

## CASE REPORT

### ACUTE PANCREATITIS ASSOCIATED WITH ACUTE VIRAL HEPATITIS: CASE REPORT AND REVIEW OF LITERATURE

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#### SUMMARY

This case report, along with the review presented, describes a patient diagnosed with acute viral hepatitis, who developed a framework of intense abdominal pain and laboratorial alterations compatible with acute pancreatitis. The association of acute pancreatitis complicating fulminant and non-fulminant acute hepatitis virus (AHV) has been reported and several mechanisms have been proposed for this complication, but so far none is clearly involved. As acute hepatitis is a common disease, it is important to stimulate the development of other studies in order to determine local incidence and profile of patients presenting this association in our environment.

**KEYWORDS:** Acute viral hepatitis; Hepatitis A virus; Acute pancreatitis; Hepatitis complications.

#### INTRODUCTION

Biliary lithiasis and alcoholism are responsible for 70 to 80% cases of acute pancreatitis<sup>3</sup>. Infectious causes were first well-documented by LEMOINE in 1905 in a patient with mumps<sup>3</sup>. Nowadays, other viruses such as Coxsackie B, Epstein-Barr virus, measles, influenza A and varicella zoster, have been implicated in acute pancreatitis<sup>3,6,8,10</sup>. In 1944, it was LINSEY who first reported the association between acute pancreatitis and infectious hepatitis<sup>7</sup>. In fulminant hepatic failure (FHF) pancreatitis occurs in up to 34% of the cases, although in non-fulminant hepatitis it is considered rare<sup>3,5,6,8</sup>. This well-known association is more frequently seen when hepatitis is due to hepatitis A (HAV) or hepatitis E (HEV), although cases are reported with hepatitis B (HBV) and C (HCV) infection as well<sup>3,6,8-10</sup>. Non-fulminant hepatitis A complicated with pancreatitis cases are described in Asia and North America, however there are no cases reported in Latin America until this moment.

In this report we present a case of acute pancreatitis complicating non-fulminant acute infectious hepatitis A.

#### CASE REPORT

A 26-year-old woman was admitted in the emergency room with severe epigastric pain with radiation to the back, nausea, anorexia, jaundice, choluria and fecal acholia, 38.5 °C fever, headache and myalgia. Two weeks before, mild symptoms had begun and in the meanwhile,

she was treated with acetaminophen, dipyron, associated carisoprodol + cafein + diclofenac + acetaminophen, cimetidin and omeprazole with partial response. Four days before admission, she presented significant aggravation of symptoms with epigastric pain associated with abdominal distension, nausea, vomit and dyspnea. She had no previous similar episodes, hepatic disease, gallstone, pancreatitis family history, recent travel, trauma, drug abuse, alcoholism or surgery.

Examination revealed a woman with severe jaundice, pallor, and epigastric abdominal pain during superficial palpation, with no peritonitis signs. Her liver was enlarged, exceeding costal margin by 2 cm.

Laboratory investigations showed (Reference ranges of laboratory data are included in parentheses): Hct 33.8% (36.7-46.4%), Hb 11.5 g/dL (12.5-15.7 g/dL), and total leukocyte count of 5,480/uL (3,800-11,000) (band neutrophils 2%, total neutrophils 51%, lymphocytes 38%, monocytes 9%, eosinophils 2%), platelets 352,000/ $\mu$ L (140,000-400,000/ $\mu$ L), total bilirubin 9.58 mg/dL ( $\leq$  1.2 mg/dL) with direct bilirubin of 7.74 mg/dL ( $\leq$  0.25 mg/dL), serum aspartate aminotransferase (AST) 1,285 IU/L (13-35 IU/dL), alanine aminotransferase (ALT) 666 IU/L (7-35 IU/dL), lipase 1,012 IU/L ( $\leq$  200 IU/L), amylase 149 IU/L (20-110UI/L), serum calcium 8.1 mg/dL (9.0-10.8 mg/dL), triglyceride 133 mg/dL ( $\leq$  150 mg/dL), serum alkaline phosphatase 278 IU/L (64-300 IU/dL), gamma-glutamyl transferase (GGT) 270 IU/L (7-32 IU/L), serum albumin 3.6 g/dL (3.5-5.0 g/dL), prothrombin time 13.8 s (INR: 1.15) ( $<$  2.0), erythrocyte

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sedimentation rate (ESR) 31 mm/h (1-20 mm/h), total anti-HBc (-), IgM anti-HBc (-), HBsAg (-), anti-HBsAg (+), total anti-HAV (+), IgM anti-HAV (+), anti-HCV (-). Abdominal ultrasonography showed a contracted gallbladder without lithiasis, normal biliary tree, liver and pancreas, small amount of fluid localized peri-hepatic and in rectouterine pouch. The patient received conservative management with analgesia, hydration and fasting. During follow-up, she remained stable, afebrile and her symptoms regressed within three days. She was discharged on the 6<sup>th</sup> day of admission after significant clinical and laboratory improvement. During ambulatory follow-up the patient presented complete resolution of the symptoms and biochemical results.

## DISCUSSION

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<sup>4</sup>. The relationship between viral hepatitis and acute pancreatitis is recognized for more than 60 years. In the majority of cases, acute pancreatitis occurs as a complication in the course of fulminant hepatic failure (FHF)<sup>3,5,6,8,9</sup>. GEOKAS *et al.* studied this association discriminating between FHF from viral etiology and toxic etiology. They found an incidence of acute pancreatitis of 44% in the first group and only 6% in the later, reinforcing the role of the virus rather than the FHF *per se* on the etiology.

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 & AMARAPURKAR, 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<sup>1</sup>. Another 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 of 5.65% of pancreatitis

from 124 patients with AVH. Analyzing only the group with severe abdominal pain, there was approximately 30% of acute pancreatitis.

BHAGAT *et al.* have recently studied 334 patients presenting with acute pancreatitis. They have found clinical and laboratorial evidence of AVH in seven of them, without any evidence for other causes of pancreatitis, like gallstone disease, alcoholism, drug ingestion, hypertriglyceridemia, hypercalcemia or trauma.

The three main series of cases published totalize 10 cases of hepatitis A and nine of hepatitis E complicated with acute pancreatitis. On the data presented by MISHRA *et al.*, in 1999, all patients were young (average age: 13.5 years), predominantly men (five of six cases), with mild to moderate pancreatitis starting between 10 and 22 days after jaundice onset. Laboratory studies showed at average serum total bilirubin of 15.6 mg/dL, ALT of 810 IU/L and serum amylase of 795 IU/L. On the cases published by JAIN *et al.* there was an average age of 23.9 years, all seven patients were men with mild pancreatitis, and this complication was diagnosed between two and 30 days of jaundice. On average, serum total bilirubin was 16.4 mg/dL, ALT was 1,371 IU/L, serum amylase was 365 IU/L and lipase was 2,495 IU/L. The series presented by BHAGAT *et al.*, in 2008, showed an average age of 19.4 years, six of seven were men, with pancreatitis initiating between three to 17 days after jaundice onset. Laboratory tests presented, on average, serum total bilirubin of 10.7 mg/dL, ALT of 484 IU/L, amylase of 1,264 IU/L and lipase of 1,382 IU/L. Our case presents a 26 year old female with mild pancreatitis starting during the first week of jaundice. Her serum total bilirubin was 9.58 mg/dL, AST was 1,285 IU/L, amylase was 149 IU/L and lipase was 1,012 IU/L. The comparison between our case and these three important series is shown on Table 1.

According to the 2006 guidelines of the American College of Gastroenterology (ACG), the diagnosis of acute pancreatitis requires the presence of at least two of the following: 1) abdominal pain typical,

**Table 1**  
Comparison between published series of acute pancreatitis associated with AVH laboratory tests at patient admission

	MISHRA <i>et al.</i>	JAIN <i>et al.</i>	BHAGAT <i>et al.</i>	Reported case
Age (years, average)	13.5	23.9	19.1	26
Sex (M/F)	5/1	7/0	6/1	F
Jaundice pain interval (days)				3
1. Average	15.3	12.0	12.0	-
2. Range	10 - 22	2 - 30	13 - 17	-
Average serum bilirubin (mg/dL)	15.6	16.4	10.7	9.58
Average serum ALT (IU/L)	810	1,371	483	666
Average serum amylase (IU/L)	795	365	1,264	149
Average serum lipase (IU/L)	-	2,495	1,012	1,012
Etiology				
1. HAV	5	2	3	+
2. HEV	1	4	4	-
3. HBV	-	1	-	-

2) amylase and/or lipase more than three times the normal and 3) characteristic findings on imaging examinations (ultrasonography, abdominal computed tomography - CT, magnetic resonance imaging)<sup>2</sup>.

Though in this patient CT scan was not performed, there was no other explanation to high level of serum amylase and the characteristic abdominal pain observed, which meets two of the criteria above; besides there was an important clinical response to conservative management as analgesia, hydration and fasting indicated to pancreatitis.

Regarding the disparity observed between the values of amylase and lipase, it is known that serum amylase is elevated in two to 12 hours of onset of symptoms and remains elevated for three to five days, while the lipase lasts more than 10 days without permanence of symptoms or development of complications, which could explain these findings.

The mechanisms involved on the development of pancreatitis associated to non-fulminant hepatic failure are 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. Other suggested mechanism is the development of ampulla of Vater edema with consequent obstruction of principal pancreatic duct<sup>3,6,8</sup>. Another hypothesis is the release of lysosomal enzymes by inflamed hepatocytes on circulation with subsequent activation of trypsinogen to trypsin from virus-damaged acinar cell membrane<sup>3</sup>. There is no direct evidence of the way by which the viruses reach the pancreas, however, bloodstream and biliary secretions have been proposed<sup>3,6,8</sup>.

On FHF, 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<sup>3,6,8</sup>.

In conclusion, as showed by the three main series published so far, acute pancreatitis complicating non-fulminant AVH is not as uncommon as previously thought. This case report comes as the first published in Latin America, where there are many endemic areas of acute viral hepatitis, mainly caused by HAV. Similar case was reported, caused by HBV, in another Brazilian region<sup>9</sup>. This report, along with the review presented, should alert physicians to the diagnosis of pancreatitis caused by HAV in patients having disproportionate abdominal pain in the course of AVH. Possibly, it will also stimulate the development of other studies in Latin America in order to determine local incidence and profile of patients presenting with pancreatitis caused by viral hepatitis, although all the cases reported until now have resolved with conservative treatment.

## RESUMO

### Pancreatite aguda associada com hepatite A aguda: relato de caso e revisão da literatura

Este relato de caso, junto com a revisão de literatura, descreve um paciente com diagnóstico de hepatite viral aguda, que desenvolveu quadro de dor abdominal intensa e alterações laboratoriais compatíveis com pancreatite aguda. Casos de pancreatite aguda complicando hepatites virais agudas fulminantes e não fulminantes tem sido esporadicamente relatados e vários mecanismos são propostos para explicar esta complicação, no entanto sua causa ainda se mantém desconhecida. Como a hepatite aguda é doença comum, é importante estimular o desenvolvimento de mais estudos na América Latina que visem determinar a incidência local e o perfil dos pacientes que apresentam esta complicação.

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