ISCHEMIC HEPATITIS

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Introduction

Abnormal liver function commonly accompanies critical illness. Severe jaundice develops in approximately 2% of patients with shock resulting from major trauma and may appear within hours [1]. In severely ill patients development of jaundice may reflect multiple organ-system failure and poor prognosis. We report two cases of multiple trauma who developed clinical and biochemical evidence of acute hepatocellular dysfunction following episode of prolonged hypotension.

Case-1

A 25-years-old man was admitted to the hospital on 10 Jun 98 with multiple injuries, sustained in a road traffic accident. He was an old case of bronchial asthma, on regular medication. His vital parameters were within normal range at the time of admission. Clinical examination, skiagrams and ultrasound scan of abdomen revealed compression fracture of Dorsal 12 vertebra, contusion of chest (Right) and blunt injury abdomen with contusion of mesentery. The patient was treated conservatively. He developed hypotension on 11 Jun 98 (BP-80/60 mm of Hg). Examination revealed tachycardia (pulse-120/min) and icterus. The abdomen was tender; there was no hepatosplenomegaly. There was no evidence of encephalopathy. Investigations revealed conjugated hyperbilirubinemia (serum bilirubin 5.8 mg%), increased serum transaminase level (AST-182 IU/L, ALT-102 IU/L) and prolonged prothrombin time (19 sec, control 13 sec). Viral hepatitis markers (HbsAg and HCV) were negative. The patient was managed conservatively with intravenous fluids, blood transfusion and sympathomimetics. The blood pressure became normal in about 24 h. The patient showed rapid recovery after correction of hypotension. His liver function normalised within 10 days. He was discharged on 11 Aug 98.

Case-2

A 27-years-old serving soldier was admitted on 11 Aug 98 with history of fall from a wall. Clinical examination revealed trochanteric fracture left femur, blunt injury left lower chest and closed head injury. There was past history of jaundice twice in 1998 and in 1991. At the time of admission, his vital parameters were stable. There was tenderness in left hypochondrium. Neurological examination was normal. He was kept on symptomatic treatment. On 12 Aug 98, he developed hypotension (BP-64/40 mm of Hg). He was managed with intravenous fluids, blood transfusion and sympathomimetics. Examination on 13 Aug 98 re-

vealed a pale, icteric patient who was drowsy and talked incoherently. There was no fresh finding on systemic examination. Investigations revealed anaemia (Hb-9.5 gm%), polymorphonuclear leucocytosis (TLC-17,300/cmm, P 83%) and conjugated hyperbilirubinemia (serum bilirubin-4.4 mg%) with raised level of serum transaminases (AST-104 IU/L, ALT-98 IU/L). Prothrombin time was prolonged to 23 sec (Control-12 sec). In view of altered sensorium, management as for hepatic encephalopathy was started with protein restriction, bowel sterilisation, vitamin supplements and maintenance of fluid and electrolyte balance. Ultrasound scan of abdomen was suggestive of approximately 50 ml of blood in splenic capsule. Splenic capsule, however, was intact. Four quadrant aspiration of abdomen led to aspiration of small amount of haemorrhagic fluid from left lower quadrant. Blood culture was sterile and peripheral blood smear did not reveal any toxic granules, thus ruling out septicemia. CT scan head showed haemorrhagic contusion right frontoparietal region. Serological tests for hepatitis B and C were negative. The patient's hypotension lasted about 12 h. His sensorium improved in next 4-5 days and liver function normalised within one week. He is asymptomatic now. Ultrasound scan of abdomen and liver function tests are normal. The jaundice in this case was due to ischemic damage to liver. However, altered sensorium was most likely due to contusion of brain. He is under follow up for chronic liver disease in view of history of jaundice twice in the past.

Discussion

Multiple factors are responsible for development of jaundice in patients suffering from severe trauma or surgery. There may be increased bilirubin load following blood transfusion (especially stored blood), resorption of haematomas or extravasated blood in the tissues and sepsis. Impaired hepato-cellular function follows trauma, surgery, drugs (e.g. halothane anaesthetics, phenacetin, non-steroidal anti-inflammatory drugs and antimicrobial agents like sulpha drugs and chloramphenicol), total parenteral nutrition and ischemia/hypoxia due to shock. Rarely cholestatic jaundice may develop.

Ischemic hepatitis (also known as hypoxic hepatitis, ischemic liver injury or ICU jaundice) is defined as marked and rapid elevation of serum transaminases in the setting of an acute fall in cardiac output [2]. Ischemic hepatitis is caused by poor hepatic perfusion

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and may affect approximately 22% of those with low cardiac output, decreased hepatic blood flow or passive venous congestion. The important causes are shock due to acute heart failure, trauma, haemorrhage, sepsis burns, peritonitis or blackwater fever; low cardiac output (ischemic heart disease or cardiomyopathy leading to congestive cardiac failure) or severe arterial hypoxaemia due to obstructive sleep apnoea [3]. Similar ischemic changes may follow cessation of hepatic blood flow during the course of hepatic transplantation or tumour resection [4]. Ischemic hepatitis is the most frequent cause of elevated serum transaminases and prolonged prothrombin time in hospitalised patients [5].

Pathologic changes are related to duration of shock. Basic pathology remains reduction in liver blood flow or reduced oxygen content of the blood. This leads to anoxia and necrosis of centrilobular cells. The centrilobular or zone 3 cells receive blood at a lower oxygen tension than the peripheral cells and are most vulnerable to ischemic insult. In addition, hepatotoxic action of the inflammatory mediators also contribute to the injury [6]. Tissue damage also occurs during reperfusion when there is flux of oxygen radicals. These initiate lipid peroxidation with disruption of membrane integrity. Liver dysfunction is associated with depression of phagocytic action of Kupffer cells which permits systemic spread of endotoxin and inflammatory mediators and thus may predispose to multiple organ failure. The left lobe of liver may suffer more than the right.

Clinical picture of ischemic hepatitis simulates that

of acute viral hepatitis. There is marked elevation of AST, ALT and LDH but bilirubin, alkaline phosphatase, gamma-glutamyl transferase and prothrombin time are slightly abnormal. Liver function returns to normal within 5-10 days with correction of underlying cause. An elaborate work-up or invasive procedure is redundant [5]. If the cause is not corrected or if the liver has been previously damaged, acute ischemic/hypoxic insult may lead to picture of fulminant hepatic failure. Mortality is high (58.6%) and depends on the underlying cause and not the liver injury [5,7]. Management is non-specific but prompt resuscitation, correction of underlying cause, definitive treatment of sepsis and meticulous supportive care are likely to reduce the incidence and severity.

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