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Liver-Kidney-Heart Axis – A Clinical Challenge

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Abstract

Background: *Cirrhosis is a chronic disease with multiple etiologies, multiple manifestations, and multi-organ involvement. It affects about 200 million people worldwide and its main complication is portal hypertension (PHT). Cirrhotic cardiomyopathy is a consequence of PHT, with heart failure (HF) being the main manifestation. On the other hand, for people with cardiopathy due to reasons beyond cirrhosis, the presence of the last could act as a trigger to acute HF. Finally, when HF and cirrhosis coexist, the renal system suffers the most, originating from type 5 cardiorenal syndrome, a complex entity with many challenges in diagnosis and treatment. This entity was recently defined and there is a lack of data on the epidemiology of this syndrome.*

Case Description: *A 77-year-old woman, with cardiovascular risk factors; heart failure with reduced ejection fraction (HFrEF), secondary ischemic and valvular cardiopathy, chronic kidney disease (CKD), and stable decompensated cirrhosis, went to the emergency department after progressive abdominal perimeter augmentation, leg edema, and hematochezia. It was assumed acute decompensated cirrhosis and acute decompensated CKD, had triggered digestive bleeding and the patient stayed hospitalized. Intravenous diuretic therapy was started but the ascites and kidney function got worse, the NT-proBNP grew until 1125000 pg/ml and transthoracic echocardiography showed important signs of congestion, isolated right ventricular dysfunction, with normal cardiac output. After teamwork's discussion, a type 5 cardiorenal syndrome was assumed deciding not to act on tricuspid regurgitation due to the maladaptive RV remodeling. Hepatorenal syndrome (HRS) treatment was begun (oral terlipressin and intravenous albumin), followed by decongestion therapy, resulting in a marked improvement in clinical presentation. The kidney, heart, and liver recovered to these basal states.*

Conclusion: *With this clinical case, the authors want to show how multidisciplinary management is important to face tricuspid regurgitation and right ventricular dysfunction.*

Keywords: type 5 cardiorenal syndrome, heart failure, cirrhosis, liver-kidney-heart axis

Abbreviations: PHT: portal hypertension; HF: heart failure; HFrEF: heart failure with reduced ejection fraction; CKD: chronic kidney disease; HRS: hepatorenal syndrome; LV: left ventricle; PM: pacemaker; CRT: cardiac resynchronization therapy; SBP: spontaneous bacterial peritonitis; SAAG: serum ascites albumin gradient

Introduction

The different organs and systems of the human body uniquely interact to maintain homeostasis. When one of them works badly, it creates a syndrome. Sometimes it is difficult to understand where the problem began.

Cirrhosis is a chronic disease with multiple etiologies, multiple manifestations, and multi-organ involvement. Portal hypertension (PHT) is the main complication of cirrhosis, and it is the main reason for the systemic manifestations of cirrhosis, independently of the etiology.

Cirrhotic cardiomyopathy is a consequence of PHT, a recent syndrome, only recognized in 2005, with a lack of epidemiological studies [1]. The manifestations of cirrhotic cardiomyopathy can be systolic heart failure (HF), diastolic dysfunction, or/and electrophysiological abnormalities. It is an exclusion diagnosis of HF [1–3] and it is a consequence of hyperdynamic circulation of the splanchnic system with increased cardiac output, reduced systemic vascular resistance, and activation of renin-angiotensin-aldosterone and arginine-vasopressin systems. In systolic dysfunction, despite the high cardiac output, the heart is unable to meet its demands to generate adequate arterial blood pressure and cardiac output to vascularize the organs [1, 2]. In diastolic HF, because of hyperdynamic circulation, the myocardium stays hypertrophic and fibrotic, increasing stiffness and impairs relaxation. These mechanisms contribute to liver decompensation because of congestive hepatopathy [1, 2]. On the other hand, one person can have cardiopathy for multiple reasons, and at the same time have cirrhosis, where the decompensation of one of them can trigger a decompensation of another [4]. When there is HF and decompensated cirrhosis, the renal system is the most affected. Because of this relationship, it is increasingly accepted that hepatorenal syndrome (HRS) is the consequence of the cardiorenal link in cirrhosis, also named type 5 cardiorenal syndrome. The hemodynamic changes that happen in the liver-heart axis explained before, proceed to renal hypoperfusion and renal venous congestion [3, 5–8].

The management of the liver-kidney-heart axis is a big and complex challenge. On one hand, we want to diminish the congestion with diuretics; on the other hand, diuretics aggravate kidney perfusion. It will limit the introduction of different drugs with prognostic value on cirrhosis and HF. The administration of vasoconstrictors like terlipressin and albumin ameliorated the kidney achievement. As a consequence, drugs with prognostic value can be restarted [2, 7, 8].

With the clinical case presented in the next words, the authors want to show the degree of complexity of one patient and the importance of teamwork to better medical treatment.

Case Description

We presented a 77-year-old woman with cardiovascular risk factors: hypertension, dyslipidemia, and obesity. Associated heart failure with reduced ejection fraction (HFrEF), secondary ischemic and valvular cardiopathy: acute myocardial infarction in 2001, complicated with left ventricle (LV) pseudoaneurysm that needed Chirurgie correction and consequently a metal mitral valve substitution. She was accompanied in cardiology consultations, and throughout the years, the patient developed a slow ventricular response atrial failure, with a pacemaker (PM) needed in 2012, and an upgrade to cardiac resynchronization therapy (CRT) in 2021. The last echocardiography in 2022 showed non-dilated left and right ventricles with reduced ejection fraction (LVEF) of 36% and normal function mitral valve prosthesis regurgitation with severe tricuspid regurgitation.

Other personal problems are chronic kidney disease (CKD), with a basal creatinine of 2 mg/dL and glomerular filtration rate of 22 ml/min/1.73 m^2 since 2016, and stable decompensated cirrhosis (some digestive bleeding by gastroduodenal varices in the past) secondary to primary biliary cirrhosis since 2021. She also has mild pancytopenia and mild hypoalbuminemia.

In July of 2023, the patient went to the emergency department after progressive abdominal perimeter augmentation, leg edema, and hematochezia. The workup showed stable anemia (10 g/dL), but worsening of kidney function, with 2.5 mg/dL of creatinine. The diagnosis paracentesis excluded spontaneous bacterial peritonitis (SBP), the serum ascites albumin gradient (SAAG) was 1.1 g/dL, and abdominal eco-Doppler excluded portal thrombosis. The NT-proBNP was 45000 pg/mL, being the basal value for this patient.

Assumed acute decompensated cirrhosis and acute decompensated CKD, having triggered digestive bleeding, and the patient stayed hospitalized.

In the first week, the patient had no other digestive bleeding and started intravenous diuretic therapy. However, the ascites got worse, with signs of tension ascites, and she presented the workup shown in the table below (Table 1).

		Normal value
NT-proBNP (pg/mL)	112500	[50–450]
Serum creatinine (mg/dL)	3.6	0.5-1.1
Hemoglobin (g/dL)	10	12–16
Transthoracic echocardiography	LVEF 30%; normal mitral prosthesis gradient; moderated reduced RVEF; severe tricuspid regurgitation; pulmonary artery systolic pressure 60 mmHg; fixed and dilated inferior vena cava; inverted flow of suprahepatic veins	_____

Table 1: Workup of the patient.

With these findings, cardiogenic shock was suspected by internal medicine, requesting the help of a multidisciplinary team. Low cardiac output (2.3 l/min/1.73 m^2) was discarded, and the patient was consequently treated suspecting HRS. The steps were evacuated paracentesis, oral terlipressin, and intravenous albumin.

Two days later, the creatinine reduced by about 25% of the last value, allowing to start the diuretic treatment.

Fourteen days after the treatment with terlipressin, albumin, and diuretic adjustment, the patient presented with 2.7 mg/dL of creatinine and 54576 pg/mL of NT-proBNP.

Nevertheless, transthoracic echocardiography showed no differences with the first one.

After a multidisciplinary team discussion, taking into account the patient's fragility and comorbidities, as well as maladaptive RV remodeling (end stage of probable postcapillary pulmonary hypertension), conservative treatment was decided. Evolution was torpid in the next months, always with cirrhosis decompensations, but with cardiac stability thanks to aggressive diuretic treatment.

Discussion

This clinical case shows perfectly the complexity of organ systems interaction, and the need for multidiscipline teamwork to better understand and better treat the patients.

The patient has three big systemic syndromes, cirrhosis, HFrEF, and CKD. Digestive bleeding was the basis of the problem. This happening is a sign of acute decompensated cirrhosis. For that, the worsening of hyperdynamic circulation and decrease of peripheric vascular resistance triggered an acute biventricular HF. The left heart, previously ill, cannot send the needed perfusion to the organs. For that, we assessed a kidney hypoperfusion.

As a consequence, the right ventricle afterload increased, and stayed dilated and a functional tricuspid regurgitation was observed. It provokes venous congestion, including renal venous congestion.

It was a big challenge to arrive at this clinical interpretation. The biggest challenge was to understand how to manage this clinical situation: the kidney needs perfusion, but the liver and heart demand decongestion. Where does the scale fall? Well, after multidisciplinary teamwork, that allowed us to mind that HRS is one example of the existence of a liver-kidney-heart axis, it allowed choosing the best medical treatment for the patient: perfuse the kidneys with effective volume and pressure (terlipressin and albumin), recover the kidneys and after that, these were prepared to decongestive treatment.

After arriving at a stable phase, the patient continued with severe tricuspid regurgitation. How we can see this patient is very complex, so the best decision was medical optimal treatment.

Conclusion

This clinical case gives us many learning points: the body's systems are interdependent, so the best way of work is like a multidisciplinary team. The sharing of knowledge allows us to remember the organs' interdependency.

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