Ischemic Hepatitis Induced by Uremic Cardiac Tamponade in a Patient with Underlying Hepatitis C with a Review of the Literature

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Abstract
Ischemic hepatitis is a rare cause of acute liver injury (ALI) and is associated with various etiologies including cardiac failure, trauma, hemorrhage, and respiratory failure that all result in poor perfusion and oxygen delivery to the liver. A 30-year-old patient complained of orthopnea with a history of hepatitis C treatment and is currently on hemodialysis (HD) due to chronic allograft rejection. Also, he had previous pericardial effusion (PEFF) due to inadequate dialysis. Laboratory tests on admission revealed urinary tract infection, HCV PCR positive, and high blood urea nitrogen. Computed tomography of the chest showed massive PEFF. Echocardiography revealed a massive PEFF that measured 3.6 cm on the apical four-chamber window, and the inferior vena cava diameter was 27 mm with a decreased collapsibility of <20% in inspiration. The patient was treated for UTI and started the treatment for HCV. Also, increased HD sessions with minimal heparinization of the dialyzer circuit were obtained along with daily monitoring of PEFF by echocardiography. At first, echocardiography did not reveal frank signs of cardiac tamponade, but after 2 sessions of HD, the patient developed chest pain, worsening orthopnea, JVP elevation, and dropping of the systolic BP. Echocardiography showed specific signs of cardiac tamponade, which included an increased effusion to 4.4 cm and changes in velocities of the mitral valve and tricuspid valve during the respiratory cycle by more than 25% and 40%, respectively. The patient was transmitted to ICU, and pericardiocentesis was
obtained. Two days later, asymptomatic ALI was noticed by elevation of the following tests: ALT, AST, LDH, PT, and INR. However, ALI exhibits a rapid and spontaneous resolution to nearly normal tests after 10 days. Although the patient was hemodynamically stable, the liver injury occurred and might be attributed to ESRD and hypertension that caused thickened heart walls, diastolic dysfunction, and subsequently hepatic congestion, in addition to previous liver injury due to HCV. We present a rare case of ALI caused by uremic pericardial tamponade with an overview of the current literature with regard to this entity. So, we emphasize monitoring liver function tests in the context of PEFF, especially in patients with chronic kidney disease.

Introduction

In 1979, Bynum et al. coined the term “ischemic hepatitis” to refer to a liver injury characterized by a centrlobular liver cell necrosis with a sharp increase in serum aminotransferase activity in the setting of cardiac failure [1]. It accounts for 1–2.5% (and occasionally up to 10%) of patients admitted to an intensive care unit (ICU) [2]. Ischemic hepatitis (IH) is a rare cause of acute liver injury (ALI) and is associated with various etiologies including cardiac failure, trauma, hemorrhage, and respiratory failure that all result in poor perfusion and oxygen delivery to the liver. When we talk about cardiac cause we mean decreased cardiac output that related to congestive heart failure or acute cardiac failure [3].

IH is usually detected first because of elevations in liver biochemical tests following a hypotensive episode that consists of a rapid rise in serum aminotransferase levels associated with an early massive rise in lactate dehydrogenase levels. Peak aminotransferase levels are typically 25–250 times the upper limit of normal and decline steadily, usually returning to normal within 7–10 days. IH is nearly always self-limited, and the patient’s overall prognosis is poor, with mortality rates of at least 25% [2]. In the study conducted in 2003, the acute cardiac failure was the underlying condition in 20 episodes of hypoxic hepatitis (14%), and causes of it included myocardial infarction (n = 8), pulmonary embolism (n = 5), thoracic trauma (n = 3), sudden arrhythmia (n = 1), and pericardial tamponade (n = 3) [3].

We present a rare case of ALI caused by uremic pericardial tamponade in a patient with hepatitis C virus (HCV) infection and on hemodialysis (HD) for 2 years due to chronic allograft rejection which required pericardiocentesis, which ultimately led to resolution of ALI. We also present an overview of the current literature with regards to this entity.

Case Report

A 30-year-old patient was admitted to the Nephrology Department of Al Assad University Hospital, who complained for 10 days of orthopnea, fever, flank pain, and oliguria. He received renal allograft 12 years ago and is currently on HD for 2 years due to chronic allograft rejection. He had hypertension (HTN) and a history of HCV treatment. Also, he had previous pericardial effusion (PEFF) due to inadequate dialysis, which was treated with pericardiocentesis and increase of HD sessions.

A physical exam showed diminished heart sounds, blood pressure (BP) 130-120/70–85 mm Hg. Laboratory tests on admission (Table 1) revealed urinary tract infection, HCV PCR positive, and high blood urea nitrogen (BUN). Computed tomography of the chest showed
massive PEFF, and electrocardiogram was normal. Echocardiography revealed a massive PEFF that measured 3.6 cm on the apical 4-chamber window, significant thickening of cardiac walls, ejection fraction of 50%, and the inferior vena cava (IVC) diameter was 27 mm with a decreased collapsibility of <20% in inspiration.

The patient was treated for urinary tract infection and started the treatment for HCV. Also, increased HD sessions with minimal heparinization of the dialyzer circuit was obtained along with daily monitoring of PEFF by echocardiography. The status was worsening, which was observed by sustained elevation of urea and hyperkalemia.

On day 4 of admission, after 2 HD sessions, the patient developed chest pain, worsening of orthopnea, jugular venous pressure (JVP) elevation, and dropping of the systolic BP to 90–100 mm Hg. The echocardiography showed previous signs of IVC, increased effusion to 4.4 cm, and changes of velocities of mitral valve (MV) and tricuspid valve (TV) during the respiratory cycle by more than 25% and 40%, respectively, but no collapse of cardiac chambers (Fig. 1). The patient was transmitted to the ICU, and pericardiocentesis was obtained, which drained 1,600 mL of bloody fluid. Laboratory and histopathologic tests of the pericardial fluid are shown in Table 1. The patient status rapidly improved, and BP increased to 130/70 mm Hg. On day 6, routine tests revealed liver injury (Table 1), which included prothrombin time

![Fig. 1. Echocardiography showed a massive PEFF on the apical four-chamber window (a), decreased velocity by 25% on MV (b), increased velocity by 40% on TV (c) during the respiratory cycle.](image-url)
20/s, international normalized ratio 3.6, alanine aminotransferase 481 U/L, aspartate aminotransferase 1,369 U/L, and lactate dehydrogenase 7,785 U/L.

By reviewing the literature, we found that, in rare cases, cardiac tamponade (CT) induced liver injury due to ischemia. Rapid resolving and self-limiting of liver injury were noticed by daily liver function tests, which returned to nearly normal after 10 days (Table 1).

Discussion

Over the past 20 years, a literature review yielded 6 patients of chronic kidney disease (CKD) associated with IH due to CT (Table 2) [4–9]. Underlying conditions that caused CT were as follows: adenocarcinoma of the lung was detected in 2 cases [7, 8], uremic pericarditis in one [9], and 3 cases had unknown etiology [4–6]. Four patients were on HD [4, 5, 7, 9], and 1 patient received HD for deterioration of CKD stage V [6]. All patients showed collapse of cardiac chambers on echocardiography.

IH, also referred as shock hepatitis, accounts for 0.16 and 2.6% of patients in the general medicine ward and ICU, respectively, with a male-to-female ratio of 2:1 [3]. The main underlying conditions are congestive heart failure (56%) and septic shock, which together accounts more than 3/4 of all episodes [3, 10]. In fact, shock hepatitis is a misnomer since up to half of patients experienced it without shock [3]. Systemic hypotension alone did not lead to IH, and this was observed in a study of 31 patients who had underlying cardiac disease that had led to passive hepatic congestion, compared to the control group [11]. The risk of developing ALI is increased in liver diseases such as cirrhosis, alcoholic liver disease, and viral hepatitis. Also, end-stage renal disease has been linked to the development of hepatic congestion due to several factors such as HTN and cardiomyopathy [5].

In the current case, although the patient was hemodynamically stable, liver injury had occurred. This might be attributed by end-stage renal disease and HTN that caused thickened heart walls, diastolic dysfunction, and subsequently hepatic congestion, in addition to previous liver injury due to HCV.

There is a known correlation between the degree of azotemia, usually BUN >60 mg/dL, and uremic pericarditis [12]. In a past series of 125 patients, the frequency of uremic pericarditis has been found in 40 patients (32%), and 5 of these patients (12.5%) developed a PEFF which was sufficient to produce CT. Seven patients in this study were treated with HD using universal heparinization, 1 patient developed CT in the first session, and all the rest of the patients on HD were without complications [13]. The bloody pericardial fluid in the context of uremic pericarditis is in part due to platelet dysfunction and the use of anticoagulant during HD [12]. With worldwide advancements of HD, pericardial involvement in CKD consists of a rare clinical condition [9].

In our patient, due to a previous history of uremic pericarditis and currently high BUN, in conjunction with pericardial fluid analysis, uremic PEFF is the most likely underlying cause. Also, the use of an anticoagulant (heparin) was the most implicated cause in increased volume of PEFF with bloody pericardial fluid after HD session, and this might clarify the specific echocardiographic findings of CT. Moreover, this case represents the second case of ALI induced by uremic pericarditis over the past 20 years.

Echocardiography is the gold standard imaging technique in the setting of PEFF and should be obtained immediately if CT is subsequently suspected. Several data of echocardiographic findings were published in the context of CT, which continue to reveal a large variability in specificity and sensitivity [14]. The sensitivity of right atria collapse ranged from 50% in early CT to 100% with progression of CT. Collapse of the right ventricle carried a high specificity (75–90%) but a relatively lower sensitivity (48–60%) to rule out CT [15]. Also, CT
| Author             | Age and stage of CKD | BP and signs                  | Features on echocardiography                                  | Laboratories                      | Complication and cause                          |
|--------------------|----------------------|-------------------------------|----------------------------------------------------------------|-----------------------------------|-----------------------------------------------|
| López-Méndez et al. [7] | 57 years ESRD on HD  | SBP 60 mm Hg, Dyspnea         | Right atrial-ventricular diastolic collapse                    | ALT: 5,054 U/L, AST: 8,747 U/L, LDH: 15,220 U/L, PT: 16/s, INR: 2.4 | Hepatic encephalopathy, Unknown               |
| Thaker et al. [8]   | 56 years ESRD on HD HCV | Hemodynamically stable, Abdominal pain, nausea | Flattening of the interventricular septum during inspiration, Right ventricular collapse, Dilated IVC (2.8 cm) | ALT: 3,600 U/L, AST: 4,200 U/L, INR: 2.9 | DIC induced by hemoperitoneum, Unknown         |
| Mitwally et al. [9] | 68 year CKD stage V  | 87/57 mm Hg, Dyspnea, lethargy, anuria | Collapse in the right ventricle and atrium                     | ALT: 1,729 U/L, AST: 1,772 U/L, PT: 25.8/s, INR: 2.3 | AKI with HD, Death, Unknown                   |
| Din et al. [6]      | 30 years ESRD on HD  | Borderline hypotensive, Abdominal pain, nausea, vomiting | Collapsing of atrial chambers                                  | ALT: 3,176, AST: 8,267             | Adenocarcinoma of lung                        |
| Boendermaker et al. [5] | 61 years CKD III      | Hypotensive, Oliguric, dyspnea | Apical of 3.2 cm and of 3.1 cm over the right ventricle, Paradoxal septal movement, Compression of the right atrium | ALT: 2,449, AST: 3,802, LDH: 3,161 | Adenocarcinoma of lung                        |
| Shoni and Rodriguez [4]* | 87 years ESRD on HD | SBP 40–60 mm Hg, Hypotension, Shortness of breath, chest pain, on HD sessions | Right atrial and ventricular collapse                           | ALT: 1,661, AST: 1,859, PTT: 72.9, INR: 5.7 | Death, Uremic pericarditis                    |

**ESRD, end-stage renal disease; HD, hemodialysis; HCV, hepatitis C virus; CKD, chronic kidney disease; SBP, systolic blood pressure; IVC, inferior vena cava; ALT, alanine aminotransferase; AST, aspartate aminotransferase; LDH, lactate dehydrogenase; PT, prothrombin time; INR, international normalized ratio; PTT, partial prothrombin time; DIC, disseminated intravascular coagulopathy; AKI, acute kidney injury.**

*INR and PTT continued to rise up unless discontinue of warfarin.
produces changes in flow velocities through MVs and TVs during the respiratory cycle. There were approximately 25% decrease and 40% increase in MV and TV inflow velocities, respectively. This may also occur with chronic obstructive pulmonary disease and pulmonary embolism [15]. In contrast to the uncertain role of IVC in the assessment of intravascular volume, the evaluation of IVC in CT is less controversial [16]. A plethoric IVC is defined as having diameter > 2.1 cm with < 50% inspiratory reduction. However, it has been reported as a very sensitive sign (95–97%) and has high negative predictive value; it has much lower specificity (40%) for CT, which can be caused by chronic obstructive pulmonary disease, tricuspid regurgitation, and congestive heart failure [15].

Herein, the first sign in our patient was plethoric IVC, which was observed for 4 days on subsequent echocardiography, and the progression of PEFF volume caused another specific radiographic sign to appear. Unfortunately, although findings of echocardiography are very helpful, none of them is 100% diagnostic of CT. Thus, the decision to manage PEFF should be guided by history and physical exam and supported by echocardiographic findings [14].

This case mentions important causes such as uremic pericardial tamponade that lead to ALI. So, we emphasize monitoring of liver function tests in the context of PEFF, especially in patients with CKD.

**Statement of Ethics**

This case report complies with the guidelines for human studies and was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. A written informed consent was obtained from the patient for publication of this case report and any accompanying images, and he has provided a copy of the consent form. This study protocol was reviewed, and the need for approval was waived by the Ethics Committee of the Damascus University Research Center.

**Conflict of Interest Statement**

The authors have no conflicts of interest to declare.

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**Author Contributions**

Mohammad Khaled Alsultan wrote and revised the manuscript and literature review and treated and followed up the patient. Aliaa Bakr wrote and revised the manuscript and literature search. Qussai Hassan made article corrections, was the supervisor, and followed up the case.

**Data Availability Statement**

All necessary details are available in the article. Further enquiries can be directed to the corresponding author.
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