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Hyperglycaemia as an indicator of concurrent acute pancreatitis in fulminant hepatic failure associated with hepatitis B infection

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ABSTRACT

Pancreatitis occurring concurrently with fulminant hepatic failure (FHF) is primarily detected on autopsy and is seldom clinically apparent. We report a fatal case of FHF in a 25-year-old woman which was related to acute hepatitis B infection. In this patient, hyperglycaemia needing insulin infusions led to the detection of acute pancreatitis. FHF complicated by acute pancreatitis has a poor prognosis. A high index of suspicion is necessary for its diagnosis. The role of orthotopic liver transplantation and use of antiviral therapies need further evaluation in this situation.

Keywords: fulminant hepatic failure, hepatitis B, hyperglycaemia, pancreatitis

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INTRODUCTION

Pancreatitis due to hepatotropic viruses is uncommon. The diagnosis of pancreatitis is made post mortem in most cases of fulminant hepatic failure (FHF). Asymptomatic pancreatitis has however been noted in over one-third of patients with FHF at autopsy[1,2]. There are a few case reports of symptomatic pancreatitis in the setting of acute viral hepatitis[3]. We report a fatal case of FHF related to acute hepatitis B infection where hyperglycaemia needing insulin infusion led to the detection of acute pancreatitis.

CASE REPORT

A 25-year-old woman presented with a two week history of fever with malaise and a one week history of jaundice. She had been delirious, agitated and finally stuporous over the last two days and was admitted into the medical intensive care unit. There was no past history of jaundice, surgical intervention, transfusion or recent drug intake. She did not consume alcohol, have a history of trauma or family history of pancreatitis. On examination, she was deeply icteric, stuporous but responding to painful stimuli (Glasgow coma scale score 6/15). Her pulse rate was 112 beats per minute and she was normotensive. Abdominal examination revealed a liver span of two intercostal spaces and no free fluid. Bowel sounds were sluggish.

Investigations revealed a haemoglobin level of 12.9 g/dL and her prothrombin time was markedly elevated (international normalised ratio 4.89). She had an elevated total bilirubin (11.5 mg/dL) and markedly raised transaminases (AST 3200 IU/L and ALT 3400 IU/L). Her hepatitis B surface antigen (HbsAg) and immunoglobulin M (IgM) antibodies to core antigen of hepatitis B (IgM core) were positive. Serology for hepatitis A (IgM HAV) and hepatitis E (IgM HEV) were negative. Blood smears for malarial parasites were negative.

After admission, she was noted to have high plasma glucose (random plasma glucose ranged from 307 mg/dL to 399 mg/dL) and needed up to 5 units/hour of regular human insulin infusion to keep her glucose levels under control. She was not on total parenteral nutrition or hyperosmolar dextrose infusions at this time. Concurrent pancreatitis was suspected and confirmed by an elevated amylase (1318 IU/L) and lipase (810 IU/L). Values were repeated the next day, and the amylase (1640 IU/L) and lipase (840 IU/L) were still found to be elevated.

A portable ultrasonographical examination of her abdomen revealed no gallstone and a normal liver. The pancreas was suboptimally visualised. Computed tomography of the abdomen was not feasible as the patient was unstable and could not be shifted out for the procedure. Despite maximal supportive therapy, including ventilatory support, she succumbed to her illness and died 72 hours after admission. A post-mortem percutaneous trucut liver biopsy showed features of massive hepatic necrosis consistent with a diagnosis of FHF. The relatives did not give consent for an autopsy.

DISCUSSION

Asymptomatic, clinically-unsuspected acute pancreatitis detected on autopsy in patients with FHF has been noted in 33%[1] and 36%[2] of patients. A prospective study involving 60 patients with FHF found

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hyperamylasaemia in 14, of which 11 had autopsy and pancreatitis was confirmed in 10[2]. It is interesting that pancreatitis in FHF is not suspected clinically but is usually an autopsy finding. In our patient, the presence of unexpected hyperglycaemia needing insulin infusion led to the diagnosis of acute pancreatitis. Spontaneous hypoglycaemia is often seen in FHF and is probably due to decreased ability to mobilise already-depleted glycogen stores and decreased gluconeogenesis[4]. Hyperglycaemia is often seen in the first few days of acute pancreatitis and improves once the pancreatitis resolves[5].

The mechanism for acute pancreatitis in the setting of FHF has been postulated to be because of a high concentration of free radicals in FHF, altered coagulation profile and presence of multiple thrombi or areas of haemorrhage in the pancreas, a component of multi-organ failure or due to the hepatitis virus infection itself[6]. The aetiology of acute pancreatitis in our case was considered to be HBV infection as there were no gallstones on ultrasonography, no history of alcohol abuse, or intake of drugs or trauma. The calcium levels were normal and her triglyceride levels were 56 mg%. The temporal profile also suggests a relationship between the two processes.

The mechanisms by which hepatitis B virus (HBV) can cause acute pancreatitits are unknown. In humans, the pancreas can be infected haematogenously or by contamination with biliary juice containing HBV[7]. HBV has been detected in pancreatic juice[8], which is secondary to replication in pancreatic acinar cells as hepatitis B viral antigens have been detected in the cytoplasm of pancreatic acinar cells[7]. Chronic HBV carrier patients have a much higher incidence of hyperamylasaemia post-liver transplant than HBV negative patients[9]. Suppressing HBV replication with lamivudine has been useful in a single case of recurrent pancreatitis associated with chronic hepatitis B infection[10]. This suggests that the HBV infection could have a role in causing pancreatitis.

Acute pancreatitis has been noted to be a poor prognostic factor when complicating acute exacerbation of chronic hepatitis B infection[11] and is associated with significantly greater mortality in patients with FHF[12]. The potential implications of this in planning liver transplantation in patients with FHF are unclear, but it has been suggested that orthotopic liver transplantation may not be warranted in the setting of concurrent acute pancreatitis and FHF[12]. Clinically-evident acute pancreatitis occurs rarely in patients with HBV-related FHF and requires a high index of suspicion. The reasons for this are unclear. The pathogenesis of pancreatitis in these patients needs to be elucidated. The literature suggests that patients with FHF and concurrent pancreatitis have a poor prognosis. The implications of this in strategies for liver transplantation need to be evaluated. It is unclear if antiviral drugs will suppress replication in extrahepatic sites and improve prognosis. As lamivudine has shown benefit in one report[10], the use of antiviral therapy in this setting needs further evaluation.

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