however, because of unforeseen complications during his hospital stay—namely, bleeding from a gastric ulcer and right upper extremity phlebitis at a previous intravenous site—full surgical assessment was delayed pending resolution of these problems. The patient was stabilized medically and dismissed; later, he underwent follow-up as an outpatient. Subsequently, pericardiectomy was done. At postoperative follow-up 2 months later, the patient still felt fatigued and had occasional chest discomfort, but he had no further ankle swelling, hypotension, syncope, or presyncope.

DISCUSSION

The initial symptoms of constrictive pericarditis include dyspnea, peripheral edema, and ascites. Syncope, as described in our patient, is an uncommon initial feature. The differential diagnosis includes right ventricular infarction, pulmonary embolus, cardiac tamponade, and restrictive cardiomyopathy, conditions that may be separated from constrictive pericarditis by distinguishing features in the history, on physical examination, and from common diagnostic tests. Most likely, despite increased venous and pulmonary pressures in our patient, the use of orally administered loop
diuretics resulted in lowered circulatory blood volume and postural changes in cardiac output and blood pressure. The most important diagnostic challenge in constrictive pericarditis (once this frequently overlooked diagnosis is considered) is distinguishing it from restrictive cardiomyopathy. Treatment of constrictive pericarditis—that is, pericardectomy—can be curative, whereas treatment of restrictive cardiomyopathy has limited results. After a thorough history, physical examination, chest roentgenography, and electrocardiography, diagnostic studies often include echocardiography, CT, cardiac catheterization, and, occasionally, endomyocardial biopsy. Even then, the diagnosis may remain uncertain, and surgical exploration may be necessary.

Echocardiography is frequently the initial diagnostic test used in assessment of patients with dyspnea, peripheral edema, jugular venous distention, or abnormal findings on cardiac auscultation. Findings on echocardiography that support the diagnosis of constrictive pericarditis as opposed to restrictive cardiomyopathy are characteristic variations in mitral and tricuspid Doppler flow patterns during respiration that are absent in restrictive cardiomyopathy. These changes include a decrease in mitral inflow early-filling velocity during inspiration in comparison with expiration and a compensatory increase in tricuspid inflow velocity during inspiration. These changes are due to the altered relationship between intrathoracic and intracardiac pressures as a result of “isolation” of the heart by a fibrous or thickened pericardium; therefore, intrathoracic respiratory pressure changes are not transmitted to the cardiac chambers. Because similar Doppler findings may be noted in patients with severe chronic obstructive pulmonary disease or mechanical ventilation, further diagnostic studies may be needed to confirm the diagnosis of pericardial constriction. Important secondary causes of restrictive cardiomyopathy include amyloidosis, eosinophilic endomyocardial disease (Löffler's syndrome), hemochromatosis, and myocardial sarcoidosis (usually in the setting of systemic sarcoidosis).

Both CT and MRI have recently emerged as helpful non-invasive procedures for diagnosing constrictive pericarditis and for distinguishing it from restrictive cardiomyopathy. Weaknesses in MRI are its inability to distinguish calcification from fibrosis and its variable image quality in comparison with conventional and especially electron beam CT—particularly with frequent ectopic beats, as in our patient. Constrictive pericarditis is an elusive disease, and delayed diagnosis is common. Frequent causes of pericarditis, which may or may not lead to hemodynamically significant constriction, include previous cardiac operation, prior chest irradiation, infection, myocardial infarction, neoplasms, or unknown factors. Other causes include blunt trauma, sarcoidosis, Wegener's granulomatosis, and mediastinal fibrosis. The most likely cause of constrictive pericarditis in our patient was a prior cardiac operation; pericarditis may have resulted from a combination of trauma and irritation of the pericardial layers with inflammation, adhesion, fibrosis, and pericardial constriction, with or without effusion. No apparent factors indicate in which patients constrictive pericarditis will develop after a cardiac operation. Patients with postpericardectomy syndrome or severe mediastinal bleeding postoperatively, however, are at increased risk. Constrictive pericarditis must be considered in the differential diagnosis in a patient with unexplained dyspnea who has previously undergone a cardiac operation.

Treatment of constrictive pericarditis varies and is influenced by the clinical response. Medical therapy involves diuretics, corticosteroids, nonsteroidal anti-inflammatory drugs, and antimicrobial agents, singly or in combination, depending on the suspected cause. Constrictive pericarditis may be transient and may not need surgical intervention. Surgical management of pericardial disease and issues such as timing of operation, type of incision, need for bypass, and extent of pericardial resection remain controversial. Preoperative disability seems to be the major indication for pericardectomies performed for constrictive pericarditis and is also the main factor that influences operative mortality.

REFERENCES
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13. Correct answers: 1. d, 2. e, 3. e, 4. e, 5. a