**Hepatic Hypoperfusion in Complex Cardiac Pathology: A Case of Ischemic Hepatitis Secondary to Congenital Heart Disease with Atrial Fibrillation and HFpEF**

**ABSTRACT**

Ischemic hepatitis (IH) is an acute liver injury caused by hepatic hypoperfusion, typically occurring in shock states. We present a 77-year-old woman with congenital heart disease (CHD), heart failure with preserved ejection fraction (HFpEF), and atrial fibrillation who developed IH without overt hypotension. She presented with dyspnea, weakness, and oliguria, accompanied by severe transaminitis (AST 6602 U/L, ALT 3886 U/L), coagulopathy (INR 7.35), and lactic acidosis (lactate 6.8 mmol/L). Echocardiography revealed atrial fibrillation with rapid ventricular response, pulmonary hypertension, and valvular abnormalities. Management included rate control, diuresis, and hepatic support. Liver enzymes improved by day 4, confirming recovery. This case demonstrates that IH can occur in HFpEF patients with CHD and arrhythmia, even in the absence of profound hypotension. Early recognition and hemodynamic optimization are critical to prevent irreversible liver damage. This case report underscores IH as a potential complication in high-risk cardiac patients, necessitating vigilant monitoring and prompt intervention.

**INTRODUCTION**

Ischemic hepatitis (IH), also known as shock liver or hypoxic hepatitis, is a diffuse liver injury caused by acute hypoperfusion. It typically follows episodes of hemodynamic instability or hypoxia, such as hemorrhage, sepsis, pulmonary embolism, heart failure, arrhythmias, acute myocardial infarction or severe respiratory distress. The condition is marked by a transient yet significant elevation of serum hepatic transaminases and is associated with centrilobular hepatic necrosis. Serum hepatic transaminase levels typically rise to 10–300 times the upper limit of normal and usually return to baseline within 5–25 days.1 In patients with chronic heart failure, severe ALT/AST elevation is less common unless accompanied by a low-output state. Ischemic hepatitis can occur in cardiogenic shock, typically in the setting of significantly reduced ejection fraction.2 Cardiogenic ischemic hepatitis, can develop after a severe hypotensive episode in patients with acute heart failure.3In heart failure patients, liver damage may manifest as chronic congestive hepatopathy or ischemic hepatopathy, also known as acute cardiogenic liver injury (ACLI).4 Ischemic hepatitis can develop from diminished hepatic blood flow due to low cardiac output, even without overt shock.5 Several studies have pointed out that the hemodynamic changes in heart failure with preserved ejection fraction (HFpEF) were different from HFrEF. This case report highlights an occurrence of ischemic hepatitis in a patient with congenital heart disease, HFpEF and atrial fibrillation.

**KEYWORDS:** Ischemic hepatitis, HFpEF, congenital heart disease, atrial fibrillation, cardiogenic liver injury

**CASE DESCRIPTION**

A 77-year-old female patient was admitted in ICU in the department of Cardiology with complaints of generalized weakness, acute dyspnea and oliguria. Her past medical history included hypothyroidism, Type 2 Diabetes Mellitus (T2DM), systemic arterial hypertension, dyslipidemia, persistent atrial fibrillation, congenital heart disease (CHD) and heart failure with preserved ejection fraction (HFpEF). Patient has no prior history of liver and pulmonary disease. The patient had been on multiple medications, including Tab Levothyroxine 150mcg once daily, Tab Metoprolol succinate 50mg twice daily, Tab Cilnidipine 10mg once daily, Tab Atorvastatin 10mg once daily, Tab Torsemide/Spironolactone 10/25mg once daily, Tab Apixaban 5mg twice daily, Tab Metformin 500mg once daily and Tab fenofibrate 160mg once daily.

On admission, cardiovascular examination revealed pansystolic murmurs, blood pressure 140/90 mmHg and a pulse rate of 112 bpm. ECG showed atrial fibrillation with fast ventricular response (AF with FVR). An echocardiography assessment showed congenital heart disease, subpulmonic ventricular septal defect with left-to-right shunt, interventricular gradient of 56 mmHg, dilated right atrium, left atrium and right ventricle, with an ejection fraction of 60%. Other findings included anterior mitral leaflet prolapse, grade 3 mitral regurgitation, mild aortic regurgitation, grade 3 tricuspid regurgitation, moderate pulmonary arterial hypertension, right ventricular systolic pressure of 54+ right atrial pressure mmHg, and a thin rim of pericardial effusion.

Pulmonary examination revealed air entry bilaterally equal, dyspnea on exertion, grade 2-3 dyspnea, bilateral basal creps. Examination revealed dyspnea secondary to cardiac illness. Chest X-ray revealed bronchovascular markings and cardiomegaly.

On admission, laboratory investigations revealed markedly elevated liver function test (LFT) parameters, with aspartate aminotransferase (AST) at 353U/L, alanine aminotransferase (ALT) at 224U/L and alkaline phosphatase (ALP) at 60U/L. Serum total bilirubin was 2.3 mg/dL, with direct bilirubin at 1.4 mg/dL. Electrolyte levels showed sodium at 131mEq/L and potassium at 4.9mEq/L. ABG shows pH 7.29, pCO2 38 mmHg and lactate levels at 6.8 mmol/L. Hematology investigations showed total counts were elevated at 13020 cells/ul and ESR of 15mmhr. CRP was elevated to 13.5mg/dl.Trop I levels showed elevation to 0.02ng/ml and BNP was elevated to 876pg/ml. Blood glucose values were elevated, with random blood sugar (GRBS) of 172 mg/dL. Urinalysis showed significant proteinuria (+++), RBCs (10-12/HPF), and a mild increase in pus cells (2-4/HPF), suggestive of possible renal involvement. Dengue IgM, leptoIgM, HBsAg, anti HCV, HIV, Anti HEV IgM and Hepatitis B were found to be negative.

On Day 2, PT and INR revealed highly elevated values of 89.1 and 7.35, Serum sodium remained at 134 mEq/L, while potassium was highly elevated to 6 mEq/L, after further management it was dropped further to 3.2 mEq/L. Blood glucose remained elevated, with FBS at 169 mg/dL and GRBS at 152 mg/d. Procalcitonin was elevated to 0.1 mcg/l.

By Day 3, repeat LFTs showed hepatic enzyme elevation, with AST at 6602 U/L, ALT at 3886 U/L and ALP of 75 U/L. Total bilirubin levels were at 2.4 mg/dL with direct bilirubin at 1.4 mg/dL. LDH was elevated to 3342 U/L, GGT elevated to 59 U/L and S. CK to 229 U/L.

On day 4, LFT parameters showed a slight improvement, with AST decreasing to 2747 U/L, ALT to 2746 U/L and ALP 76U/L.Total bilirubin levels were at 2.6 mg/dL with direct bilirubin at 1.6 mg/dL. Electrolytes showed stabilization, with sodium and potassium were improved following supplementation.

During stay in the hospital, Tab Fenofibrate 160 mg was stopped in view of elevated LFT. The patient received Inj Calcium Gluconate 1 ampule stat and Neb Salbutamol 4 respules stat for hyperkalemia, InjMeropenem 1 g three times daily for 5 days for infection and was switched to oral Ofloxacin 200 mg once daily, Inj Pantoprazole 40mg once daily, Tab Metoprolol succinate 50 mg twice daily for rate control in atrial fibrillation, Tab Apixaban 5 mg twice daily was given for atrial fibrillation and was temporarily stopped from second day of admission due to elevated INR and was restarted when INR came to 2.5 during discharge, Tab torsemide/spironolactone 10/25 mg once daily was stopped temporarily and started Inj Furosemide 20mg twice daily was given for a day and then changed dose to 10 mg twice daily in view of decreased urine output and mild volume overload and was stopped after 2 days, Tab Sildenafil 20 mg twice daily was given in view of pulmonary hypertension, Tab Ursodeoxycholic acid 300 mg twice daily, Syp lactulose 30 ml twice daily for hepatic dysfunction, Tab Sodium bicarbonate 500 mg three times daily, and his past medications were continued.

At discharge, the patient was prescribed with a structured medication regimen, including anti-hypertensives, metformin, thyroxine and supportive therapies. She was advised to follow up in the cardiology outpatient department after five days with repeat laboratory investigations, including a complete blood count (CBC), renal function tests (RFT), serum sodium (Na) and potassium (K) levels, international normalized ratio (INR) and liver function tests (LFT).

**DISCUSSION**

The pathophysiology of ischemic hepatitis involves impaired hepatic perfusion, primarily from low cardiac output or systemic hypotension. Though once attributed mainly to shock, forward failure is now a recognized cause. The liver, receiving 25% of cardiac output mostly via the portal vein relies on compensatory mechanisms like hepatic artery buffering, passive reservoir drainage, and the hepatorenal reflex to maintain perfusion and prevent ischemia during hemodynamic stress.1

Heart failure is classified based on left ventricular ejection fraction (LVEF) into two main categories: heart failure with preserved ejection fraction (HFpEF), defined as LVEF ≥ 50%, and heart failure with reduced ejection fraction (HFrEF), characterized by LVEF < 40%.4AF frequently coexists with HFpEF (62% prevalence), increasing mortality by 11% and independently predicting cardiovascular death. Shared pathophysiology leads to cardiac output decline, elevated filling pressures, and right heart failure. Hepatic congestion from venous hypertension causes transaminase elevation, which worsens dramatically during hypotensive episodes, precipitating ischemic hepatitis.2

The role of systemic hypotension as a key pathogenic factor was recognized over four decades ago, giving rise to the clinical term shock liver. Among patients studied, cardiogenic causes such as acute myocardial infarction, arrhythmias, cardiac tamponade and acute pulmonary embolism were the predominant triggers of hypotension, accounting for 77% (24 out of 31) of cases.5

In hypoxic hepatitis, LDH rises early within 12-48 hours often with an ALT/LDH ratio <1.5. AST elevations typically exceed ALT, with aminotransferases and LDH reaching 10–20 times normal limits, especially in acute congestive liver injury (ACLI) following heart failure decompensation. These markers decline rapidly if perfusion improves, usually normalizing in 7-10 days. ALT decline within 72 hours helps distinguish ACLI from viral, alcoholic, or drug-induced hepatitis. Bilirubin, INR, and creatinine are often mildly elevated, while alkaline phosphatase rarely exceeds twice the upper limit. Renal dysfunction is frequent, and prolonged prothrombin time is seen in most cases. LDH, though underused, is a valuable diagnostic clue.1,4,5

Dalos et al. first identified serum gamma-GT as an independent prognostic marker in HFpEF, comparable to hemoglobin and NT-proBNP. While gamma-GT correlates with diastolic dysfunction and right atrial pressures, its exact mechanism remains uncertain, potentially reflecting hepatic congestion from elevated cardiac filling pressures, systemic inflammation, or both. This highlights a critical knowledge gap regarding liver biomarkers in HFpEF pathophysiology.8

Ischemic hepatitis results from combined hypoperfusion, hypoxia, or endotoxemia. Respiratory failure exacerbates risk through hepatic congestion. Transaminases >20×ULN require differentiation from viral, toxic, and ischemic causes with the latter's rapid rise and fall pattern being specific.1

Our patient's presentation was classically characteristic for ischemic hepatitis: exclusion of viral/hepatotoxic causes, underlying HFpEF/CHD, rapid aminotransferase elevation (>20×ULN) with normal ALP, and prominent LDH rise. The characteristic biochemical pattern coupled with hemodynamic compromise confirmed diagnosis, though select cases may require biopsy. Definitive diagnosis rests on clinical context and typical enzyme kinetics.

The diagnosis of hypoxic hepatitis typically relies on a combination of hemodynamic disruptions and signs of acute liver damage, and in certain instances, a liver biopsy may be required.9

In HFrEF and acute heart failure, elevated AST and ALT often result from low cardiac output. In contrast, HFpEF patients, as in the TOPCAT trial, are less prone to hypoperfusion. Instead, hepatic congestion from elevated central venous pressure impairs biliary function, with Allen et al. noting higher bilirubin in volume-overloaded patients.6,11

The clinical signs of liver injury remained generally in the background of the clinical signs of the underlying condition, while the dramatic but rapidly resolving elevation of serum enzyme activities, the profound fall of prothrombin activity, and the frequent alteration of renal function formed a triad of bio chemical abnormalities that is unusual in cases of viral or drug-induced hepatitis and that strongly suggests the diagnosis of hypoxic hepatitis.10 The presence of liver changes in individuals with heart failure may affect the pharmacokinetics and pharmacodynamics of cardiovascular medications. Drugs frequently prescribed, including beta-blockers, statins, antiarrhythmic agents, anticoagulants and antibiotics, may accumulate to harmful levels in these patients, resulting in both cardiac and non-cardiac adverse effects. A highly debated topic is the influence of liver dysfunction on patients receiving anticoagulant therapy. The administration of novel anticoagulants such as dabigatran, rivaroxaban or apixaban is particularly contentious; hence, their use is often restricted in cases of hepatic congestion.4

There is no designated treatment for IH. However, key components of management include quickly restoring cardiac output and addressing the root cause of the hemodynamic instability. Typically, the prognosis is primarily influenced by the underlying cause rather than the resulting hepatic dysfunction.12

**CONCLUSION**

In summary, when transaminase levels exceed 1000 IU/L without an identifiable hepatic cause, ischemic hepatitis should be suspected. This case underscores that ischemic hepatitis can develop in patients with heart failure with preserved ejection fraction (HFpEF). It results from impaired diastolic function, leading to reduced cardiac output, increased filling pressures, and/or right-sided congestive heart failure. Our findings highlight the importance of physician awareness of this condition, as it can occur even in patients with normal blood pressure.This case highlights the significance of ischemic hepatitis in the setting of atrial fibrillation and HFpEF. Though IH was the primary diagnosis, concomitant sepsis and prior fenofibrate use may have contributed to the severity of liver injury.The timely discontinuation of fenofibrate was crucial in preventing further hepatic injury. Optimized cardiac and diabetic management contributed to patient recovery. Long-term follow-up is essential to ensure stabilization of liver function and cardiovascular health.

**Declaration of patient’s consent**

The authors certify that all necessary patient consent forms have been obtained. In these forms, the patient(s) have granted permission for their images and other clinical information to be published in the journal. The patients are aware that their names and initials will not be disclosed, and every effort will be made to protect their identity, though complete anonymity cannot be guaranteed.

**ETHICAL STATEMENT**

Ethical approval is not applicable in this case report.

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