Pancreatic Involvement in Non Fulminant Acute Viral Hepatitis

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ABSTRACT

BACKGROUND: Biliary pathology and alcoholism are responsible for 70 to 80% cases of acute pancreatitis. Viral etiology is not uncommon.

OBJECTIVE: To study association of nonfulminant acute hepatitis with acute pancreatitis.

METHODS: We undertook a prospective study over 3 years from Jan 2009 to Dec 2011, during which 950 patients got admitted as acute pancreatitis.

RESULTS: Four patients (4.2%) were diagnosed with acute pancreatitis which developed after acute hepatitis. All patients were young (15-36 years); three males and one female. Two patients had pancreatitis in first week and two in third week, after onset of jaundice. Three patients had mild pancreatitis and one had severe pancreatitis. The etiology of pancreatitis was hepatitis A in two, and hepatitis E and hepatitis B in one each. All patients were managed conservatively and recovered completely.

CONCLUSIONS: Association between acute pancreatitis and acute viral hepatitis is now more frequently recognized; more commonly in young males, between 1st and third week of hepatitis illness. JMS 2012;15(1):44-46.

Key Words: Pancreatitis, Acute hepatitis, Hepatotrophic virus

Common causes of acute pancreatitis worldwide are biliary pathology and alcoholism accounting for 70 to 80% of cases.¹ Although hepatitis viruses have a strong tropism for hepatocytes, viral antigens have also been detected in other tissues such as the pancreas and gall bladder.² Several viral infections have been implicated as an etiological factor of acute pancreatitis. The viruses most frequently responsible are Mumps virus, Coxsackie B virus, Epstein-Barr virus, varicella zoster and Measles virus.^{3,4} Fulminant hepatic

failure (FHF) pancreatitis occurs in up to 34% of the cases, although in non-fulminant hepatitis it is considered rare.^{5,6} Acute pancreatitis is not uncommon in fulminant hepatic failure (FHF) and has been confirmed based on histology or serology.^{7,8} It has been reported with hepatitis A (HAV), hepatitis B (HBV) and non-A-non-B (blood-borne) and hepatitis E virus (HEV) infection.^{9,10}

The aim of present study was to determine the occurrence, characteristics and outcome of acute pancreatic involvement in the course of non fulminant acute viral hepatitis.

Methods

This was a prospective study conducted in department of Gastroenterology of Sher-i-Kashmir Institute of Medical Sciences over 2 years from Jan 2010 to Dec 2011. During this

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period 950 patients got admitted as acute pancreatitis. Acute pancreatitis was diagnosed on the basis of pancreatic type of pain, high biochemical marker (amylase, lipase) with ultrasound abdomen (US) and or contrast enhanced computed tomography (CECT) abdomen suggestive of acute pancreatitis. Patients were treated with intravenous fluids, analgesics and other supportive treatment. Etiological profile for acute pancreatitis was ascertained by taking history of alcohol intake, abdominal trauma. Serum calcium and triglyceride levels were done to rule out metabolic cause of acute pancreatitis. US abdomen, CECT abdomen, viral serology for hepatic viruses was done. Stool examination for egg of ascariasis was also done to ascertain etiology of pancreatitis.

Results

Of these 950 patients only 4 patients were diagnosed as acute pancreatitis were associated with acute viral hepatitis. The mean age was 27.5 years(range 15-36), there were 3male and one female patient All 4 patients presented at admission with pancreatic type of pain with high amylase mean1421(range 654-2156)u/l, serum lipase mean 730(560-1500)u/l. All patients had US, CECT abdomen and Magnetic resonance imaging (MRI) suggestive of acute pancreatitis with normal hepatobiliary system. All 4 patients were non alcoholic with normal serum calcium and triglyceride level. There was history of viral hepatitis present in all 4 patients, one to three weeks before present admission and all patients were having jaundice at presentation. Two patients were evaluated prior to their admission and were positive for hepatitis A (IgM Anti- HAV) and second positive for hepatitis E (IgM Anti- HEV). Among other two patients one was found to be positive for hepatitis A (IgM Anti- HAV) and other positive for acute hepatitis B infection (HBsAg, IgM Anti- HBc). Mean bilirubin was 22(range12-35) mg/dl, mean AST402 (range156-567) u/l mean ALT 496(range 300-750) u/l, mean ALP 238(range 175-300) u/l. All patients were negative for other viral and etiological profile for acute pancreatitis. Two patients had pancreatitis in Cholestatic phase and other two in acute phase of acute hepatitis. Three patients were having mild and one had severe pancreatitis. All 4 patients were managed conservatively for acute pancreatitis and hepatitis. All patients had benign course of illness and recovered. Patients were discharged in good health within average of 6 days. On follow up all patients had normal liver function tests with seroconversion of hepatitis B. (Table 1)

Discussion

The etiology of pancreatitis in our series was considered to be due to a hepatitis virus in all patients, as there was no evidence of gallstones, sludge, alcohol, drugs, trauma or metabolic causes in all our patients with only viral serology positive, however incidence of acute pancreatitis was very low in our series.

Table 1. Shows clinical and laboratory profile of patients

	Case 1	Case 2	Case 3	Case 4
Age(Yr)	15	25	34	36
Gender	M	F	M	M
Pain interval after onset of jaundice (weekly)	1	2	3	1
Hepatomegaly (cm below subcostal margin)	3	3	2	2
Etiology	Hepatitis A	Hepatitis B	Hepatitis A	Hepatitis E
Hospital Stay (Days)	5	5	10	5
Recovery	Complete	Complete	Complete	Complete
Bilirubin (mg/dl)	16	12	35	26
AST (IU/L)	156	567	300	588
ALT (IU/L)	300	750	200	734
Alkaline phosphates (IUL)	200	230	320	180
Amylase (IU/L)	2156	1222	654	1654
Corrected serum calcium (mg/dl)	8	9	8	9
Serum triglyceride (mg/dl)	96	124	98	123
US/ CECT/MRI for GB and Biliary Tree	Normal	Normal	Normal	Normal

Viral etiology of pancreatitis is well established. In adults, mumps virus is the most commonly associated with pancreatitis occurring even in the absence of parotiditis.¹¹ In the autopsy series of Ham and Fitzpatrick, 1 of the 42 (33%) patients with ALF had acute pancreatitis,¹² the majority being of viral etiology. Most of the patients reported had presented with symptomatic pancreatitis in the early phase of the hepatitis illness Mishra *et al*⁷ reported 6 patients at wk 2 or 3 after the onset of jaundice. Bhagat *et al* also reported 7 patients of acute pancreatitis due to viral hepatitis.³ Our series had four patients presenting as acute pancreatitis in setting of acute hepatitis. Two patients presented in the first week, one in the second week and one in third week after the onset of jaundice. No patient had biliary sludge or any other biliary abnormality on USG, CECT or MRI.

Acute pancreatitis in nonfulminant acute viral hepatitis covers the full range of clinical severity. Subclinical pancreatic involvement in viral hepatitis may occur more commonly than is appreciated. The pancreatitis in our patients was mild as reported previously.^{7,13,14} One of our patients had severe pancreatitis with necrosis on CECT abdomen with bilateral pleural effusion and minimal ascites, this patient had prolonged course in hospital and was discharged after 10 days. This patient had pancreatitis due to hepatitis A virus.

In other study in India, by Jain *et al*, in 2007, which was designed to determine more accurately the frequency of pancreatic involvement in the course of acute viral hepatitis, found an incidence 5.65% of pancreatitis from 124 patients

with acute viral hepatitis.⁶ In their study all patients were male and hepatitis E related pancreatitis was common, were as in our series there were 3 male and 1 female patients and hepatitis A related pancreatitis was common.

Extrahepatic manifestations of viral hepatitis appear in 6.4% of cases, as shown in a series of 448 cases of viral hepatitis studied in India by Amarapurkar *et al* in 2002. The most common in chronic viral hepatitis were glomerulonephritis, polyarteritis nodosa and cryoglobulinemia. In acute viral hepatitis (AVH), four cases of thrombocytopenia and one case of acute pancreatitis were reported.¹⁵ The mechanism involved on the development of pancreatitis associated to non fulminant hepatic failure is unknown and probably multifactorial. Many hypotheses have been presented, including direct cytopathic effect of hepatitis viruses on acinar pancreatic cells and/or immunomediated aggression against infected pancreatic cells. There are studies demonstrating surface and core antigens of HBV in pancreatic tissue and secretions. Others suggested mechanism is the development of ampulla of Vater edema with consequent obstruction of principal pancreatic duct. Another hypothesis is the release of lysosomal enzyme by inflamed hepatocytes on circulation with subsequent activation of trypsinogens to trypsin from virus-damaged acinar cell membrane.⁸ There is no direct evidence of the way by which the viruses reach the pancreases, however blood-stream and biliary secretions have been proposed a great number of factors could contribute, such as hypotension, infections, drug induced injuries and hepatic failure itself causing intra-pancreatic hemorrhage related to hypoprothrombinemia or disseminated intravascular coagulation.^{3,6,7}

In conclusion, as shown by the three main series published so far acute pancreatitis complicating non fulminant AVH is not as uncommon as previously thought. Our data, along with the review presented, should alert physicians to the diagnosis of pancreatitis caused by acute non fulminant viral hepatitis in patients having disproportionate abdominal pain in the course of disease.

Conclusion

In conclusion, acute pancreatitis is not uncommon. In a patient with acute viral hepatitis. Acute or disproportionate abdominal pain, acute pancreatitis should be kept as a possibility even in cholestasis phase. Acute pancreatitis due to

acute viral hepatitis is usually mild and resolves on conservative management.

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