Stripping off the pericardium: Cures the liver and the kidneys and dries up the ascites

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Case history

A 62 year-old Caucasian male, with past medical history of coronary heart disease, type-2 diabetes mellitus, obstructive sleep apnea, and hyperlipidemia, admitted to the hospital with an episode of hypoglycemia and unresponsiveness. He was diagnosed in the past by his gastro-enterologist as having "liver disease", the nature of which was not clear. His physical examination showed that he was well nourished man with regular heart rate, no edema or jugular venous distension but his serum creatinine was 1.9 mg/dl and had un-quantifiable proteinuria in his urine analysis which initiate a nephrology consultation. He returned to the nephrology clinic after discharge from the hospital on 12/15/16 with increasing serum creatinine from 1.9 to 2.5 mg/dl and an estimated GFR of 30 ml/min. During this encounter he denies any nausea, vomiting, diarrhea, or use of non-steroidal anti-inflammatory medications (NSAID). In the interim, he stated that he had paracentesis of 17 liters on 12/07/16 for his ascites.

On his follow up visit on 1/31/17 his examination was unremarkable and his serum creatinine had gone down to 1.9 mg/dl. During this time he was diagnosed with liver cirrhosis but had no liver biopsy or more detailed information about the diagnosis. His hepatitis serology was negative and liver function test were within normal range. He returned to the nephrology clinic on 3/8/17 with increasing serum creatinine to 3.82mg/dl and blood urea nitrogen (BUN) increasing from 37 to 73 mg/dl. He had a transthoracic echocardiogram which showed left ventricular dysfunction.

The patient returned to the nephrology clinic once again on the 3/17/17, with stable serum creatinine of 3.8 and BUN of 79 mg/dl. But this time he had fluid overloaded with increased edema of the lower extremities and tense ascites. He stated that he had been scheduled for paracentesis and cardiac catheterization on 3/29/17.

On the next visit on 4/24/17, his eGFR had gone down and was classified to CKD stage-4. During this visit he was diagnosed with chronic constrictive pericarditis (CP) on cardiac catheterization. His edema had been controlled with medications, and paracentesis. He was scheduled to have pericardiectomy in the following few days. His serum creatinine had gone up to 4.4 mg/dl. He continued to have paracentesis and hemodialysis to control his edema and renal function. His last paracentesis was on 5/8/17 with 10.7 L removed.

On 5/17 he had surgery on the pericardium with chest tube insertion x 3. During this hospital admission and following surgical procedure his heart function, renal function, and urine output had improved. He was taken off hemodialysis and his final serum creatinine was 1.53 mg/dl before discharge. He had a total of 4 cardiac catheterizations and the diagnosis of CP was clenched on the 3rd catheterization. He had

multiple paracentesis with total fluid loss of 111 Lb. and total fluid removal by paracentesis of 21.6 L.

Discussion of the case

This case illustrated the importance of vanishing arts of clinical history, examination, and analytical data interpretation. The patient presented with edema, ascites, fluid overload, normal hepatitis serology and liver function, and progressive increase in blood urea nitrogen (BUN) and creatinine. He underwent a total of 4 cardiac catheterization before the final clinical diagnosis is attained. The sensitivity of transthoracic echocardiography (TTE) is not high (40%) compared with the trans-esophageal (TEE) for the diagnosis of valvular diseases, diseases of the myocardium, and pericardium linings [1].

Serology for hepatitis B and C were negative as other liver function tests. A diagnosis of cirrhosis without liver biopsy was given because of ascites. Considerations of pre-hepatic, hepatic and post-hepatic causes of ascites were not analyzed in the context of patient's history and clinical examinations. As a matter of fact very often CP is misdiagnosed as cirrhosis because of hepatomegaly and ascites. On the other hand ultra-sound examination of the abdomen in this case revealed no splenomegaly, evidence of fibrosis, or obstruction to the portal or hepatic veins. I am not sure if portal vein and hepatic venous pressures and their variation with respiration were measured during this encounter. The patient was treated symptomatically with diuretics, paracentesis, and eventually hemodialysis to control ascites, peripheral edema, and deteriorated kidney function.

The case is also unique as it presented with increasing BUN and creatinine in the absence of significant proteinuria, making intrinsic renal disease unlikely. The ultra-sound of the kidneys excluded obstruction of the genitourinary tract making pre-renal diseases with congestive nephropathy a more likely scenario. One wonders why cardiac catheterization were performed in more than 3 occasions to achieve the diagnosis. I do not know whether the intra-cardiac pressures were measured in the first 2 catheterizations or not.

On 5/12/16 both right and left cardiac catheterization was done which showed no coronary artery disease or evidence of CP. His

transthoracic echocardiogram was also normal with ejection fraction of 60% which is very commonly encountered in CP.

If we trace his serum creatinine as far back as 1/27/14 and 6/26/15 (1.0 and 0.84 mg/dl, respectively), one would find that his serum creatinine were normal to start with and progressively getting worse up until his recent admission and the time of surgery after which relief of congestion and improvement of kidney function began to appear, (Table 1).

Constrictive pericarditis is a scaring process which causes loss of normal elasticity of the pericardial sac. It is typically chronic disease which impedes cardiac filling by the external forces. In the most severe form of CP the pericardium becomes almost inelastic which compromises volume changes during respiration.

In normal situation the normal pericardium does not interfere with the decrease in intra-thoracic pressure during inspiration which leads to increase in venous return to the right side of the heart. This increase in venous return to the right side of the heart does not impair left ventricular filling.

However, in CP cardiac volume is constrained which prevents normal inspiratory decrease in intra-thoracic pressure from being transmitted to the heart chambers. Pulmonary venous pressure decrease during inspiration, however, left ventricular pressure does not. This divergences will results in decreased left ventricular volume as a results of a decrease in trans-pulmonary gradient. These pathophysiological abnormalities lead to shifting of interventricular septum to the left during expansion of the right ventricle further compromising left ventricular end-diastolic volume. In severe CP the ventricular filling occurs in early diastole with little or no filling subsequently. As CP becomes more severe the ventricular volumes and stroke volumes are reduced [2,3].

The etiology of CP are identified in case series reported by previous workers [4-9].

- Idiopathic or viral   42-61%
- Post-radiation   20-31%
- Connective tissue disorders   3-7%
- Post-cardiac surgery   11-37%
- Post-infectious   3-15%
- Miscellaneous causes (malignancy, Trauma, drug induced, asbestosis, Sarcoidosis, uremic pericarditis)   up to 10%

Table 1. Time-line for serum creatinine.

Date	5/11/16	12/25/16	1/31/17	3/8/17	3/17/17	4/24/17	5/22/17	7/8/17
Serum creatinine in mg/dl	1.38	2.5	1.9	3.82	3.8	4.4	2.41	1.8

Table 2. Differences between constrictive pericarditis and restrictive cardiomyopathy.

Characteristics	CP	RCMP
History - Prior pericarditis - Cardiac surgery - Irradiation - DM, amyloidosis, sarcoidosis	Yes Yes Yes No	No No No/Yes Yes
Physical examination - JVP - Pericardial knock - S3	more common Yes No	Yes No Yes
ECG findings - BBB - Ventricular hypertrophy - Pathological Q wave - impaired atrio-ventricular conduction	No No No No	Yes Yes Yes Yes
B-type BNP	Usually in normal range	Usually raised
CXR - Calcification - cardiomegaly	Yes No	No Yes
Imaging (Doppler, echo, CT, CMR) - increased thickens of pericardium or calcification - Thick ventricular wall or septum - MR or TR	Yes No No	No Yes Yes
Doppler - Respiratory variation in ventricular filling velocity - Hepatic venous flow reversal - Diastolic MR	High usually in 30-40% Expiratory No	Minimal <10% Inspiratory Yes
Tissue Doppler imaging - Early diastolic Doppler tissue velocity @M annulus (E') - Doppler myocardial velocity gradient @ LVW in early diastole and during ventricular ejection	Increased >12 cm/sec Comparable to normal	Decreased to <8cm/sec Significantly lower
Cardiac catheterization - Right and left ventricular end-diastolic pressure (RVEDP & LVEDP)	Equal or near equal	LVEDP>RVEDP
Biopsy - Endomyocardium or less commonly pericardium	May be helpful	May be helpful
CP- constrictive pericarditis, RCMP- restrictive cardiomyopathy		

Orthotopic heart transplant and tuberculous pericarditis have been associated with high incidence of CP (49%) in developing world [10,11]. IgG4 diseases and Whipple's disease have also been incriminated in cases of CP [12,13].

The clinical presentation of CP are protean, and includes volume overload manifested as peripheral edema, ascites and anasraca, low cardiac output with exertional dyspnea, fatigability and signs of heart failure or symptoms of cardiac tamponed.

On physical examination, patients with CP often exhibit raised jugular venous pressure (JVP), pulsus paradoxus [4,14], Kussmaul's signs [8,9], a pericardial knock [8], edema, ascites, pulsatile liver, and cachexia. JVP is reported in 93% of cases of CP [8]. Unexplained raised JVP in patients with predisposing conditions like malignancy, irradiation, or pervious cardiac surgery should alert the physician to the presence of CP.

Evaluation of CP should include chest x-ray which might show calcification. Echocardiography both 2-D and M-mode which can be done as transthoracic or trans-esophageal echocardiography (TTE or TEE). The TEE is more sensitive [1-3,15-20]. CT and cardiac magnetic resonance (CMR) are very sensitive modalities for detection of pericardial thickening and calcification in CP [3,15] [21-24]. Hemodynamic evaluation during cardiac catheterization are sometimes needed to confirm the diagnosis of CP [2,3,15,25].

Plasma BNP are elevated in cardiomyopathy and left ventricular dysfunction but less so in CP. The differential diagnoses of CP includes cardiac tamponade, restrictive cardiomyopathy, and cirrhosis. Table 2 showed the difference between CP and restrictive cardiomyopathy.

Acute kidney injury (AKI) is rare manifestation of CP. The pathophysiology is probably linked to congestive nephropathy with high renal vein pressure and little in the way of proteinuria as illustrated in this case. The high pressures in the renal veins are transmitted back to the glomeruli with decrease in the glomerular filtration rate. Once the pressure is relieved by pericardiectomy the renal function usually reverted to normal.

The treatment of CP is pericardiectomy [26-29]. Striping of as much as possible of the pericardium is advisable to have the gratifying effects of surgery especially if surgery is carried out early in the disease process. In many instants relief of ascites, peripheral edema and congestive hepatopathy and nephropathy would ensue more quickly.

The take home message in this case is never abandoned good clinical history, physical examination looking for signs of CP especially raised JVP, pulsatile liver, and ascites. The art of history taking and physical examination together with analytical interpretation of the data will sharpen our clinical acumen and in most cases would lead you to the correct diagnosis.

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