Constrictive Pericarditis as a Long-term Undetermined Etiology of Ascites and Edema

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Abstract:
Constrictive pericarditis (CP) is defined as impedance to diastolic filling caused by a fibrotic pericardium. The diagnosis of CP is a clinical challenge and requires a high index of clinical suspicion. The signs and symptoms of CP include fatigue, edema, ascites, and liver dysfunction. These can be mistakenly diagnosed as primary liver disease. We present the case of a 69-year-old woman with a 7-year history of leg edema and a 2-year history of ascites who was initially diagnosed with cryptogenic liver cirrhosis and was finally diagnosed with CP.

Key words: ascites, constrictive pericarditis

Case Report

A 69-year-old Japanese woman with a history of atrial fibrillation presented to our hospital with a 7-year history of intermittent leg edema and 2-year history of ascites. She began to experience fatigue, exertional dyspnea, and leg edema 7 years prior to her admission; these were improved by diuresis with azosemide. However, 2 years prior to her admission, she had recurrent leg edema and abdominal distention. Ascites was found by the primary care physician and she was referred to a tertiary care center. Various tests, including blood tests, echocardiography, and chest and abdominal CT scans, were performed. However, no specific etiology was determined, even after consulting with various subspecialists, including a cardiologist, nephrologist, gastroenterologist, and gynecologist. Her serum brain natriuretic peptide (BNP) level was checked several times, and it remained between approximately 120 and 180 pg/ml. She had received care from a gastroenterologist, who made a presumptive diagnosis of cryptogenic cirrhotic ascites. To obtain a second opinion, she visited our outpatient clinic. She did not have any other medical history.

A physical examination revealed that her blood pressure was 101/72 mmHg and her pulse rate was 53/minute. She
had a normal respiratory rate and temperature. Jugular venous distention (JVD), which was elevated to the edge of the submandibular bone on sitting in the upright position, was noted; her estimated jugular venous pressure was 20 cm. Her JVD became more engorged on inspiration and lessened on expiration (Kussmaul’s sign). Her heart sounds were irregular. Severe pitting edema in the bilateral legs and abdominal distension were noted. Blood test results indicated a normal blood cell count. A liver function test revealed normal aspartate transaminase (AST), normal alanine transaminase (ALT), elevated alkaline phosphatase (436 IU/L), and elevated gamma-glutamyl transferase (235 IU/L). Her serum creatinine level was 0.81 mg/dL. Her BNP level was 188.2 pg/ml. A chest x-ray film showed dullness in the costophrenic angle bilaterally, which was consistent with bilateral pleural effusion. Electrocardiography revealed a heart rate of 70 beats/minute, atrial fibrillation, and no ST-T change.

Echocardiography showed marked biatrial enlargement, a thickened posterior pericardium, respiration-related ventricular septal shift, shortening of the deceleration time of the E wave in mitral inflow (90.2 ms), normal early diastolic velocity of the mitral annulus (E’) (septal, 12.7 cm/second; lateral, 10.2 cm/second) by tissue Doppler wave form (Fig. 1), normal E/E’ (6.2), and normal left ventricular ejection fraction (LVEF) (67%). A careful examination revealed that the mitral inflow velocity decreased on the first beat of inspiration and increased on the first beat after expiration; contrary to this, tricuspid inflow velocity had the opposite changes. CP was suspected based on these suggestive findings (4-6). Subsequently, a computed tomography (CT) scan of the chest showed the marked thickening of the pericardium (Fig. 2). Cardiac catheterization revealed a diastolic dip and plateau pattern in the left ventricular (LV) and right ventricular (RV) pressure traces (Fig. 3A, B), elevation and equalization of the end-diastolic pressure of the right and left heart, the mean right atrial pressure and the mean pulmonary artery wedge pressure (28, 29, 26, and 28 mmHg, respectively). Reciprocal respiratory variation in the RV/LV peak systolic pressure was also noted (Fig. 3C). She was diagnosed with CP and pericardiectomy was successfully performed. The operative findings included severe restricted posterior motion, thickened pericardium adhering to heart, posterior pericardium that was even thicker than the other part of pericardium, and no calcification of the pericardium. The pathology of the pericardium revealed fibrotic thickening and chronic lymphoplasmacytic inflammation, but no specific cause was found. Thereafter, her fatigue, exertional dyspnea, ascites, JVD, and Kussmaul’s sign resolved, even after the discontinuation of diuretics. At three years after the operation, she is still doing well.
Discussion

The diagnosis of CP requires a high degree of clinical suspicion because the signs and symptoms of this disease can be falsely attributed to other causes. The common manifestations, in cases of severe CP, include ascites (37%), hepatomegaly (53%), pleural effusion (35%), and peripheral edema (76%) (3). These often lead to the misdiagnosis of chronic liver disease (7). The median duration of symptoms before pericardiectomy was 11.7 months (range, 3 days to 29.1 years) (3). In a study of 218 patients with ascites, the reported causes were cirrhosis (n=162, 74%), heart failure (n =44, 20%), peritoneal disease (n=10, 5%), and constrictive pericarditis (n=2, <1%) patients (8). Although CP is not common, we should be aware of this condition when the etiology of ascites is not disclosed.

For patients with cirrhosis due to other causes, the jugular venous pressure is generally normal or quite decreased (with the exception of patients with tense ascites) in patients with CP, and their elevated jugular venous pressure is often found to be elevated (93%) (3). Normally, inspiration decreases the intrathoracic pressure, which is transmitted to the heart with a resultant respiratory drop in JVD. Because of the impaired filling of the right heart, patients with CP lack this drop and even the JVD increases during inspiration (Kussmaul’s sign) (1). Although this sign was noted in 13-21% of patients with CP (3, 9), it is not specific for CP and may also occur in any condition associated with elevated right-side pressure, such as tricuspid stenosis, RV infarction, and restrictive cardiomyopathy (1). The presence of JVD and Kussmaul’s sign should lead physicians to investigate these cardiac conditions.

Transthoracic echocardiography is an essential diagnostic test for patients being evaluated for CP. It typically shows pericardial thickening (4). Enhanced interventricular interaction and dissociation between intrathoracic and intracardiac pressure are pathophysiological findings in cases of CP (1). These are manifested by the abrupt displacement of the interventricular septum in early diastole with inspiration (septal shudder and bounce), a maximal significant decline in the mitral E flow immediately after inspiration, and a maximal significant decline in the tricuspid E flow immediately after expiration along with hepatic vein reversal (4, 10, 11). These findings were shown to be sensitive and specific to CP (4); however, echocardiography must be performed very carefully with a high index of suspicion for CP. These findings were also significantly associated with CP in the subset of patients with atrial fibrillation (4). Atrial enlargement may be seen, especially in patients with long-standing constrictive physiology (10). The early diastolic Doppler tissue velocity at the mitral annulus (E’) is usually reduced with diastolic dysfunction and increased filling pressures. Because transmural inflow early velocity (E) increases progressively with higher filling pressures, E/E’ has been shown to have a strong positive relationship with the pulmonary capillary wedge pressure (PCWP) and LV end-diastolic pressure. However, in many patients with CP, E’ is prominent despite diastolic dysfunction because the longitudinal movement of the wall is increased (4, 6, 10). As a result, the usually positive linear relation between E/E’ is reversed in patients with CP (6). When an enlarged atrium is found with normal E’ and E/E’, like in our case, CP should be considered.

BNP is primarily stored in the ventricular myocardium and is released when the ventricular diastolic pressure increases and the wall stretches. The degree of plasma BNP elevation in CP should be much less in comparison to other types of cardiomyopathy because the wall stretch is limited.

Figure 3. A) A right ventricular (RV) pressure trace. B) A left ventricular (LV) pressure trace. C) A simultaneous RV and LV pressure trace. The dip and plateau pattern or square root sign was observed in the RV pressure (A) and LV pressure (B) traces. The diastolic pressures in both ventricles were equal (A) (B) (C). The height of the LV rapid filling wave (LVRFW) (up-down arrow) was 9 mmHg (B). A simultaneous RV and LV pressure trace showed ventricular discordance; the peak LV systolic pressure (solid line) was reduced with the corresponding increase in the peak RV pressure (dotted line) during inspiration (C).
by the thickened stiff pericardium. In one study, the mean serum BNP level of CP patients was 128.0 pg/mL (standard deviation, 52.7 pg/mL; range, 88-186 pg/mL) (12). Although normal E/E’ and LVEF values on echocardiography and a lower BNP level-as was observed in our case-are consistent with CP, patients with these signs may be misdiagnosed as having a normal heart function.

In normal individuals, the ventricular diastolic pressures vary independently and remain unaffected by the ventricle (13). Because of the stiff pericardium, which equally limits the expansion of all chambers, the elevation (approximately 20 mmHg) and equalization (within 5 mmHg) of the diastolic pressures at approximately 20 mmHg in all chambers is noted in patients with CP. An early marked diastolic dip followed by a plateau (dip and plateau sign or square root sign) are often noted in both the RV and LV pressure traces. Early diastolic filling of the ventricles is increased, which is represented by a deep rapid filling wave (RFW). An LV RFW of >7 mmHg is reported to show 93% sensitivity and 57% specificity in the diagnosis of CP (13). The RV systolic pressure is elevated but limited to <50 mmHg (13). The RV diastolic pressure is usually elevated to more than one-third of the RV systolic pressure (13). Because of the exaggerated ventricular interdependence, increased RV filling during inspiration shifts the septum toward the left ventricle, leading to decreased LV filling. As a result, the peak systolic pressures of the RV and LV show discordant changes during each respiratory phase (13, 14). All of these hemodynamic features were observed in our patient (Fig. 3A-C).

The possible causes of ascites in this case include increased pressure in the hepatic veins with resultant portal hypertension and veins draining the peritoneum as well as liver cirrhosis due to prolonged cardiac hepatopathy (15). In cases of ascites due to heart failure without cirrhosis, the serum albumin level is generally normal; an ascites analysis demonstrates a serum ascites albumin gradient (SAAG) of ≥1.1 g/dL and an ascites protein level of ≥2.5 mg/dL, with 63% sensitivity and 93% specificity (8). It has been reported that in cases of liver cirrhosis, although the SAAG is ≥1.1 g/dL, the ascites protein level is <2.5 mg/dL in 87% of cases (8). In our patient, the serum albumin level was normal and the results of a coagulation panel were within normal limits; thus, there was no evidence of liver cirrhosis. The patient had never experienced abdominal paracentesis. Soon after surgical treatment, her ascites diminished without diuretics, suggesting that the ascites was more likely related to associated with heart failure due to CP than liver cirrhosis.

Although idiopathic pericarditis is the most common (known) antecedent cause of CP, the most common type is CP with no recognized antecedent (1). Other possible etiologies includes infection (virus, bacteria, tuberculosis, etc.), connective tissue disease, neoplasm, trauma, postcardiac surgical procedures, radiation therapy, end-stage renal disease, and cardiac pacemaker insertion (1). Our patient did not have any recognized history of pericarditis. Considering that her condition improved after surgery, malignancy or active tuberculosis was unlikely. She did not show any signs and symptoms of connective tissue disease. With regard to the possible etiology of CP, a pathological examination of the surgical specimen only revealed non-specific inflammation and fibrosis, which was suggestive of idiopathic pericarditis.

In the present case, although the patient had been evaluated by a cardiologist, the patient had been experiencing symptoms of CP for years before a correct diagnosis was made. However, when JVD elevation is detected and a patient is positive for Kussmaul’s sign, a careful evaluation with echocardiography based on the suspicion of CP can help to prevent a misdiagnosis. Physicians should be aware of this condition when they encounter patients with chronic edema, ascites, or liver dysfunction of unknown etiology and should evaluate the jugular vein and echocardiography results with a high index of suspicion for CP.

The authors state that they have no Conflict of Interest (COI).

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