Leptospirosis and Pancreatitis Complication

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ABSTRACT

Leptospirosis is a wide-spread zoonosis in the world, especially in the tropical countries. Ninety percent of cases are characterized by abrupt fever and have good prognosis, but in 10% of cases, exacerbation will occur and the mortality rate is about 10%. Leptospirosis may strike the entire organ, including gastrointestinal tract. Pancreatitis in leptospira is characterized by increased serum amylase levels, with mean values of five times normal. Early diagnosis and prompt treatment will engender good prognosis. Treatment of acute pancreatitis caused by leptospira is similar with other acute pancreatitis treatment caused by other agents. The pathophysiology of leptospira infection includes endotoxin, hemolysis and lipase.

Keywords: *Leptospirosis, pancreatitis, diagnosis*

INTRODUCTION

Leptospirosis is a zoonosis disease caused by leptospira. Leptospira consisted of pathogenic strains - *L. interrogans* and non-pathogenic *L. biflexa*. It is widely-spread almost all over the word, especially in tropical, warm-climate and humid countries.[1,2]

The clinical manifestations of leptospirosis vary form asymptomatic to severe symptoms. Generally, the early diagnosis of leptospirosis is difficult because the patient usually came with meningitis, hepatitis, nephritis, pneumonia, influenza, toxic-shock syndrome, fever of unknown origin, and some of cases present with pancreatitis.[1,3] Diagnosis of leptospirosis is based on history (there are some inquired risk factor), physical examination and laboratory. Definite diagnosis is based on leptospira findings in the blood, urine or cerebrospinal culture or serologic proof of its existence. The standard serologic method of *microscopic agglutination test (MAT)* is widely used in the world because it has high sensitivity and accuracy. The standard titer, which is utilized by Balitvet in order to determine positive value of Leptospira serum level is 100 in accordance to the international standard.[1,3]

Acute pancreatitis is an acute inflammation reaction of the pancreas, it is a gastrointestinal emergency, which is frequently found in clinical setting. The natural history of this disease has a lot of variation, from *self limited* to very severe type which is accompanied by potential fatal shock.[5,6] In the foreign countries, the causes of acute pancreatitis are alcoholism (30% - 45%), biliary disorder (30% - 45%), idiopathic (10% - 30%) and other causes such as auto-immune, genetic, infection, traumatic (10%). A study in Cipto Mangunkusumo Hospital in 1996 indicated that the most common causes of acute pancreatitis were leptospirosis (21.5%), gallstone (12.2%), typhoid fever (9.2%), dengue fever (6.1%) and idiopathic in 45.2%.[5,7]

The diagnosis of acute pancreatitis is based on history, clinical manifestations, laboratory, ultra-sonography or CT-scan examination. Clinically, there is persistent abdominal pain in epigastric and right-upper quadrant region, nausea and vomiting. The patient

generally presents of moderate to severe dyspepsia, nervous, and may be accompanied by loss of consciousness, fever and jaundice. The laboratory examination reveals increased serum amylase and lipase level. The ultrasonograph or CT-scan reveal inflammation feature of pancreas.[5,2] The treatment is dependent on the severity of pancreatitis, the causes and the presence of complication.[8,9,10]

In order to determine the prognosis, we should identify mild or severe cases. Some criteria may be applied, i.e. Ranson, Imrie and APACHE.[9,10] The Ranson criteria consist of admission evaluation, i.e. age, leukocyte amount, glucose, LDH and ALT level and 48 hours-care evaluation, i.e. decreased hematocryt value, increased BUN level, calcium level, arterial PO_2, base deficit and the amount of fluid. Leptospira may also cause renal complication, i.e. acute renal failure in 16% - 40% cases, which is characterized by increased ureum-creatinine level. The patient of pre renal phase in acute renal failure has good response to adequate fluid treatment.[11,12,13]

This case is being proposed because Indonesia is a tropical country, which develops many leptospirosis, and pancreatitis is one of the most common complications in clinical setting. By early diagnosis and adequate treatment in a right time, it is expected that we may prevent the fatal multiple organ failure.

CASE REPORT

Male patient, 30 years old, was admitted to our hospital, on 25th March 2004 with chief complaint of fever since 8 days before admission. He was referred from other private hospital with the explanations of DHF observation, anemia, and anuria. Since 8 days before admission, he had high fluctuating fever, there was no chilled, he had nausea and vomiting. Three days later the patient went to General Hospital with fluctuating fever, jaundice eyes, epigastric pain, muscle pain especially in his calf region, he had diarrhea every 3 hours of liquid-yellowish stool, and the urination was normal.

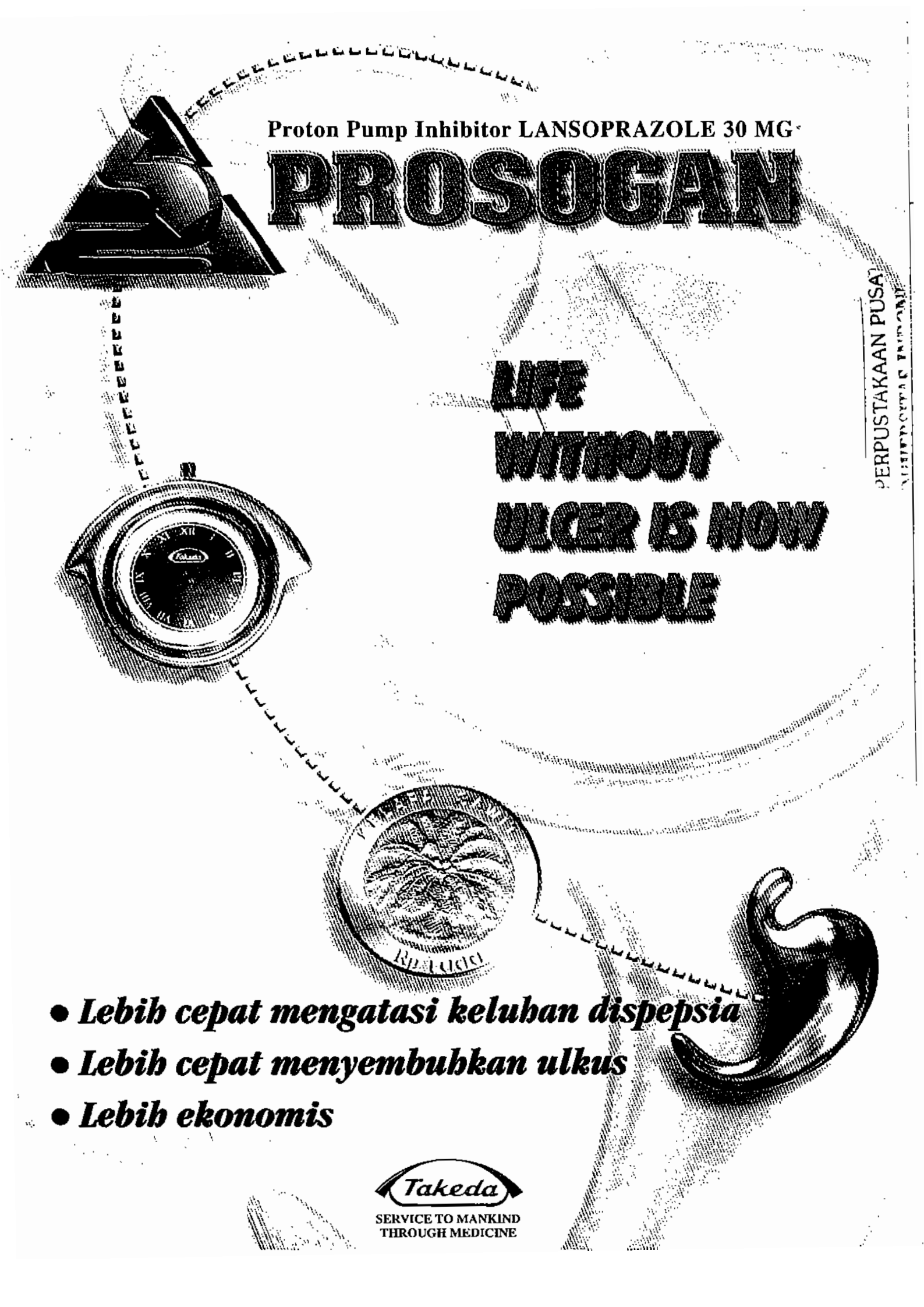
On the 3rd day of hospitalization, he was admitted to the ICU because of his weaker condition and a nasogastric tube (NGT) was inserted, revealed 300 cc of green fluid. Because the patient cannot urinate, then catheter was inserted. The patient was having a fasting and he had some treatment, i.e. intravenous Ringer lactate 1500 cc/24 hours, intravenous dextrose 5% for 100 cc + furosemide 16 ampoule 24 hours, triofusin 1000 cc/ 24 hours, hepar aminofusin 500 cc/24 hours, cefotaxime injection 2 x 1 g, gastridine injection 3 x 1 ampul. During hospitalization, there was no bleeding. After that, he was referred to Cipto Mangunkusumo hospital for hemodialysis. The patient works as a minibus driver, he lives in the area that frequently hit by flood, he denied any alcohol consumption or intravenous drugs, the history of a journey to malaria-endemic region was also denied.

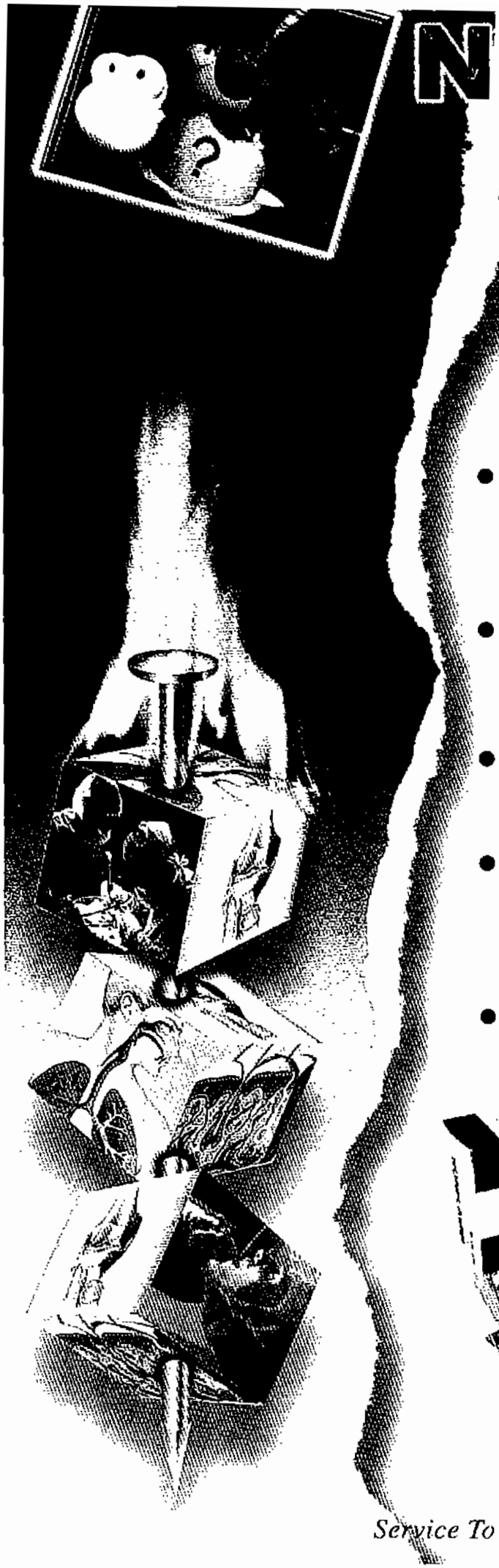
On physical examination, the patient was moderately ill, alert, and fully oriented. Blood pressure was 120/80 mmHg, pulse rate was 100 beats per minute, temperature was 36.0°C, and respiratory rate was 20 times per minute. Conjunctiva was pale, and his sclera was jaundice. Normal heart and lungs based on chest examination. On abdominal examination, there was liver enlargement of 3 fingers below the costae archs, two fingers below the processus xyphoid, sharp edge, tenderness, unpalpable spleen. Normal bowel sound. On the extremities, there was pressure tenderness on gastrocnemius muscles.

On laboratory examination revealed hemoglobin 8.4 g/dL, hematocryt 24%, leukocyte 12,600/µL, platelet count 78,000/µL, MCV 81, MCH 29, MCHC 36, sodium 127 meq/L, potassium 3.0 meq/L, chloride 92 meq/L, ureum 210 mg/dL, creatinin 7.4 mg/dL, amylase 367 U/L, lipase 445 U/L, ALT 94 mg/dL, AST 73 mg/dL. Dengue IgG negative, IgM negative, CRP positive. The urine examination revealed; leukocyte 2-3, a lot of erithrocyte, urine quantitative protein 1,547/24 hours. Blood gas analysis: pH 7.41 / PCO_2 113 / HCO_3 22 / SBC 22 / SBE -3 / SO_2 98 / TCO_2 51. The abdominal USG showed mild hepatomegaly of left lobe with chronic parenchymal liver disease and parenchymal renal disease. The chest X-ray was normal.

The management included fasting in order to give his pancreas a rest and nasogastric tube (NGT) had been inserted for gastric and duodenum content drainage and for reducing abdominal distention. During hospitalization, he had fasting up to the fifth day of hospitalization (8 days total of NGT insertion). At that time, there was no abdominal pain, no vomiting, and the NGT drainage was not produced since a day before, the amylase/ lipase level was 566/744. After that he had gradual feeding i.e. 1st pancreatic diet through NGT for 2 (two) days, then he had gradual 2nd pancreatic diet i.e. refined porridge for 2 (two) days. Because he was getting better then the diet was improved to coarse/crude porridge (3rdpancreatic diet) and soft diet and finally he had the regular diet. During fasting, the patient had total parenteral nutrition which is consist of intravenous triofusin 1000/12 hour, intravenous NaCl 5% dextrose = 1 : 1 /12 hour.

On the first day of hospitalization, there was renal improvement, which was characterized by 2,000 cc of 24 hours urine production. The result of ureum-





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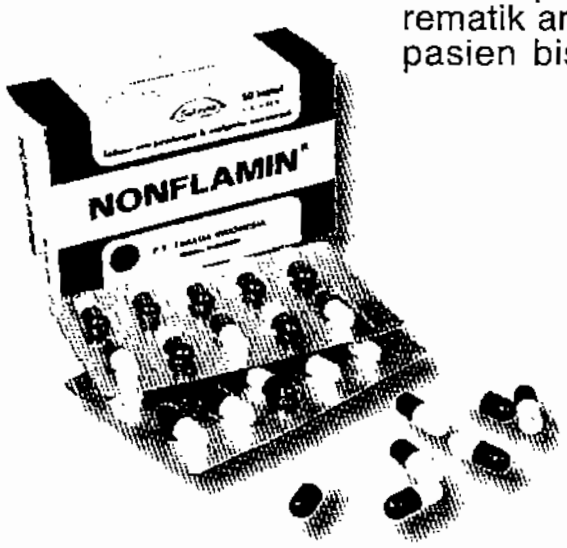

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creatinine reexamination was 172/6.9. During hospitalization, the patient had not had any diuretics and there was improvement of ureum/creatinine level. So hemodialysis was not indicated for this patient.

The patient had cefoperazone antibiotics because we considered previously he had already received cefotaxime for 6 days and the leucocytes were still at 12,600/ml level and he also had already renal impairment. During hospitalization care, he had analgesics such as tramadol in order to relieve pain and it was quite effective. The patient had not received any treatment of anti pancreatic secretion drugs such as somatostatin and octreotide because the given treatment has showed improvement and also because of cost benefits consideration. Besides, the anti pancreatic secretion drugs are still controversial and there are lack of proof that they could improve the complication. Hemodialysis was not done, because adequate treatment had caused renal improvement, which is indicated by decreased ureum-creatinine level.

Base on serologic examination, the serum contains antibody against [Bataviae] with 1:400 titer. The given antibiotics were not changed into penicillin procaine (the drug of choice of leptospirosis) because we considered that the patient's condition was getting better, there was no sign and symptom of any recurrent complication, while the cefoperazone antibiotics were continued for 2 days. We have not done any CT scan examination for this patient because we considered that pancreatitis may be established based on history, physical examination and laboratory and during hospitalization, the patient's general condition is improved. The patient was discharged on the 12th day of hospitalization the laboratory result was improved hemoglobin 8.4 g/dL, leukocytes 6.6/ml, platelet count 354/ml, ureum 28 mg/dL, creatinin 0.9 mg/dL, amylase 147 U/L, lipase 537 U/L, hematuria (-), sodium 138 meq/L, potassium 4.0 meq/L, seromarker (-) H, Widal (-), CRP 10.

DISCUSSION

Leptospirosis has many clinical manifestation from mild to severe. Hence, at early stage, there is a lot differential diagnosis consideration. Dengue hemorrhagic fever (DHF) may cause similar clinical manifestation, but the fever in this patient was longer than 7 (seven) days. During hospitalization, there was some improvement of platelet count and negative dengue blot; so that we could exclude the diagnosis of dengue hemorrhagic fever. There was small possibilities of malaria diagnosis, because there was no history of outer city journey, no chill which was accompanied by fever and heavy sweating. The differential diagnosis of typhoid can be excluded by negative widal test, while acute hepatitis was not proven by serologic test. The definite diagnosis of leptospirosis is based on *MAT* serology result that indicates positive *L. bataviae* with titer of 400 (the standard titer of *MAT*, which is utilized by Balitvet to determine positive serum of leptospira is 100).[2]

Diagnosis of pancreatitis in this patient is based on abdominal pain. On physical examination, there was epigastric pain and laboratory result revealed increased serum amilase and lipase over 5 times of normal value.[2,6,8]

The etiology of pancreatitis in this patient is leptospirosis infection; which is indicated by positive serology result, negative HbsAg seromarker, anti HCV and widal result. Pathogenesis of leptospira pancreatitis is not clearly mentioned in the literatures, but it is assumed that leptospira endotoxin may induce auto-digestion.[2,5] The literature said that gastrointestinal manifestations of leptospirosis are jaundice, hepatitis, cholecystitis, pancreatitis and gastrointestinal bleeding. A Hawaian serial case reported 10 patients with leptospira pancreatitis (8 of them were children); revealed increased serum amylase and lipase level. These enzymes elevation occurred on the 8th - 10th day and it also revealed abdominal pain on the 3rd - 11th day.

The patient's ultrasonography examination does not revealed any pancreatic defect, and in the literature, it is said that 33% of pancreatic cases seem normal.[6] There was no pancreatic stone in the pancreas. It is important because pancreatic stone is one of important risk factor in pancreatitis.

The symptomatic and supportive management of acute pancreatitis patient provide a good result. Based on literature, it is said that conservative treatment also provides a good result. A good management of acute pancreatitis includes prevention of severe condition with multi-organ failure, which necessitates intensive care unit and surgery. Because the patient had fasting, we should concern about fluid and electrolyte balance, as well as rehydration. Moreover, both of them may cause renal complication, characterized by symptoms of uremia and anuria.

The literature said that pancreatitis may induce the third compartment, which cause reduced intravascular volume. Therefore, in hospitalization care, we need hematocrit monitoring and also hematocrit elevation; positive renal disorders indicate inadequate fluid therapy. In this patient, adequate fluid-intake demonstrated improved renal function. In some of literatures, NGT insertion has been obsolete, except for vomiting patient.[2,6]

Main treatment for leptospirosis is antibiotics, the drug

of choice is penicillin procaine, but cefoperazone was given in this patient because we consider that definite diagnosis of leptospira was established on the 6th day of hospitalization and because there was an assumption of secondary infection in this patient, as well as renal impairment; therefore the selected antibiotics must be wide-spectrum antibiotics but safe for the kidney. Antibiotics administration in acute pancreatitis is not a main therapy, but it is given in order to prevent infected pancreas by migrated micro organism.

Most of patients with acute pancreatitis have mild symptoms and they have immediate recovery by conservative treatment, and also have better prognosis. This patient only has 1 Ranson sign, i.e. increased BUN > 5 mg% and has a good prognosis

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