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Case Report

Severe Acute Pancreatitis Associated with Weil's Disease

Meriem Guechi[1*], Wahiba Guenifi[1,2], Abdelkader Gasmi[1,2], Amel Ouyahia[1,2], Mounira Rais[1,2], Houda Boukhrissa[1,2], Salah Mechakra[1,2], Habiba Hemamid[2,3], Abdelmalek Hakimi[2,3], Abdelmadjid Lacheheb[1,2]

[1]Infectious Diseases Department, Teaching Hospital, Setif, Algeria
[2]Faculty of Medicine University Ferhat Abbes, Setif, Algeria
[3]Department of Medical Intensive Care, Teaching Hospital, Setif, Algeria

Abstract

Leptospirosis is an emerging zoonosis of worldwide importance. Its distribution is closely linked to hydrometric conditions. It is characterized by a wide clinical range, from the subclinical form, or one with few symptoms; which resolves spontaneously, to the multi-visceral form, known as icterrohemorrhagic disease or Weil's disease, with a lethal risk. All organs can be affected but with variable frequency. Pancreatic involvement is not well documented. We describe a 45-year-old man with Weil's disease associated with acute necrotizing pancreatitis. The evolution was favorable but required a three-week stay in the intensive care unit.

Keywords: Leptospirosis, Weil's disease, Acute pancreatitis

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Introduction

Leptospirosis is a zoonotic threat of global importance, an emerging disease caused by a pathogenic bacterium, *Leptospira interrogans*, which infects humans as well as wild and domestic animals. The World Health Organization (WHO) reports 500 000 annual cases worldwide with a mortality rate of 5% to 25%.[1] The epidemiology of leptospirosis is closely linked to hydrometric conditions. The incidence is 50 or 100 times higher in tropical regions, and many countries of Latin America and Southeast Asia. The disease is known in North Africa but the incidence and prevalence remain difficult to assess. In Algeria, seroprevalence studies in cattle confirm the circulation of *Leptospira interrogans*. In addition, several epidemics have been reported in humans.[2]

The seasonality of the disease is highly marked, with a summer-autumn recrudescence linked to heat and precipitation. Transmission occurs through water contaminated by the urine of rodents, particularly rats, and occurs preferentially in exposed persons (farmers, gardeners, sewage workers) or when bathing in rivers, ponds, or gravel pits, usually during summertime. The number of cases is underestimated because of the lack of specificity of the clinical character, which leads to the discussion of several diagnoses, and the lack of means of confirming the diagnosis in many regions of the world.

Leptospirosis is very variable in terms of its severity. The mildest forms may remain sub-clinical or be limited to a non-specific febrile episode. Other forms are severe and life-threatening. All organs may be affected and the disease may be systemic. The association of hepatorenal involvement with hemorrhagic manifestations defines the potentially lethal Weil syndrome.[3] Although there are a significant number of cases documented in the literature, pancreatitis is described as a rare complication of leptospirosis. This article reports a case of ictero-hemorrhagic leptospirosis complicated by acute necrotizing pancreatitis that required admission to the intensive care unit and progressed favorably under medical treatment.

Case Report

A 47-year-old man, a primary school director in Aïn Trik-Sétif, followed by goiter in euthyroidism, was admitted on September 26, 2020 to the Infectious Diseases Department of the University Hospital of Sétif-Algeria for acute febrile hepatonephritis. The interrogation did not reveal any notion of alcohol consumption or a journey to a malaria-endemic area; however, he participated in renovation work on his house one month before.

The onset was one week ago, marked by a high fever, repeated chills, and diffuse myalgias, followed 4 days later by mucocutaneous jaundice, yellowish diarrhea (more than 4 stools/day), and abdominal pain more localized in the right hypochondrium. On examination, the patient was altered, dehydrated, and conscious. The temperature was 38°C, blood pressure at 90/70 mm Hg, and oxygen saturation in the air 98%. The jaundice was flaring and the liver and spleen were normal in size.

The paraclinical evaluation revealed: white blood cells at 29 000/mm^3 of which 91% were neutrophils, hemoglobin at 8.7 g/dL (normochromic, normocytic),

*Corresponding Author: Meriem Guechi, Email: meriem.guechi@gmail.com

and platelet counts at 30 000/mm^3. On renal workup: serum creatinine at 76 mg/L, urea at 1.38 g/L, and on liver workup: alanine aminotransferase at 140 IU/L, aspartate aminotransferases at 180 UI/L, alkaline phosphatase at 194 IU/L, total bilirubin at 425 mg/L, of which 80% was conjugated and the prothrombin level at 95%. The lumbar puncture brought back a clear cerebrospinal fluid, and cytochemical normal.

The chest radiograph was unremarkable and abdominopelvic ultrasound showed a normal-sized liver, non-dilated bile ducts, and low abundance fluid effusion.

The patient was treated with ceftriaxone + ciprofloxacin + metronidazole + parenteral rehydration, in the hypothesis of leptospirosis or sepsis with a digestive origin. On the 3rd day, the blood pressure dropped to 60/40 mm Hg. He presented with moderate hematemesis and was unable to eat due to abdominal pain and nausea. The abdomen was tense and bloated but depressible to palpation. The transit was preserved and the diuresis was null.

Biologically, there was a worsening of renal insufficiency (urea: 3.31 g/L, creatinine: 106 mg/L, hyponatremia at 115 mEq/L), a fall in hemoglobin levels to 6.7 g/dL, procalcitonin at 111 ng/mL, creatine phosphokinase at 833 IU/L, lactate dehydrogenase at 955 IU/L, lipaemia at 273 IU/L (normal value less than 67 IU/L), and amylasemia at 429 IU/L. Electrocardiography and echocardiography were without abnormalities.

Abdominal computed tomographic (CT) angiography showed an enlarged pancreas at the expense of its caudal part losing the lobulated aspect opposite, slight densification of the peri-caudal fat, and a necrosis flow at the level of the back cavity of the omentums. Elsewhere, there was liquid digestive distension with a hydro-aeric level reaching 38 mm in diameter, a densification of the mesenteric fat opposite, and an intraperitoneal effusion of medium abundance under the subhepatic, peri splenic, gutters, inter handles, and pelvic level (Figures 1 and 2).

The patient was transferred to the medical resuscitation service where he was put on noradrenaline associated with appropriate vascular filling, blood transfusions, extrarenal purification sessions, and Inexium. Antibiotic therapy was maintained.

A gradual improvement (clinical and biological) was observed. The patient initiated a diuresis and his colors return. On the 17th day, the kidney and liver tests were correct.

In terms of infection, blood cultures did not isolate pathogenic germs; HBsAg, anti-HAV IgM, anti-HCV antibodies, and HIV serology were negative. The search for SARS-CoV-2 viral RNA on nasopharyngeal swabs by polymerase chain reaction (PCR) was negative. Martin and Pettit's (MAT) serology was performed on 10/17/2020, which was positive for *Leptospira biflexa* (Patoc strain) at 1/400.

The patient was followed up several times, after his discharge from the hospital. No complication was noted.

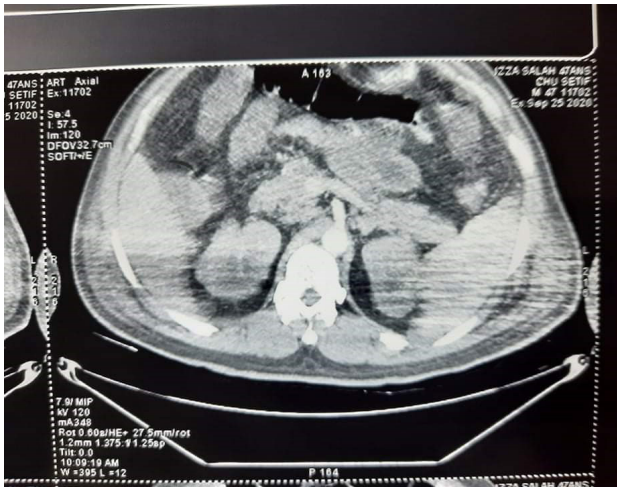

Figure 1. Necrosis flow at the level of the back cavity of the omentums

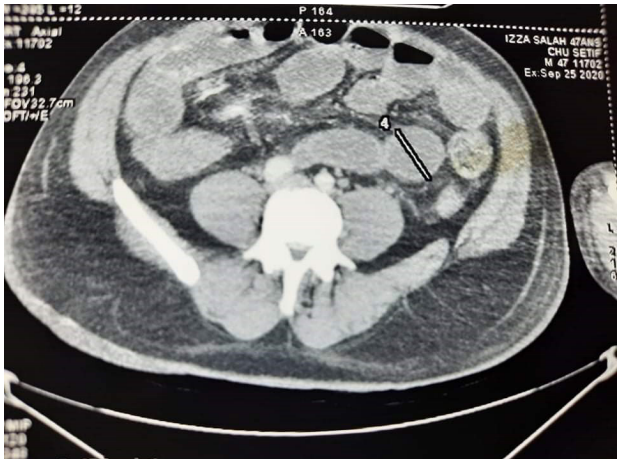

Figure 2. Liquid digestive distension

Discussion

Leptospirosis is caused by spirochetes of the genus *Leptospira*, we distinguish *L. biflexa* and *L. interrogans* which is pathogenic for humans. Its serological classification identifies 23 serogroups and more than 255 serovars. Serious forms can be observed with all serogroups, but Leptospira ictero hemorragiae is most often responsible.[1]

Leptospires can cause diffuse organ damage due to extensive vasculitis. Most complications are well documented: renal (60%), hepatic (75%), hematological (thrombocytopenia [70%]), meningeal (25%), pulmonary, and more rarely myocardial and ocular.[3] In this case, the disease involved several organs that are usually affected but also associated with acute pancreatitis. The involvement of this organ is not well studied in human leptospirosis.

Various microorganisms can cause acute pancreatitis: viruses (hepatotropic virus, coxsackie virus, cytomegalovirus, HIV, herpes virus, etc), fungi (aspergillus), parasites (toxoplasma, cryptosporidium, and ascaris), and bacteria (*Mycoplasma, Legionella, Campylobacter jejuni, Salmonella, Chlamydia trachomatis,*

Brucella, and *Leptospira*).[4,5]

The first descriptions of the association between pancreatitis and leptospirosis date back to the 1950s through clinical observations.[6] Since then, several case series have been published in both adults and children.[7-12] In 2003, the first study involving 33 patients who died from fatal leptospirosis and submitted for autopsy, found that 12 (36.6%) had pancreatic involvement.[13] Another study in 2013 involving 20 cases found 13 cases of pancreatic damage, including four aspects of fatty necrosis.[14] The pancreatic lesions were variable and sometimes of multiple severities: pancreatic edema, inflammatory polynuclear or lymphocyte infiltrate hemorrhagic lesions or necrotic lesions. Forms of pseudocyst or abscess have been reported. Smiti and colleagues were interested in changes in abdominal ultrasound and found two cases of pancreatitis among 51 cases of leptospirosis.[15]

The common clinical signs of acute pancreatitis were present in our patient. Biologically, lipasemia, whose increase is generally sufficient for the diagnosis, was in favor of the diagnosis (more than 4 times the normal rate).

Abdominal CT confirmed pancreatic involvement and specified the extent of the lesions. CT scan identified signs of pancreatic and peripancreatic inflammation and foci of pancreatic necrosis. The positive predictive value of CT for the diagnosis of pancreatic necrosis is up to 92%. The presence of signs of necrosis defines severe pancreatitis. The vital prognosis is at stake and mortality can reach 20%.[16] Jointly, abdominal CT and ultrasonography allowed us to eliminate cholelithiasis or choledocholithiasis in the patient, the main etiology of acute pancreatitis.

The MAT serology confirmed the leptospirosis origin in the patient. It is a reference test for the serological diagnosis of leptospirosis. A rate > 1/400 is very suggestive even in endemic areas.[3,17]

Leptospira biflexa is a non-pathogenic strain. The agglutination detection with *L. biflexa* is due to cross-reactions. In MAT serology, 22 strains are used including the non-pathogenic *L. biflexa* strain Patoc 1, which has the particularity of crossing with many pathogenic serogroup antigens.[1,3,17] Also, it has been reported that there is not always a match between the serogroup identified by MAT and that obtained by identification when the strain is isolated.[18,19]

A negative MAT result does not exclude infection because the patient may be infected with a serotype absent in the test antigen battery. Sometimes early antibiotic therapy can abort the immune response and prevent seroconversion. PCR seems to be the future solution for the diagnosis, allowing earlier antibiotic treatment.[1,3]

The medical treatment was sufficient and allowed the resolution of the clinical signs and the normalization of the patient's paraclinical assessment. Recourse to surgery has been reported by some authors and consisted of the evacuation of pancreatic abscesses or drainage and washing of peritoneal or retroperitoneal extensions.[20,21]

Conclusion

According to the reported literature, it seems to us that pancreatitis is wrongly considered exceptional during leptospirosis. The systematic search for pancreatitis by lipasemia and abdominal CT would make it possible to assess its frequency during leptospirosis. Pancreatitis associated with acute hepatonephritis should be investigated for leptospirosis.

Competing Interests

The authors declare no conflict of interest related to this work.

Ethical Approval

None.

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