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Hemorrhagic Fever with Renal Syndrome Associated with Acute Pancreatitis

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Abstract: Hemorrhagic fever with renal syndrome (HFRS) is a systemic infectious disease caused by Hantaviruses and characterized by fevers, bleeding tendencies, gastrointestinal symptoms and renal failure. It encompasses a broad spectrum of clinical presentations, ranging from unapparent or mild illnesses to fulminant hemorrhagic processes. Among the various complications of HFRS, acute pancreatitis is a rare find. In this report, based on clinical data, laboratory and radiologic examination findings, we describe a clinical case, with HFRS from Dobrava virus, associated with acute pancreatitis. The patient was successfully treated by supportive management. Clinicians should be alert to the possibility of HFRS when examining patients with epidemiological data and symptoms of acute pancreatitis.

Key words: Hemorrhagic fever with renal syndrome (HFRS); Pancreatitis, Dobrava virus

INTRODUCTION

Acute pancreatitis is defined as an acute inflammatory process of the pancreas that may also involve peri-pancreatic tissues. Gallstones and alcohol abuse are the leading causes of acute pancreatitis [1,6,8]. Viral infection is a rare cause of acute pancreatitis including HFRS. Clinical manifestations range from mild epigastric discomfort to critical illness and death. Clinical manifestations are characterized by gastrointestinal symptoms including: nausea, vomiting and abdominal pain. Diagnosis of acute pancreatitis is based on clinical features, biochemical tests and image studies[1,2,6,8]. On the other hand, abdominal pain is also a common initial symptom in patients with hemorrhagic fever with renal syndrome (HFRS). Acute pancreatitis is not commonly associated with HFRS. Hemorrhagic fever with renal syndrome is a systemic infectious disease caused by Hantaviruses and characterized by fever, bleeding tendencies, gastrointestinal symptoms and renal failure [4,7]. The most severe form of HFRS is caused by Dobrava virus

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(DOBV) and Hantaan virus (HTNV) infection. Increased vascular permeability plays a general role in the pathogenesis of severe Hantavirus infection [4]. In this report we describe a clinical case, serologically confirmed with HFRS from Dobrava virus associated with pancreatitis and a good outcome.

CASE PRESENTATION

A 53-year-old male was admitted to the hospital with a history of high fever, abdominal pain, muscle pain, headaches, backaches and chills. The physical examination on admission revealed: temperature was 39.5 °C, blood pressure was 90/50 mmHg, the pulse rate 110/min, and the respiration 20/min. His sclera was with conjunctivitis. Chest radiography was normal. Abdominal ultrasound examination a few hours after admission revealed minimal ascitic fluid. Laboratory findings were as follows:

Elevated liver enzymes (aspartate aminotransferase [AST] 61 U/L, alanine aminotransferase [ALT] 29 U/L), White blood cell count (WBC) 5100/μL, with segments 76.8%, Hematocrit 52.2% (37.0-50.0), Platelet count 102×10^3/μL, Erythrocyte sedimentation rate (ESR) 31 mm/h, Creatinin 1.13 mg/dL, Blood urea nitrogen (BUN) 44.9 mg/dL, Glicemia 168 mg/dL (70-110), C Reactive protein 5 mg/L (0-0.5), Amylasemi 33.4 U/L, Lipasemi 85 U/L, Procalcitonin 0.92 ng/mL (0.5-2). Other routine laboratory values within normal range.

The patient was oliguric with urine volumes less than 24-30 mL/h and the urinalysis showed proteinuria, microscopic haematuria and granular casts. On the next day the patient complained about more abdominal pain, nausea and vomiting(Table 1). Elevated serum amylase and lipase levels, in combination with severe abdominal pain, suggested an initial diagnosis of acute pancreatitis. Computed tomography of the thoraco–abdominal region, revealed small pleural effusions, minimal pericardial liquid, increase of peritoneal liquid and edema of the pancreas and peripancreatic tissues. The patient had no history of alcohol abuse, and we excluded infection of the biliary tree, gallbladder stones, microlithiasis, and hypertrigliceridemia(Fig. 1). We asked him where he had been in the last month and he told us that he had made an excursion to a northeastern mountain in Albania, an area where rodents infected by (DOBV) are found. Based on the clinical manifestation, epidemiologic data, and laboratory parameters, HFRS was suspected. On the following day we tested him for HFRS, Crimean-Congo of hemorrhagic fever (CCHF) and Leptospirosis. These gave positive results, detected by enzyme-linked immunosorbent assay (ELISA), for immunoglobulin M(IgM) antibodies and immunoglobulin G (IgM 1.487, cut-off value <0.8 and IgG 2.215) specific to DOB. An immunofluoreshence assay IFA IgM; IgG was also positive. Screening for CCHF and Leptospira were negative.

The main treatment during hospitalization was supportive therapy: (fresh frozen plasma), manage-ment of the patient's fluid (hydration and that use of

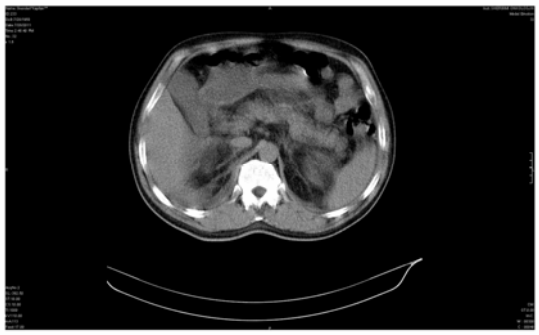

Fig. 1. Abdominal CT. Peritoneal liquid and edema of the pancreas and peripancreatic tissues.

Table 1. Laboratory follow up of progress of the disease

	White blood cell count	Platelet count	Creatinine	Blood urea nitrogen	Amylasemia	Lipasemia	AST	ALT
Normal range	4.0-10.0×10^3/μL	150-400×10^3/μL	0.66 – 1.44 mg/dL	10.0-43.0 mg/dL	28-100 U/L	13-60 U/L	0-35 U/L	0-45 U/L
Day 0	5100	102	1.13	44.9	33.4	85	61	29
Day 1	15100	61	2.39	93.8	63	105	44	31
Day 2	12200	65	2.84	104	78	141.3	49	30
Day 3	11900	71	3.32	107.9	75	138	51	30
Day 4	13100	108	4.06	126.6	72.3	124.4	75	53
Day 5	12000	154	4.16	181	68	111	95	89
Day 6	9700	205	3.81	149	54	85.6	88	107
Day 7	8700	235	2.72	136	45	56.9	70	98
Day 8	8500	350	2.21	114	45	43	64	90
Day 13	6500	310	1.6	68	28	40	41	53

diuretics) and electrolyte levels (e.g. sodium, potassium, chloride), also treatment with antibiotics. He became polyuric on day 5 after admission, with urine output of 200-250 mL/h and gradual recovery of renal function in the following days. After recovery, the patient was discharged from the hospital on the 15th day of hospitalization. He remained well at the 1.5 month follow-up.

DISCUSSION

Acute pancreatitis is defined as an acute inflammatory process of the pancreas that may also involve peri-pancreatic tissues. Diagnosis of acute pancreatitis can be difficult [6]. The diagnosis is based on clinical presentation in association with increased pancreatic enzymes, (amylase and lipase) and radiologic studies [1,6,8]. Gallstones and alcohol abuse are the leading cause of acute pancreatitis[1,6]. Infrequent—but not rare—causes of the disorder include: drug reaction (usually idiosyncratic); pancreatic and ampullary tumours; hypertriglyceridaemia; hypercalcaemia; hypothermia; congenital anomalies of pancreatic and biliary anatomy; trauma; and infectious or parasitic organisms [1,6]. Rare causes include bites of certain spiders, scorpions, and the Gila Monster lizard. In the other hand gastrointestinal disorders (abdominal pain, nausea and vomiting) are found in several acute diseases [6].

About 90% of patients with HFRS complain of abdominal pain[3]. Implication of pancreas during HFRS course is also suggested by other authors such as Eun S Kang, Bui-Mansfield and Bren *et al*. [2,4]. Combination of the serum amylase level with results of either CT or ultrasound of the pancreas and biliary tree leads to the correct diagnosis in 81–95% of patients [6]. Serum lipase concentration rises within 4-8 h of an episode of acute pancreatitis, peaks at 24 h, and returns to normal after 8-14 days, making it another useful diagnostic method in patients presenting late (eg, >24 h from onset of pain) [6]. Abdominal pain, nausea, vomiting, an increase of lipase and amilasemia occurred the day after admission. Based on clinical presentation, level of pancreatic enzymes, abdominal imaging by CT scan and serological test for HFRS, we evaluated this case as a pancreatitis caused by Dobrava virus infection. Our patient stated that he worked and had travelled in the region of Macukulli an area in northeastern

Albania where rodents infected by Dobrava virus are found. This is a mountainous area with altitudes between 608-1191 m. During recent years, it has become clear that infections from Dobrava virus are more common than in the past. During the last two years we have had three patients from this region. In general, after infection with HTNV or DOBV, there is a 2 to 3-week incubation period followed by a typical five-period clinical course, namely, febrile stage, hypotensive stage, oliguric stage, diuretic stage and convalescent stage [7].

Increased vascular permeability plays a general role in the pathogenesis of severe Hantavirus infection [4]. Clinically, retroperitoneal oedema and free liquid accumulation in the body cavities with hemo-concentration reflect the vascular failure in HFRS. Increased vascular permeability raises the possibly of increased protein loss via the intestinal tract [5]. This explains the pleural effusion and free abdominal liquid of our patient during the hipotensive stage of the HFRS course. Potential mediators, which increase vascular permeability during the acute stage of HFRS, are tumor necrosis factor (TNF)-alpha, interleukin 1 and 2, and nitric oxide [5]. Activation of inflammation mediators during the hipotensive stage of HFRS, seems to be caused by an inflammatory cascade mediated by cytokines, immunocytes, and the complement system. Inflammatory cytokines cause macrophages to migrate into tissues distant from the pancreas, including the lungs and kidneys. Immunocytes attracted by cytokines released from macrophages release more cytokines, free radicals, and nitric oxide. Some of these cytokines are implicated in the progression of the disease —eg, interleukin 1 and tumour necrosis factor (TNF); interleukins 6 and 8 are useful for monitoring the course of the disease. Since the endocrine and exocrine pancreas reside in the same anatomic domain, it is not surprising that factors that result in widespread cellular and vascular damage should result in injury to both parts of the organ. A decrease in islet function appears to occur in acute pancreatitis, although some controversy still exists [3].

CONCLUSION

1. Although rare, one of viral cases that cause acute pancreatitis is the Dobrava virus.

2. One cause of abdominal pain in patients with HFRS by Dobrava virus infection is acute pancreatitis.

3. Diagnosis and treatment of acute pancreatitis in patients with HFRS, is still basically the same as that due to other causes.

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