Case Report

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Gallbladder Sludge and Acute Pancreatitis Induced by Acute Hepatitis A

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Key Words

Infection · Hepatitis A, acute · Pancreatitis, acute · Gallbladder sludge · Hepatic enzymes

Abstract

In this case report, a young woman with gallbladder sludge and acute pancreatitis due to acute hepatitis A (HAV) is presented. She was admitted to our hospital with abnormal hepatic enzymes. Five days prior to her admission, an initial abdominal ultrasound was performed at another hospital and revealed no abnormality, while her serum aspartate aminotransferase (AST) level was at the upper limit of normal (ULN) × 8. A second ultrasound was performed at our hospital and revealed a gallbladder wall thickness (9.3 mm), gallbladder sludge in the gallbladder lumen, pancreatic edema, ascites, and hepatomegaly while AST was at the ULN × 50. Magnetic resonance imaging and magnetic resonance cholangiopancreatography revealed imaging features of an acute stage of pancreatitis and gallbladder wall thickness with coexisting sludge in the gallbladder lumen. HAV infection was diagnosed by the detection of immunoglobulin M against HAV in the serum. The patient underwent two repeated abdominal ultrasound examinations on the 5th (AST was at the ULN × 3) and the 20th days (AST was at the normal) after her discharge, and both revealed normal findings. In our case, we observed reversible changes in the hepatobiliary and pancreatic system which was related to the severity of hepatic necroinflammation. HAV-associated pancreatitis may be due to the formation of biliary sludge during the acute phase of the viral illness, but this association needs further investigation.

Acute pancreatitis is usually associated with gallstones and alcohol consumption in adults [1, 2]. In the current literature viral infections have rarely been reported as a cause of acute pancreatitis [3]. In this article, we present the case of a young woman with gallbladder sludge and acute pancreatitis induced by acute hepatitis A (HAV). A brief literature review of the cases of acute pancreatitis due to HAV follows and includes discussion of the possible underlying mechanisms.

Case Report

A 20-year-old woman was admitted to our hospital with fatigue, jaundice, abdominal pain, nausea, and vomiting. There was no history of alcohol intake, ingestion of any form of drug, herbal medicine or smoking. She was not on a diet or oral contraceptives and not sexually active. She had no prior history of jaundice, hepatitis,

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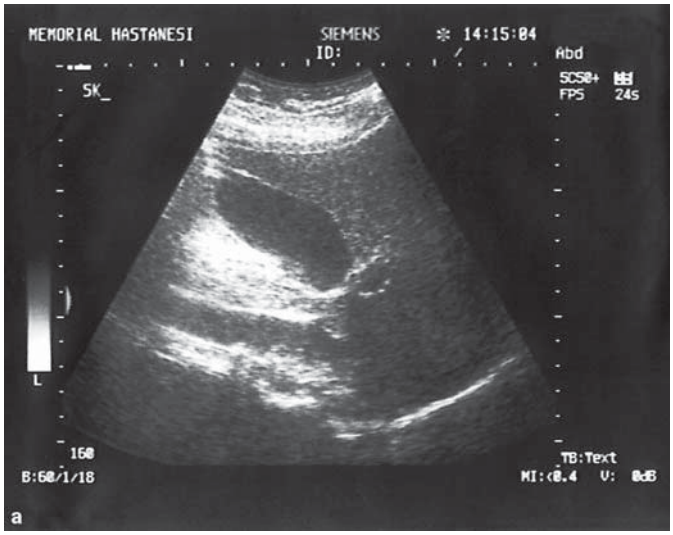

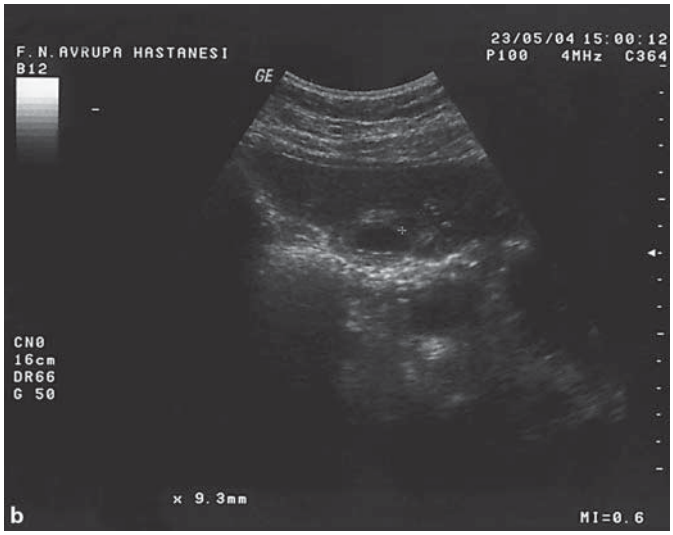

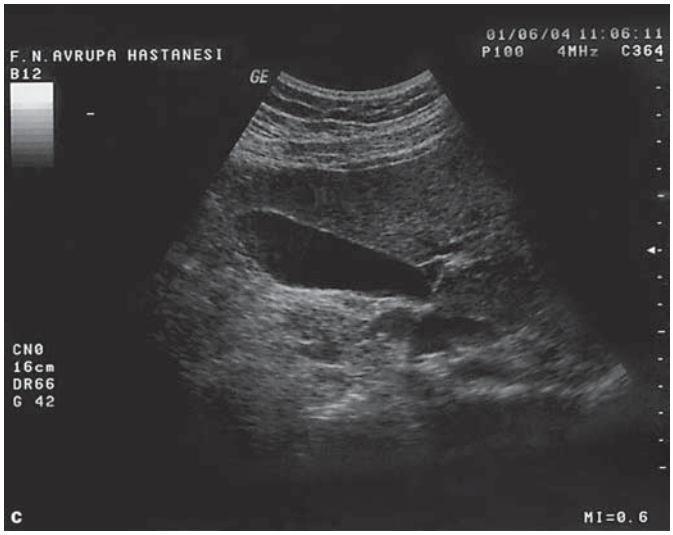

parasitic infections, gallstones, peptic ulcer or abdominal trauma. She also did not describe any recent traveling outside her home country, a dental examination, blood transfusion or surgery for the last 6 months. There was no family history of hepatitis, parasitic infection or gallstones.

She had gone to another hospital with nausea and fatigue 5 days prior to being admitted to our hospital. Her serum aspartate aminotransferase (AST) value was at the upper limit of normal (ULN) × 8 [AST 306 (normal < 31) IU/l; alanine aminotransferase (ALT) 339 (normal <32) IU/l; γ-glutamyltransferase (GGT) 45 (normal 11–50) IU/l]. Serum triglyceride and cholesterol levels and urinalysis were all normal. Abdominal ultrasound revealed no pathology (fig. 1a). The patient was sent home to rest without any medication. Two days later, a sudden onset of abdominal pain, jaundice, and vomiting was observed. She was then referred to our hospital for further investigations.

On physical examination, she had mild jaundice, moderately decreased bowel sounds, epigastric and umbilical tenderness, and a tender liver palpable 1.5 cm below the right costal margin in the mid-clavicular line. She was overweight with a body mass index of 28. There was no fever, rash or any chronic liver disease stigmata. Laboratory evaluations revealed hemoglobin of 12.5 g/dl, white blood cell count of 2,800/mm^3, with 44% neutrophils and 56% lymphocytes, and platelet count of 168,000/mm^3. The erythrocyte sedimentation rate was 16 mm/h. Urea and creatinine were 13 and 0.7 mg/dl, respectively. Her serum liver function tests and pancreatic enzymes were all elevated (AST 1,850 IU/l; ALT 2,890 IU/l; alkaline phosphatase (ALP) 612 IU/l; total bilirubin 3.96 mg/dl, and amylase 443 IU/l). Hepatitis A virus immunoglobulin M was positive. Viral serology screen was negative for hepatitis B surface antigen, hepatitis B core immunoglobulin G and M, anti-hepatitis C virus and anti-HIV. The following laboratory tests were within normal limits: serum albumin, globulin, α_1-antitrypsine, cholesterol, triglyceride, fasting sugar, sodium, calcium, magnesium, immunoglobulin levels, and prothrombin time and the international normalized ratio of prothrombin time. Results of autoantibody tests (smooth muscle antibodies, antibodies to liver/kidney microsome type-1, mitochondrial antibodies and antinuclear antibodies) and the Venereal Disease Research Laboratory test for syphilis were also negative.

Upright abdominal X-ray showed no abnormality. Abdominal ultrasound revealed gallbladder wall thickening (9.3 mm) and irregularity of the gallbladder internal echo, biliary sludge and edema of the pancreas while AST was measured at ULN × 50 (fig. 1b). Magnetic resonance imaging and magnetic resonance cholangiopancreatography were performed and showed the same features (fig. 2). Liver function tests and pancreatic enzymes were elevated (AST 1,620 IU/l; ALT 2,500 IU/l; ALP 411 IU/l; GGT 520 IU/l; total bilirubin 3.6 mg/dl; amylase 167 IU/l, and lipase 509 IU/l).

Fig. 1. Abdominal ultrasound revealed: no abnormality initially while AST was at the ULN × 8 (**a**); gallbladder wall thickening (9.3 mm) and irregularity of the gallbladder internal echo like carcinoma of the gallbladder, sludge in the gallbladder and both edema and enlargement of the pancreas while AST was at the ULN × 50 (**b**); no abnormality while AST was at the ULN × 3 (**c**).

She was closely monitored. Because oral intake provoked her vomiting, oral feeding was stopped and aggressive intravenous fluids, electrolytes, protein solutions and a proton pump inhibitor were all started. The patient gradually recovered, and watery oral feeding was started without fat on the 3rd day. A diet with fat was allowed on the 4th day. Improvement in hepatic and pancreatic enzymes was observed on the 5th day of hospitalization and the patient was discharged.

Five days after her discharge while the AST value was ULN × 3, she had no complaints and her physical examination was normal. The pancreas and gallbladder were within normal limits on abdominal ultrasound (fig. 1c). Twenty days later, abdominal ultrasound revealed no pathology and AST was normal.

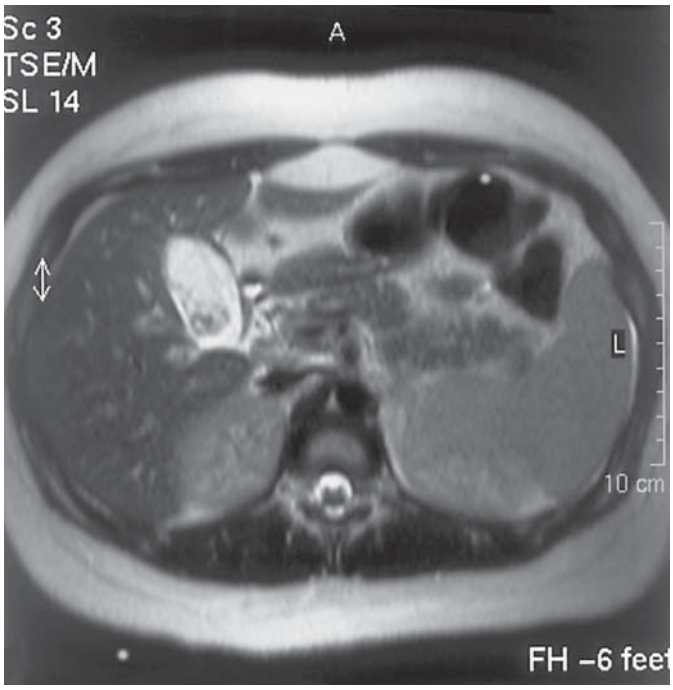

Fig. 2. Magnetic resonance imaging revealed gallbladder wall edema, biliary sludge in the lumen of the gallbladder, perihepatic and perisplenic minimal amount ascites, decreased pancreatic gland signal and arterial capillary phase contrast enhancement of the pancreatic corpus and particularly of its tail compatible with acute pancreatitis.

Discussion

Although different kinds of viruses such as A, B, C, and E have been reported as causes of acute pancreatitis, they are still uncommon conditions [3–9]. The pathogenesis of this kind of pancreatitis has yet not been fully understood. There are some theories such as edema of the ampulla of Vater and pancreatic ducts, immunologic or autoimmune mechanisms, and direct viral destruction of the pancreas [10].

Acute pancreatitis induced by HAV is usually mild or moderate in clinical severity and its response to conservative therapy is always satisfactory. Furthermore, problems related to acute pancreatitis, such as pseudocyst, abscesses, chronic pancreatitis and recurrence of pancreatitis, have never been reported. This kind of pancreatitis could be seen in all stages of HAV, even after resolution of hepatitis. In our case, abdominal pain and jaundice were observed simultaneously. Then, acute pancreatitis was diagnosed by further tests (elevated pancreatic enzymes, abdominal ultrasound, magnetic resonance imaging, and magnetic resonance cholangiopancreatography). Clinical and laboratory recovery of the pancreatitis occurred immediately together with acute hepatitis resolution.

In this case, initial abdominal ultrasound revealed no abnormality regarding the gallbladder and pancreas while inflammation of the liver was moderate (AST was at ULN × 8). Then, marked gallbladder wall changes (thickening), gallbladder sludge formation and acute pancreatitis signs were observed together with an increase in hepatic inflammation and necrosis (AST was at ULN × 50). The difference in ultrasound findings regarding sludge formation and gallbladder wall edema may be explained by the increased dysmotility of the gallbladder during the increase phase of hepatic inflammation. Ultrasound is an operator-dependent imaging modality, that also needs to be considered as a possible failure in the initial examination of our case. Thickening of the gallbladder wall in patients with acute hepatitis, as in our case, has been reported previously [11–13]. As opposed to previous studies, we observed that there was also a correlation between these changes and the severity of liver necrosis and inflammation. Furthermore, we also observed sludge in the gallbladder lumen during the course of the HAV. Our thesis for these observations is that decreased gallbladder muscle contractions due to the inflammation and edema of the organ (gallbladder wall thickening), inhibition of the general activity of the patient, and diet changes with starvation due to nausea and other problems of acute hepatitis may have caused the precipitation of cholesterol into solid crystals and biliary sludge formation in the gallbladder lumen.

Biliary sludge can appear, disappear, and reappear [14–16]. Its formation is a dynamic, reversible process. Hepatitis A may induce hypomotility and/or dysmotility of the gallbladder that may lead to sludge formation as observed in our case. A partial blockage to the flow of bile

may occur when sludge blocks any part of the biliary ductal system. If the common channel or pancreatic duct is obstructed by sludge, pancreatic juice and/or bile reflux into the pancreatic duct may occur. This may explain the onset of the acute pancreatitis attack in our case. Clinical conditions and events associated with the formation of biliary sludge include rapid weight loss, pregnancy, ceftriaxone therapy, octreotide therapy and bone marrow or solid organ transplantation [17–19]. In the presented case, there was no associated condition as mentioned above.

All the changes described regarding the biliary system and pancreas resolved with the recovery from the hepatitis in our patient. These observations lead us to consider that gallbladder sludge formation during the acute phase of HAV might be a cause for the development of acute pancreatitis as well as the other factors mentioned above.

This idea should be verified by further well-designed, prospective studies in which several patients are followed up from the very beginning of the HAV infection with abdominal ultrasound demonstrating biliary sludge formation and the correlation of gallbladder wall changes with pancreatitis.

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