Symptomatic Cirrhotic Cardiomyopathy: About Three Cases Seen in Yaounde Central Hospital, Cameroon

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Abstract

The term "cirrhotic cardiomyopathy" encompasses a wide range of clinical, ultrasounds and biological features pertaining to some anatomical, physiological and biochemical changes at the level of the heart and vessels of patients with liver cirrhosis. Mostly evolving in a silent pattern, cirrhotic cardiomyopathy can result in clinical manifestations of heart failure. Here we describe the case of three patients with liver cirrhosis who presented signs of heart failure. Two of the three patients had serological markers of viral hepatitis B and one had hepatitis C. Cardiac abnormalities on ultrasound were various and one patient had an altered left ventricular ejection fraction. The three patients were successfully managed by fluid restriction and intravenous diuretics. In this article, we also shortly revisit the pathogenesis, diagnosis and management of cardiac and circulatory impairment secondary to chronic liver diseases and especially to liver cirrhosis.

Keywords: Hepato-Cardiac Disorders; Heart Failure; Liver Cirrhosis; Cameroon

Introduction

A wide range of physiological, anatomical and biochemical changes of the heart can be seen in patients with chronic hepatic diseases [1-3]. Cardiac impairment secondary to liver cirrhosis belong to a group of disorders called hepato-cardiac syndromes, and this entity also encompasses heart diseases complicated by liver dysfunctions [2,4,5]. Indeed, the heart, blood vessels and liver are tightly linked...
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particularly through hemodynamic mechanisms related to the sympathetic system [4]. Thus, it is proven that chronic liver diseases can cause a wide range of cardiac abnormalities, including the “cirrhotic cardiomyopathy”, and each of them can lead to chronic heart failure [1,2,4]. First described by Kowalski and Abelmann in 1953, the hyperdynamic circulation syndrome, mostly pertaining to liver cirrhosis, is at the centre of the pathophysiology of heart and/or vascular impairment in patients with chronic liver illness [6-8]. Generally cardiac involvement includes systolic and/or diastolic dysfunction and some electrophysiological abnormalities such as prolonged QT interval [5,9]. This deeply assessed relationship in literature between hepatic and cardiac disorders should justify a complete and timely evaluation of the functional state of the heart and the liver, in order to adequately manage concerned patients considering both organ dysfunction, and so ameliorate the prognosis [3,10]. Indeed, heart failure in liver failure can render difficult or contraindicate invasive therapeutic procedures such as insertion of a Transjugular Intrahepatic Portosystemic Shunt also known as TIPS, and liver transplantation [4,5,11].

Here we describe cardiac complications with heart failure in three Cameroonian patients with liver cirrhosis.

Case Report

Case 1

A 63 year-old woman presented to the emergency unit of the Yaoundé Central Hospital for progressively increasing dyspnoea first on exertion and later at rest, associated with generalised body swelling, all evolving for a period of 3 months. She had past medical history of arterial hypertension known since three years without treatment, Human Immunodeficiency Virus (HIV) infection known since nine months and treated by a fix association of Tenofovir (TDF), Lamivudine (3TC), Efavirenz (EFV).

The physical examination on entry revealed, a blood pressure of 150/76 mmHg, Heart Rate of 98 beats per minute Respiratory Rate of 26 breaths per minute. The patient also had altered general state, signs of right heart failure (distended neck veins, hepatojugular reflux, Harzer’s sign, painful liver and bilateral pedal pitting edema) and signs of left heart failure (orthopnoea, bilateral basithoracic crackles, pansystolic grade 5 mitral murmur and Gallop rhythm). The diagnosis made based on the clinical exam was decompensated global heart failure.

Biological paraclinical investigations revealed mild normochromic normocytic anaemia (Haemoglobin of 10.7 g/dl), normal CD4 count, hyperuricemia (89 mg/l), low plasma potassium (2.9 mmol/l), elevated liver enzymes (96 UI/l for Aspartate Amino-Transferase and 69 UI/l for Alanine Amino-Transferase), normal pro thrombin time, elevated gamma GT (345 UI/l). Also, serum protein electrophoresis shown an augmentation of gamma globulins and beta 2 globulins giving a beta gamma bloc, and the patient had negative serological tests for hepatitis B virus, and positive ones for hepatitis C virus. On electrocardiogram the patient had left atrial and ventricular hypertrophy, and prolonged QT interval. Cardiac ultrasound revealed a dilated left ventricle, moderate mitral and severe tricuspid insufficiency, grade 3 diastolic dysfunction and a severe pulmonary hypertension (See figure 1 and 2). The Left Ventricular Ejection Fraction (LVEF) was 76% according to Teichholz formula. Abdominal echography shown a heterogeneous and micro nodular liver with crenelated outlines, and ascites (see figure 3).

We so concluded in heart abnormalities associated with post-viral hepatitis C liver cirrhosis. Initial management consisted in the administration of perindopril 5 mg per day, and reduction of fluid overload with diuretics (furosemide at 80 mg/8h). The evolution of the clinical state respect to heart failure symptoms was favourable and after ten days the patient was oriented to a gastroenterologist.
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Figure 1

Figure 2

Case 2

A 69 years old male came at the emergency unit of the Yaoundé Central Hospital for productive cough with mild pinkish expectorations, and progressively increasing dyspnoea, since four weeks prior to consultation. She had no relevant past medical history. Findings on the initial evaluation were an altered general state, fever (38.5°C) with regular tachycardia with heart rate at 122 beats per minute, signs of both left and right heart failure and reduced urine output. The clinical presumptive diagnosis was a global heart failure decompensated by an infectious state associated with a functional acute kidney injury.

Relevant results concerning lab exams were: high serum creatinine (23 mg/l) and urea (2.13 g/l), normocytic normochromic moderate anaemia (9.2 g/dl), moderate neutropenia (900 cells/mm3), moderate thrombopenia (70000 cells/mm3), positive malaria test (for *Plasmodium falciparum*), C reactive protein at 48 mg/l. Chest X-ray shown a bilateral interstitial syndrome with linear opacities and a cardiomegaly. Cardiac ultrasound concluded on: dilated cardiac cavities with a LVEF of 29%, myocardial hypokinesis, diastolic dysfunction, and moderate pulmonary hypertension.
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About the management, pharmacological treatment was made of fluid restriction (750 ml/24h), intravenous diuretics (furosemide at 20 mg/8h), injectable artesunate, associated with non-pharmacological measures including water and salt oral intake restriction. The evolution was marked by the reduction of symptom’s severity (especially breathing difficulties), but at day six of hospitalisation in the Cardiology Unit where he was later transferred, he developed jaundice, flapping tremor and signs of ascites. Paraclinical investigations for liver functional and structural evaluation revealed hepatocellular insufficiency with low pro thrombin time and elevated liver enzymes (SGOT and SGPT), and ultrasound abnormalities of a cirrhotic liver (heteronodular enlarged liver with heterogeneous echogenicity). Serological tests were positive for hepatitis C virus. The evolution was good and after two weeks he was authorized to discharge, and actually is followed by a cardiologist and a gastroenterologist.

Case 3

A 76 years old man presented since four months gradually painful and distended abdomen with bilateral ankle pitting edema and mild progressively increased breathing difficulties. He had past medical history of chronic viral hepatitis B infection without any other chronic infections or cardiometabolic illnesses, and didn’t drink alcohol. The initial physical exam found an agitated ill looking patient with a blood pressure of 114/69 mmHg, heart rate of 76 bpm, respiratory rate of 22 cycles per minute (without orthopnoea), temperature of 37.1 degrees and oxygen saturation at 91%. The patients also had signs of ascites without liver or spleen enlargement, bilateral tender lower limbs edema, bilateral coarse crackles at the lower pulmonary fields and skin and mucosal pallor. Otherwise he didn’t have signs of hepatocellular insufficiency, or abnormalities on cardiac auscultation. The diagnosis made was decompensated post viral hepatitis B liver cirrhosis with as probable precipitating factor an infectious illness (possible locations: ascites, lung, blood notably *Plasmodium falciparum* infection). The associated diagnosis of heart failure was also made respect to progressive dyspnoea and crackles topography.

Biological exams revealed severe macrocytic anemia (5.5 g/dl), with mild thrombocytopenia (95000 cells/mm³), elevated serum urea (0.84 g/l), creatinine (19.81 mg/l), hyponatremia (128.39 mmol/l), normal serum albumin levels, low pro thrombin time (50.9%), with International Normalised Ratio (INR) at 1.75, elevated liver enzymes, C-reactive protein at 24 mg/l and negative thick smear. On cardiac ultrasound the patient had concentric hypertrophy of the left ventricle, grade 1 diastolic dysfunction, grade 2 mitral and aortic insufficiency with degenerative look (see figure 4). The Left Ventricular Ejection Fraction was 79%. Abdominal ultrasound showed a heterogeneous and micro nodular liver with normal size and crenelated wall, and ascites of great abundance without other pathological findings (Figure 5). The treatment consisted of fluid restriction after carefully monitored blood transfusion, intravenous diuretics (furosemide at 40 mg/12h), preventive treatment of constipation with lactulose and oral antibiotic regimen with ciprofloxacin twice per day. The evolution was favourable and the patients discharge was done after 10 days in hospitalisation.

Discussion

General overview

As previously said a wide range of liver diseases, mainly chronic ones, could result to numerous cardiovascular damages and this spectrum of disorders is called hepatocardiac syndromes [5,12]. Chronic hepatic disorders which can lead to heart complications are chronic hepatitis, liver cirrhosis, non-alcoholic fatty liver diseases, primary biliary cirrhosis, hepatocellular carcinoma and all other liver causes of portal hypertension [3,5,12]. The three patients we described had liver cirrhosis with two due to hepatitis C virus and one to viral hepatitis B infection. In the case of liver cirrhosis, the cardiac impairment is traditionally called cirrhotic cardiomyopathy or cirrhotic heart and the diagnosis is made according to well defined criteria [1].

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Figure 4

Figure 5

Data concerning the frequency of cirrhotic cardiomyopathy are scarce due to the silent evolutionary pattern of the disease with near normal cardiac function unless the patients are exposed to stress [8,9]. Nevertheless, it has been estimated that approximately 50% of patients undergoing liver transplantation developed some signs of cardiac dysfunction and about 7 - 21% of patients died from heart failure in the post liver transplantation period [13,14].

Pathogenesis of cardiovascular complications of liver cirrhosis

The pathogenesis of cardiovascular diseases in liver cirrhosis is sustained by many mechanisms of which physiological alterations with autonomic cardiovascular dysfunction and biochemical modifications involving endocannabinoids, nitric oxide and carbon monoxide [4,11,12].

Concerning the autonomic nervous system, a decreased responsiveness to adrenergic response is well documented in patients with liver cirrhosis [5,7,12]. Many explanations can support this findings, notably interaction with the stimulation of beta adrenergic receptor system through binding proteins (stimulatory Gs-protein) and adenylyl cyclase abnormal functions, and alterations of cardiomyocyte cell membrane fluidity with dysfunction of membrane-bounded ion channels (Ca++ an K+ channels) [11,15]. Also, with liver cirrhosis there is an enhanced muscarinic receptor activity resulting in an inotropic effect on the myocardial wall [4,5,11]. The variable grade of inflammation pertaining to liver cirrhosis with elevated inflammatory markers (Tumor Necrosis Alpha), as well as bacterial endotoxin transfer in the systemic circulation, can conduct to an excessive production of nitric oxide (NO), a vascular (arterial) relaxing factor. NO will provide reduced coronary vascular tone and myocardial contractile response resulting to a negative inotropic and chronotropic effect [8,11,16]. Finally, carbon monoxide production and endocannabinoids signalling pathway have been found to be upregulated in human and animal models of liver cirrhosis, and this upregulations are associated with a negative inotropic effect on the cardiac muscle [11,15].

These biochemical and physiological changes, alone or in a complex interactivity, would therefore lead to systolic and/or diastolic dysfunctions which represent the key elements of the cirrhotic cardiomyopathy. Systolic dysfunction is characterized by the inability of the heart to ensure organs demands in oxygen and nutrients. Pathological findings frequently encountered at the level of the heart wall are myocardial hypertrophy, extended fibrosis and subendothelial edema [11,12,17].

An overview of anatomical and physiological changes of the heart in patients with chronic liver disease is given in figure 6.
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Manifestations of cardiovascular complications of liver cirrhosis

Cirrhotic patients have clinical symptoms of palmar erythema, reddish skin, raised and bounding pulse, low blood pressure all secondary to systemic vasodilatation [12,15,18].

Cirrhotic cardiomyopathy is cardiac dysfunction in patients with cirrhosis characterized by systolic and diastolic dysfunction, and electro physiological abnormalities in the absence of known cardiac disease. Systolic dysfunction entails a normal left ventricular ejection fraction at rest which decreases during stress, exercise. It has an impact in the development of complications such as sodium and water retention, ascites formation, development of renal dysfunction and on the prognosis of the patient [1,4,19].

All of our patients had ascites and two of them presented symptoms of global heart failure of which one had preserved Left Ventricular Ejection Fraction. Diastolic dysfunction is an increase in the stiffness of the myocardial wall owing to myocardial hypertrophy and fibrosis [3,5,12,20]. It is reported in 45 to 50% of cases and is characterized by myocardial hypertrophy, contractile dysfunction, changes in heart volume and an ultrasound finding of an E/A < 1 [5,9,11]. Electrocardiographic abnormalities include tachycardia, left ventricular hypertrophy and prolonged QT interval. Finally some cardiac biomarkers can be raised in patients with cirrhotic cardiomyopathy such as Brain Natriuretic Peptide (BNP), NT-proBNP and cardiac Troponin I [1,2,8,15].

Diagnostic criteria for cirrhotic cardiomyopathy were agreed at the 2005 World Congress of Gastroenterology and are [1]: (1) systolic dysfunction: blunted increase in cardiac output on exercise, volume challenge or pharmacological stimuli or resting ejection fraction < 55%, (2) diastolic dysfunction: the ratio of early to late (atrial) phases of ventricular filling or E/A ratio < 1.0 (age-corrected), prolonged deceleration time (> 200 ms), or prolonged isovolumetric relaxation time (> 80 ms). Some supportive criteria were also defined and in-
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clude: electrophysiological abnormalities, abnormal chronotropic response, electromechanical uncoupling/dyssynchrony, prolonged QTc interval, enlarged left atrium, increased myocardial mass, increased brain natriuretic peptide (BNP) and pro-BNP, or increased troponin I.

Management of symptomatic cardiac involvement in patients with liver cirrhosis: The case of the cirrhotic cardiomyopathy

Of our knowledge, no guidelines exist concerning the management of heart diseases complicating liver cirrhosis, especially the cirrhotic heart [9]. Until the conditions remain asymptomatic there is no particularly specific therapeutic measure. When the patient develops symptoms, the treatment is almost the same than the one of patients without liver cirrhosis. This includes salt and fluid restriction, diuretics and afterload reduction which can be more difficult because of the hypotension frequently encountered in cirrhotic patients [9,11,12]. Our two patients who presented signs of global heart failure were successfully treated by fluid restriction and diuretics.

Although there is no clearly significant benefit of beta-blockers in heart damage of cirrhotic patients, combination of β-blockers and aldosterone antagonists might have additive effects in improving their cardiac function [9,15]. Indeed, anti-aldosterone agents (K-Canrenone for example), due to their anti-fibrotic properties, can significantly reduce hepatic venous pressure gradient, left ventricular wall thickness and left ventricular end-diastolic volume [9,16]. However there is not a significant improve in diastolic dysfunction with this therapeutic class [9].

Of note, cardiac glycosides, such as digitalis, might not be effective in increasing cardiac contraction in cirrhotic patients [9,15].

Conclusion

The cases described draw again physicians and researchers attention on the relationship between the heart and the liver. Indeed, even though cardiac dysfunction of liver cirrhosis is in most of the cases asymptomatic, we can have clinical features of right, left or global heart failure [15]. Until the establishment of specific and universally accepted guidelines for the treatment of heart failure, symptomatic or not in patients with chronic hepatic disease especially liver cirrhosis (“cirrhotic cardiomyopathy”), the management remains the same as for patients without liver disease [9]. Nevertheless it has to be carefully conducted and monitored considering circulatory changes specific to cirrhotic patients [9,11].

Ethical Considerations

The patient’s consents were obtained prior to the elaboration of this article.

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Disclosure

No conflict of interest.

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