Diagnostic problems of right-sided heart failure patient with cardiomyopathy cirrhosis

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Abstract

Heart failure may cause liver damage, known as cardiomyopathy cirrhosis. Conversely, liver disease could also lead to heart failure and cardiovascular abnormalities. Cirrhotic cardiomyopathy is a relatively rare disease. Diagnosis should be found out as early as possible to prevent complications. Unfortunately, epidemiology data of cirrhotic cardiomyopathy is still limited, and the prevalence is still not precisely known. Hence, we reported a case of a young man with the main problem of right-sided heart failure and suspected cardiac cirrhosis with unclear manifestation. This case has a good outcome so that we hope this report could give a great reference on treating cardiomyopathy cirrhosis.

Keywords: *Cardiomyopathy cirrhosis, Male, Heart failure, Pulmonary hypertension*

Introduction

Heart failure may cause liver damage, known as cardiomyopathy cirrhosis. Conversely, liver disease also can lead to heart failure and cardiovascular abnormalities. We found a very rare case in a young adult man that comes to our hospital with an unclear manifestation of right-sided heart failure.

Currently, cirrhotic cardiomyopathy is not widely recognized and is often misdiagnosed as alcoholic cardiomyopathy. This disorder is often neglected despite the changes found in cirrhotic cardiomyopathy. Overt heart failure is not a common feature of cirrhotic cardiomyopathy because hyperdynamic circulation coexists with peripheral vasodilatation, significantly reducing ventricular afterload. Epidemiology data of cirrhotic cardiomyopathy is still limited, and the prevalence is still not precisely known. Diagnosis is often difficult as the cardiac function at rest approaches normal function. Most patients are diagnosed in a decompensated phase of cirrhosis, with the presence of diastolic heart failure and/or high-output heart failure.¹⁻⁴

Hence, we reported a case of a young man with the main problem of right-sided heart failure and suspected coincidence with cardiomyopathy cirrhosis.

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Case Report

A 29-year-old male reported shortness of breath for the last six months and has worsened in the past two days. A dry cough accompanied this shortness of breath. He had to use two or more pillows while he slept. On physical examination, there was swelling on both legs, icteric sclera, ascites, and signs of cirrhosis. Table 1 shows the patient's laboratory results during patient care and follow-up. In summary, we found elevated liver function test on his laboratory results and cardiac enlargement represented of mitral heart disease on his chest X-ray shown in Figure 1.

Table 1. Patient's Laboratory Results

Parameters	Result	Normal Range
Complete Blood		
Count		
Leukocyte	5.4×10^3	$4.5 - 11 \times 10^3$
Erythrocyte	4.3×10^6	$4.2 - 5.4 \times 10^6$
Hemoglobin	13.5	12-16
Hematocrit	38.3	38-47
MCV	89	79-99
MCH	31	33-37
MCHC	35	33-37
Thrombocyte	21×10^3	$150 - 440 \times 10^3$
Liver Function Test		
SGOT	60 (on the day of admission) 368 (7 days after admission)	8-38 (IU/L)
SGPT	47 (on the day of admission) 352 (7 days after admission)	10-35 (IU/L)
Albumin	2.8	>3.5 mg/dL
Direct bilirubin	4.10	0.1-0.3
Indirect bilirubin	1.25	0.1-1.0
Renal function Test		
Blood urea nitrogen (BUN)	34	10-50
Creatinine	1.2	0.8-1.3
Virus Marker		
HbsAg	Reactive	Non Reactive

Figure 1. Chest X-ray showed the sign of cardiomegaly and mitral heart disease

An electrocardiogram showed inverted T waves in lead III, aVF, V4, V5, V6 (Figure 2). Echocardiography examination was done, and we found right-sided heart failure with pulmonary arterial hypertension (Figure 3). Hepatitis virus marker test showed positivity for HbsAg (Table 1).

Figure 2. ECG showed inverted T waves in lead III, aVF, V4, V5, V6

Figure 3. Patient's echocardiography, showing signs of right-sided heart failure and Pulmonary Arterial Hypertension

Based on anamnesis, physical examination, and further diagnostic examination, we suggested a diagnosis of right-sided heart failure with the suspicion of cirrhosis cardiomyopathy with hypoalbuminemia, pre-renal acute kidney failure, hepatic cirrhosis, and general weakness.

We suspected two coincidences between liver function disorders (hepatic cirrhosis) and right-sided heart failure, so we did additional examination such as echocardiography in our diagnostic plan (see discussion below).

Treatment of the underlying disease is essential in managing patients. Jaundice and ascites usually respond well to a diuretic. If the heart failure is successfully treated, early histologic changes in cirrhotic cardiomyopathy can be resolved, and even cardiac fibrosis may be clinically and histologically regress. Once the patient is stable, beta-blockers and ACE inhibitors can be given if the heart failure begins with the left ventricle. Spironolactone can be provided if a patient is classified in NYHA class III or IV. Currently, there are no specific studies on the management of cirrhotic cardiomyopathy. The management practice, in this case, was intended to treat cardiac dysfunction and hepatic cirrhosis.

We gave pharmacologic therapy including infusion of 0.9% saline:aminoleban 1:1 intravenous 20 drops per minutes (DPM), dopamine drip 3µg (1 ampule of dopamine in 500ml of 0.9% saline with a rate of 25 ml/h), furosemide drip 3mg/h, beraprost sodium (prostacyclin synthetic analog) 20mg twice daily, spironolactone 25mg once daily, digoxin 0.25mg once daily, tenofovir 300mg once daily, fondaparinux (low molecular weight heparin) 5mg once daily, and oral supplementation of albumin. We also provided education to the patient and his family that the patient's condition needed to be handled thoroughly by specialist doctors, especially internists.

Discussion

Cardiomyopathy cirrhosis is defined as cardiac dysfunction in patients with cirrhosis, characterized by impaired contractile responsiveness to stress and/or altered diastolic relaxation, with electrophysiological abnormalities, in the absence of other known cardiac disorders.¹⁻³

Cirrhotic cardiomyopathy is defined as the presence of the signs of portal hypertension or the results of congestive heart failure. In chronic congestion, sustained hypoxia inhibits hepatocellular regeneration and causes fibrotic tissue formation, leading to cardiac cirrhosis. Heart failure is a multisystem disorder in which there is

impairment of skeletal muscles and renal function, sympathetic nervous system stimulation, and complex neurohormonal changes.⁵⁻⁸ As the theory mentioned above, the patient has fulfilled the criteria of cirrhotic condition and congestive condition. Based on theory, we must see the relationship between the two requirements below.

In cirrhotic cardiomyopathy, there is primary diastolic dysfunction with left ventricular hypertrophy, left atrial enlargement, prolonged isovolumic relaxation time (IVRT), and decreased early to late diastolic flow ratio. At rest, the systolic function is normal, and in stress conditions, there is systolic dysfunction due to disturbed inotropic and chronotropic responses.^{4,9}

Right ventricular and pulmonary artery pressure, pulmonary capillary wedge pressure (PCWP) is slightly increased. Increased cardiac output and intravascular plasma volume cause volume overload in the myocardium, causing myocardial hypertrophy. Cardiac dysfunction at rest is not evident because of the decreased left ventricular afterload caused by peripheral vasodilatation. The pathogenesis of cirrhotic cardiomyopathy is not fully understood. Interaction between various factors plays a role in causing this disorder.^{6,10}

Table 2. *Diagnosis Criteria of Cirrhotic Cardiomyopathy*⁷

Name Of Criteria	Parameter
Systolic Dysfunction	A marked elevation of Cardiac Output, volume changes or pharmacologic changes, or reduced ejection fraction below 55%
Diastolic Dysfunction	E/A ratio under 1.0 Increased deceleration time Prolonged isovolumetric relaxation time
Supportive Criteria	Electrophysiological abnormalities Abnormal chronotropic response Prolonged Q-Tc interval Left atrial enlargement Elevated mass of myocardial Elevated BNP and pro-BNP level Elevated troponin I

The sympathetic nervous system mainly regulates the contraction of cardiac muscle via the β -adrenergic (β -AR) receptor. β agonists bind to β_1 and β_2 , then activate adenylyl cyclase through G (Gs) protein stimulation. This results in the production of cyclic adenosine

monophosphate (cAMP) from adenosine triphosphate (ATP). In cAMP, protein kinase A (PKA) undergoes phosphorylation into several substrates, including calcium release receptors found in the sarcoplasmic reticulum. Gs protein also directly activates sarcolemma L-type calcium channels. This causes an influx of calcium into the cardiomyocyte cytosol, causing actin binding to myosin myofibrils and resulting in cellular contraction.¹⁰⁻¹²

We compared the diagnostic criteria of cirrhotic heart disease from Table 2 to our patient's presentation. The ejection fraction of our patient did not fulfill the criteria of cirrhotic cardiomyopathy, but other echocardiography parameters such as prolonged isovolumetric contraction time and increased LV volume were fulfilled. We decided to continue to focus our treatment for cirrhotic cardiomyopathy, even though not all criteria of cirrhotic cardiomyopathy were satisfied.

Animal studies regarding cirrhotic cardiomyopathy have resulted in a subnormal response of left ventricular contractility to sympathetic stimulation. It is discovered that the density of β -AR, Gs protein, and adenylyl cyclase activity was decreased. They lead to a reduced cAMP formation. Membrane fluidity also changes due to the changes in lipid composition in the cardiomyocyte plasma membrane. It blocks the function of membrane binding receptors such as β -AR. In addition, there were also abnormalities of transduction signal due to overexpression of several protein inhibitor genes and decreased expression of adenylyl cyclase genes. All of these factors harm the cardiomyocyte contractility.¹²

Cannabinoid subtype-1 (CB-1) receptor in cardiomyocytes has a negative inotropic effect by activating G inhibitor (Gi) protein. Gi protein inhibits adenylyl cyclase activity, decreasing cAMP production, resulting in decreased calcium influx to the cardiomyocyte cytosol. In the study of rat cardiac muscle, there was a weak contraction in response to isoproterenol, and it is improved by administration of CB-1 receptor antagonist. Nitric oxide (NO) and carbon monoxide (CO) negatively affect the contractility of cardiomyocytes. In the patient with hepatic cirrhosis, NO and CO level is elevated due to increased synthesis of inducible NO (iNO) and heme oxygenase activity.¹²

Cardiac abnormalities with mild or moderate left ventricular failure could have similar characteristics with cirrhotic cardiomyopathy. Patients with hepatic cirrhosis can also coexist with primary heart diseases such as ischemic heart disease, hypertension, cardiomyopathy, or alcoholic cardiotoxicity. It remains unclear whether the patient with hepatic cirrhosis is protected from coronary atherosclerosis. Some pieces of evidence suggest that hepatic cirrhosis patients may develop severe coronary artery disease. In western

countries where alcohol is the leading cause of hepatic cirrhosis, alcohol can induce or worsen heart disease in two ways. First, excessive and long-term alcohol consumption is directly cardiotoxic. Second, hypertension becomes more severe or uncontrolled in an alcoholic person. A detailed history of alcohol consumption and careful examination about the presence of hypertension signs such as retinal vascular changes and diagnostic tests such as exercise stress electrocardiography, nuclear cardiac scan, and coronary angiography may be helpful to distinguish these disorders from cirrhotic cardiomyopathy.¹¹⁻¹²

Most cases of cirrhotic cardiomyopathy are clinically insignificant and asymptomatic. This led to little interest in studying the treatment of cirrhotic cardiomyopathy. When heart failure clinically occurs due to any form of stress, management follows the guidelines of a non-cirrhotic patient. In the late stage of cirrhosis, there is an overactivity of the renin-angiotensin-aldosterone system. In a study about the role of angiotensin II in regulating renal sodium retention in pre-ascites cirrhosis. Low dose losartan (7.5mg) has a natriuretic effect without negative effects on the kidney and systemic hemodynamics. However, long-term administration of these drugs does not reduce portal pressure.¹³ Conversely, higher doses of losartan or irbesartan decrease the portal venous pressure gradient but with negative circulatory effects, especially severe hypotension in hepatic cirrhosis patients with pre-ascites or ascites.¹²

Captopril, an angiotensin-converting enzyme inhibitor, can suppress hyperaldosteronism without impairing renal function. It was reported that after oral captopril administration in cirrhotic patients with ascites, there were no changes in cardiac output and renal blood flow, but mean arterial pressure, renal and systemic vascular resistance decreased significantly. They concluded that captopril caused hypotension due to increased renal vasodilation.¹⁴ Administration of low dose captopril to prevent changes in arterial pressure in cirrhotic patients with or without ascites. There was a decrease in renal filtration rate and urinary sodium excretion followed by local inhibition of angiotensin II.¹⁵ Transplantation is the curative therapy of hepatic cirrhosis patients and its complications. Successful liver transplantation is thought to improve all the organ-related hemodynamic dysfunctions, including hepatopulmonary syndrome, cerebral hypoperfusion, hepatorenal syndrome, and cirrhotic cardiomyopathy.¹²

The patient also showed signs of right-sided heart failure in our study, with significant pulmonary hypertension on echocardiography. Therefore, patient management was focused on treating each disorder; by giving diuretics, prostacyclin analog,

potassium blocking diuretics, and anti-hypertension like ACE inhibitor and treating the cirrhosis itself by anti-viral, good nutrition, and symptomatic treatment. During follow-up, the patient has improved and was discharged from the hospital.

Conclusion

Treatment of underlying disease is essential for patient management. In this case, the management of the patient was tended to treat right-sided heart failure and hepatic cirrhosis simultaneously. As a result, an excellent clinical response was obtained, and periodic monitoring was required.

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