Case Report

HYPOXIC LIVER INJURY IN PROLONGED HYPOTENSION AND SEPSIS
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Abstract
Hypoxic liver injury is not an uncommon condition in critical care setup. This condition is characterized by a massive but transient increase in serum transaminase levels usually associated with hypoxia and persistent hypotension. A 25-year male was admitted with history of blunt trauma abdomen in road traffic accident. Subsequently patient had developed renal failure, sepsis and persistent hypotension. Hypoxic liver injury was an incidental finding at autopsy. We present a case report and discuss the importance of this condition as a co-morbid state affecting the prognosis.

Key words: Liver, hypoxia, hepatopathy, death, autopsy, ischemia, sepsis

Introduction
The liver is generally protected from ischemic insult because of dual blood supply via the hepatic artery and portal vein. Therefore true hepatic infarction is rare and its incidence varies from zero in 3,500 autopsies to one in 88 autopsies. However, in critical care setting, hypoxic liver injury (HLI) appears to be more common than has been previously recognized with a reported prevalence of 0.6-1.5%. The identification of this condition is important as the mortality rate varies from 25-73%. To draw attention towards this important issue, herein we are presenting a case report and discuss its importance as a co-morbid state.

Case report
A 25-year male was admitted to a critical care center with history of road traffic accident. The patient had sustained blunt trauma abdomen. His sigmoid and rectum was contused and undergone colostomy. During the course he developed renal failure and had regular hemodialysis. Subsequently patient developed sepsis and needed ionotropic and ventilatory support. In the initial period complete blood counts revealed hemoglobin: 10.5 g/dl, white blood cell count: 11,400 /cumm and platelet count: 2.75 lac/cumm. Biochemical investigations revealed blood urea: 300 mg/dl, serum creatinine 4 mg/dl, total bilirubin: 1.2 mg/dl, SGOT: 40 IU and SGPT: 23 IU. Subsequent hematological and biochemical investigations were not available for review. On 31st day after admission, patient sustained cardiorespiratory arrest and declared dead.

Autopsy examination revealed multiple ecchymotic areas over skin, icterus and infected tracheostomy, colostomy and laprotomy wound with laprotomy wound dehiscence. Brain was congested and oedematous. Pleural cavity contained 600 ml reddish colour fluid on each side. Lungs showed patchy consolidation. Epicardium showed multiple petechial hemorrhages. Peritoneal cavity contained 1000 ml turbid fluid with signs of peritonitis. Liver was enlarged weighing 2600 g. Cut surface of both lobes showed multiple areas of focal fatty infiltration with multiple necrotic areas in the parenchyma (Fig 1). Spleen was enlarged weighing 300 g. Suprarenals showed hemorrhages in the cortex. Sigmoid and rectum showed ischemic infarction. Microscopic examination revealed congested brain and spleen. Lungs showed congestion, oedema and bronco-pneumonia. Myocardium showed focal areas of necrosis with marked acute inflammatory infiltrate. Adrenal revealed congestion and loss of vacuolation. Liver showed congestion and coagulative necrosis with mononuclear cell
infiltration with presence of few areas of normal hepatic architecture with fatty change and chronic venous congestion (Fig 2).

Figure 1 cut surface of liver showing areas of necrosis and fatty infiltration

Figure 2 photomicrograph of liver showing coagulative necrosis with mononuclear cell infiltration (H and E, X 40)

Discussion

The liver receives about 20% to 25% of the cardiac output, 70% via the portal vein and 30% from the hepatic artery. The hepatic artery receives a fixed percentage of the cardiac output, which decreases as cardiac output decreases. Its blood flow varies inversely with that in the portal vein \(^3, 4\). Profound hepatic hypoperfusion (66% reduction of portal flow during ischemia and 80% reduction in hepatic artery flow during reperfusion) producing temporary acute hepatic dysfunction has been found in an experiment involving intestinal ischemia-reperfusion injury in rats.\(^5\) From clinical and experimental studies, it has been found that liver is affected during certain hypotensive state; recognized as “hypoxic liver injury”\(^2, 6\). This disorder is often not suspected clinically but may be detected incidentally at autopsy.

HLI is also known as shock liver, hypoxic hepatitis, hypoxic hepatopathy or ischemic liver. HLI is due to inadequate oxygen uptake by the centrilobular hepatocytes resulting in necrosis. The most common cause is insufficient hepatic perfusion in the setting of passive liver congestion or chronic liver disease \(^3, 7\). Profound and prolonged shock, leading to low hepatic perfusion and hepatocytes hypoxia, appears important for the development of HLI. However, other pathogenic mechanisms have also been identified to cause HLI and include low blood flow secondary to congestive cardiac failure, blood loss, and hypoxia from sepsis or respiratory failure, inadequate oxygen extraction by the hepatocytes, chronic pericardial constriction and increase metabolic demands \(^7-11\).

Clinically the manifestations include weakness, shortness of breath and right upper abdominal pain from enlarged, congested liver. Clinical appearance of jaundice is unusual. HLI is associated with transient and dramatic elevations of serum aminotransferase activity. The raised value occurs after 24–48 hours following hypoxic insult. Alanine transaminase (ALT) elevations greater than 20 times the normal level have been considered by some investigator to be the minimum requirement \(^3\). Similarly serum lactate may be elevated due to inadequate removal of lactate. Lactate dehydrogenase (LDH) level increases and the peak value reaches before transaminase levels. The international normalized ratio (INR) may increase, usually after the peak in the transaminase level. The prothrombin time and partial prothromboplastin may be raised. Microscopic examination shows centrilobular necrosis.
The diagnosis has to be established on clinical and biochemical criteria, as role of interventional procedure such as biopsy remains limited. The condition has to be differentiated from viral hepatitis, drug-induced/toxic hepatitis and hepatic trauma. Sudden and transient increase in transaminase level differentiates between HLI, toxic hepatitis and viral hepatitis. The transaminase level in viral hepatitis decreases slowly in comparison with HLI and toxic/drug induced hepatitis. Similarly elevation of INR occurs early in HLI. The ALT-LDH ratio is considerably low in HLI and toxic hepatitis in comparison with viral hepatitis. Histologically venous congestion with centrilobular necrosis will be evident in HLI whereas hyperplasia, panlobular infiltration with mononuclear cells, inflammation, variable degree of cholestasis and regeneration, characteristic features of hepatitis, will be absent.

In the present case, the patient was admitted for a month and developed renal failure and sepsis. In the later course he required ventilatory assistance and inotropic support since he was having persistent hypotension. He was given blood components to correct coagulopathy. Unfortunately subsequent hematological or biochemical investigation reports were not available for evaluation. HLI was an incidental finding noted at autopsy and was thought to be due hypoxia, resulting from prolonged hypotension and sepsis. It was demonstrated by Shibayama that in addition to circulatory disturbances, sepsis could also cause liver injury. In septic shock, HLI is produced due to increased metabolic demands of hepatocytes along with their inability to extract adequate oxygen from the blood. The presence of hypoxia in the present case can also be demonstrated by the presence of focal fatty deposition. It was considered that hypoxia is a key factor and inadequate local tissue perfusion leads to focal fatty infiltration in the hypoperfused area.

On most of the occasions, HLI have a benign course and the transaminase levels return rapidly to normal state with the correction of the underlying cause. However, in about 6% of cases, HLI may progress to acute liver failure. While dealing in autopsy practice, identification and interpretation of this state is vital to arrive at a conclusion. Such findings are frequent in patients who are hospitalized and later require ventilatory assistance and inotropic support and have multi-organ failure. Presence of such finding indicates a state of prolonged persistent hypotension and/or sepsis.

In conclusion, HLI is not rare in critical care setting and this reversible subclinical condition needs attention since this co-morbid state may affect the outcome of the underlying condition. Similarly identification of this state is essential for forensic pathologist to arrive at a conclusion.

References


