Case Report

Hepatitis B induced fulminant liver failure: A call for prevention

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ABSTRACT

Acute fulminant hepatic failure is a condition in which a healthy liver deteriorates rapidly following an insult, resulting in the impairment of its synthetic functions. This condition is rare and is associated with high fatality rates. We report the case of a 19-year-old male who was brought to the emergency room in an unconscious state with jaundice and persistent fever for 2–3 weeks after recently commencing intravenous use of morphine. He was found to be hepatitis B surface antigen reactive, and his laboratory tests indicated severe liver dysfunction with elevated levels of serum bilirubin, aspartate transaminase, alanine transaminase, gamma-glutamyl transferase, and International normalized ratio. The patient was diagnosed with fulminant liver failure with coagulopathy and hepatic encephalopathy. The patient's family was addressed and counseled regarding the urgent need for liver transplantation. However, due to a lack of funds and insurance, supportive treatment was the only option left. Despite all supportive measures, the patient expired within 48 h. This case highlights the importance of various socioeconomic issues involved with liver transplantation, as in a resource-limited setting, urgent transplantation seems nearly impossible. In addition, this case report raises certain ethical issues that need consideration, particularly in an injection drug use scenario. It also highlights the importance of addressing the rising issue of injection drug use among youth, particularly in the regions of Punjab.

Key words: Fulminant liver failure, Hepatitis B, Injection drug use, Liver transplantation

In India, the prevalence of Hepatitis B virus (HBV) in the general population is 2.4% [1]. HBV is transmitted through horizontal transmission (sexual route and parenteral route) and vertical transmission. Sexual transmission occurs when bodily fluids come into contact with broken skin or mucous membranes. Parenteral transmission occurs through contaminated needles that come into contact with the blood of the infected person, blood transfusions, and organ transplants. Studies suggest that HBV in India is mainly transmitted horizontally [1]. According to the report by the all India institute of medical sciences, the most often utilized drug is alcohol, followed by marijuana, and opioids [2]. Approximately, 2.1% of people are reported to use opioids, with heroin use accounting for 1.14% of this total, pharmaceutical opioid use coming in at 0.96%, and opium use at 0.52% [2]. India is reported to have a thrice higher rate of opioid use than the rest of the world [2]. The state with the most injection drug users is Uttar Pradesh, with 100,113 persons who inject drugs (PWID), followed by Punjab with 88,165 PWID, and Delhi with 86,909 PWID [3].

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Most of the cases of Hepatitis B remain asymptomatic or develop mild inflammation, which resolves in a few weeks to months. However, 5% of adults and 90% of infants develop chronic hepatitis, and only 0.5% of adults develop fulminant hepatitis [4]. Fulminant hepatic failure (FHF) is an acute condition with a high fatality rate. It is characterized by massive necrosis of hepatocytes, leading to liver dysfunction, which can result in jaundice, coagulopathy, thrombocytopenia, metabolic derangements, and hepatic encephalopathy. FHF can be categorized as hyperacute (encephalopathy occurring within 7 days of the onset of jaundice), acute (encephalopathy occurring between 8 and 28 days), or subacute (encephalopathy occurring between 5 and 12 weeks) [5]. To meet the criteria for FHF, a patient should have two of the three: bilirubin >10 mg/dL, International normalized ratio (INR) >1.6, and signs and symptoms of hepatic encephalopathy. These patients need antiviral treatment [6] and surgical intervention in the form of liver transplantation. However, liver transplantation is associated with several socioeconomic, donor-related, and ethical challenges that need consideration.

In this case report, we shall discuss the case of a 19-year-old male with fulminant liver failure secondary to Hepatitis B infection due to injection drug use, highlighting the pathophysiology of the disease,

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ethical challenges in the management of fulminant liver failure, and the growing issue of injection drug use in the youth of Punjab.

CASE PRESENTATION

A 19-year-old daily wage laborer was brought to the emergency room in an unconscious state with chief complaints of fatigue, yellow discoloration of the eyes and skin, and fever for 2–3 weeks. His condition worsened 3–4 days ago when he felt dizzy and disoriented and started experiencing altered mental status. According to his family, the patient had been using injection drugs for 1 month and smoking for 1 year. There was no history of alcohol consumption. His family denied any recent travel or prior illness. According to them, the patient was unmarried and sexually inactive. He had no history of blood transfusions in the past.

On examination, the patient was somnolescent and responded only to painful stimuli with eye-opening. He did not respond to verbal or tactile stimuli. His Glasgow coma scale (GCS) score was 5. His examination findings were suggestive of Grade 3 encephalopathy. He had severe jaundice with yellow discoloration of the sclera and skin. On abdominal examination, the liver was palpable at two fingers below the right costal margin.

The laboratory results showed an abnormal liver function test with significantly increased levels of total bilirubin, aspartate transaminase, alanine transaminase, alkaline phosphatase, gamma-glutamyl transferase, and INR (Table 1). The patient was found to be positive for hepatitis B surface antigen and negative for anti-hepatitis C virus antibody and anti-HIV antibody. His complete blood counts showed an elevated total leukocyte count of 18,600/cmm with neutrophilic predominance.

The patient was diagnosed with fulminant liver failure secondary to hepatitis B infection with Grade 3 hepatic encephalopathy and coagulopathy. He was shifted to the intensive care unit after admission. Due to his poor GCS, he was intubated and started on mechanical ventilation. He was started on supportive therapy, including intravenous fluid, inotropes, vasopressors, and an anti-hepatic coma regimen consisting of L-Ornithine L-Aspartate, lactulose, and rifaximin. Persistent bradycardia (in the 50s) was present, which was suggestive of increased intracranial pressure, and therefore, a bolus of mannitol was given at 1.25 g/kg. The patient was also administered 4 units of fresh frozen plasma. His blood sugar levels and electrolytes were monitored at regular intervals and managed accordingly. His model for end-stage liver disease score was 40, predicting a poor prognosis without liver transplantation.

The patient's family was addressed and counseled regarding the urgent need for liver transplantation. However, due to their poor financial condition and lack of funds and insurance, they refused to take the patient to a transplant center and insisted on continuing with the supportive therapy. Regardless of all the possible interventions by the medical and intensive care teams, the patient's condition deteriorated further to the stage of coma and Grade 4 encephalopathy. Despite all supportive measures, the patient expired within 48 h.

Table 1: Laboratory parameters of the patient

Lab parameter	Result	Normal range
TLC	18,600/cmm	4000–11,000/cmm
Polymorphs	77%	40–75%
RBC count	5.7 lacs/cmm	4.5–5.5 lacs/cmm
MCV	75.8 fL	77–93 fL
MCHC	36.6 g/dL	31–35 g/dL
PT	51.2 seconds	13.1–15.3 s
Total bilirubin	40.7 mg/dL	0.2–1.2 mg/dL
Direct Bilirubin	21.2 mg/dL	
AST	2246 U/L	10–35 U/L
ALT	1765 U/L	10–40 U/L
ALP	263 U/L	44–147 U/L
GGT	121 U/L	5–40 U/L
INR	3.99	0.9–1.L
BUN	13 mg/dL	5–20 mg/dL
Serum creatinine	1.6 mg/dL	0.6–1.3 mg/dL.
Sodium (Na)	139 mmol/L	135–145 mmol/L
Potassium (K)	4.3 mEq/L	3.5–5.2 mEq/L
HBSAGRT	Reactive	Non-reactive
AHCVAb	Non-reactive	Non-reactive
AHIVAB	Non-reactive	Non-reactive

INR: International normalized ratio, TLC: Total leukocyte count, MCV: Mean corpuscular volume, MCHC: Mean corpuscular hemoglobin concentration, PT: Prothrombin time, AST: Aspartate transaminase, ALT: Alanine transaminase, ALP: Alkaline phosphatase, GGT: Gamma-glutamyl transferase, BUN: Blood urea nitrogen, HBSAGRT: HBsAg rapid test, AHCVAb: Anti-HCV Ab rapid test, AHIVAB: Anti-HIV Ab rapid test

DISCUSSION

Two mechanisms of liver injury contribute to acute liver failure (ALF): Direct damage and immune-mediated damage. HBV causes liver damage through the immune-mediated pathway. Just like septic shock, ALF also displays immune paralysis, in which there are opposing pro- and anti-inflammatory cytokines [7]. Many studies have shown circulating inflammatory cytokines in ALF, such as tumor necrosis factor (TNF)-α, interleukin (IL)-1, IL-6, and IL-8 [7]. Furthermore, death receptors associated with the liver such as Fas (CD95), TNF-R1, and TRAIL-R work by engaging with their corresponding ligands (Fas-L, TNF-α, and TRAIL) and causing apoptosis [7]. HBV-specific CD8+T cells also have a role, as they may directly kill virus-infected hepatocytes and contribute to liver injury [7]. In ALF due to Hepatitis B, the liver shows portal and lobular inflammation with irregular areas of hepatocyte ballooning and necrosis. This necrosis may become confluent while bridging from lobule to lobule and may become multilobar [8]. This may result in a complete shutdown of the liver's synthetic function and, at the same time, involve other organ systems that may result in rapid deterioration in the patient.

The management of these patients is best done in a transplant center by a multidisciplinary team of health-care providers [9,10]. However, supportive management such as fluid administration, inotropes, vasopressors, and ventilator support becomes critical until a transplant option is available. Furthermore, ALF patients may have complications such as bleeding, acute kidney injury,

infections, and intracranial hypertension, which should be treated accordingly [11]. However, these interventions may not prove beneficial in the setting of multiorgan failure. Hence, the single most important intervention in hepatitis B-related ALF to consider is timely liver transplantation. Patients who receive liver transplants have 1- and 5-year survival rates of approximately 84% and 75%, respectively [10]. However, in a resource-limited setting, LT can have several restrictions, such as limited funds, no insurance, donor-related problems, and severe clinical deterioration (e.g., uncontrolled sepsis), severe comorbidities, and substance abuse [11].

Many ethical dilemmas may need to be resolved while considering a transplant. First, a psychological assessment of the patient is not possible in such cases, and the patient's familial relationship can influence the decision for transplantation [12]. Second, in a patient with injection drug use, compliance with the treatment and abstinence from drug use following a transplant cannot be determined [12]. Hence, to consider it, a contraindication to transplantation is ethically challenging [12]. Therefore, a clear rationale may be required to overcome such ethical issues. In this view, it is vital to discuss that one of the important aspects of Hepatitis B infection spread in India, particularly in the Punjab region, is the use of injection drugs, where it is observed that every third person is using drugs other than tobacco and alcohol [13]. The prevalence of heroin abuse has increased over time [13,14]. Easy access to morphine and a lack of education is among the other culprits in drug use [13]. Most of the youth who indulge in injection drug use come from lower socioeconomic backgrounds. It is ironic that they can get access to drugs such as heroin but do not have enough funds when it comes to acquiring medical facilities. Another issue that needs to be addressed is the lack of education regarding infections spread by sharing needles. Although the state government has banned the sale of syringes without a prescription [15], it is important to search for loopholes in the system. One important question that needs clarification is whether the banning of non-prescription syringes has led to increased needle sharing among drug abusers.

CONCLUSION

Fulminant liver failure following hepatitis B infection is rare and requires liver transplantation for survival. However, liver transplantation is influenced not only by medical guidelines but also by the availability of grafts, affordability, and ethical issues. The lower-class population of society is adversely affected due to a lack of funds and education and the high prevalence of injection drug use. This puts the population at high risk of the infection spreading. Hence, the prevention of viral hepatitis seems to be the best cure so far.

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