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Case Report

A rare case of complicated pancreatitis due to leptospirosis

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ABSTRACT

The COVID-19 pandemic and the actions taken to combat it have greatly impacted the health infrastructure of all nations. Here we present a rare case of leptospirosis with severe acute pancreatitis, bilateral peripheral gangrene, disseminated intravascular coagulopathy and multiorgan failure. This is a rare presentation of leptospirosis wherein the patient had no history suggestive of acquisition of leptospires. The patient was started on doxycycline but still could not be saved due to the multisystem involvement.

1. Introduction

The COVID-19 pandemic and the actions taken to combat the pandemic is being seen to have impact on the psychosocial, economic and health infrastructure of the various countries across the globe. This is especially true for the low-to-middle income countries having a high population burden with a poor infrastructure. As the world leaders are concerned about the impact of COVID on the diseases like TB, HIV and malaria, the other tropical diseases like scrub typhus, leptospirosis etc are getting neglected [1]. Diagnosing these diseases at an early stage could enable timely treatment and thus save the patient [2]. Here, we present a case of leptospirosis presenting with pancreatitis, acute respiratory distress syndrome, Disseminated Intravascular coagulopathy and acral gangrene.

2. Case

An adult non-alcoholic labourer was bought to the medical emergency of a large tertiary care hospital of India with a history of non-radiating abdominal pain with persistent vomiting for 4 days along with altered sensorium and respiratory distress for one day. There was no history of fever, radiation of pain, abdominal distension, hematemesis or melena. On examination the patient had icterus and tachypnea. The patient was tested COVID negative by Xpert SARS CoV2 (Cepheid, Danaher, CA, USA) in the emergency and his other hematological and biochemical investigations were sent. His laboratory parameters revealed anemia (Hb – 8.1 g/dL, MCV – 107 fl and RDW - 20) with neutrophilic leukocytosis (TLC– 29000/μL) and thrombocytopenia (platelet count– 62,000/μL). Peripheral smear showed macrocytic RBC with neutrophilic leukocytosis with left shift and toxic granulations and low platelet count. INR was 1.4 and DIC profile showed mildly prolonged PT and aPTT (PT = 16.8s with control of 12s and aPTT was 44s with control of 40s) with normal thrombin time and fibrinogen levels. He had acute kidney injury (Blood urea – 147 mg/dL and serum creatinine – 8.4 mg/dL) with oliguria and metabolic acidosis (pH-7.3). Liver biochemical tests done on second day of illness showed hepatocellular type of jaundice (total bilirubin – 5.4 mg/dL with conjugated fraction being 4 mg/dL; ALT/AST/ALP = 623/209/287; serum albumin – 2.6 g/dL). Serum amylase and lipase on day 2 of pain were 1422 U/L and 2900 U/L, respectively. Arterial blood gas analysis showed metabolic acidosis with hypoxic respiratory failure with PaO2/FiO2 ratio of 201. Ultrasound abdomen at admission showed bulky and heterogenous pancreas with mild hepatosplenomegaly and normal outline of liver with moderate ascites. Gall bladder was normal. Ascitic fluid work up showed low SAAG, high protein ascites with high amylase with cell count of 120/μL with 60% polymorphs. Two possible syndromic diagnoses were considered. One was severe acute pancreatitis with multiorgan dysfunction syndrome and the second was acute infective etiology (tropical illness in monsoon season) with multiorgan failure and associated acute pancreatitis. He was empirically started on intravenous piperacillin/tazobactum and doxycycline from day of admission and was put on hemodialysis.
From Day 2 onwards, the patient also developed fever along with blackish discoloration of the extremities followed by dry gangrene of tips of fingers, toes and over the surface of palms and soles (Fig. 1). Jaundice worsened with rise in bilirubin levels to maximum of 19 mg/dL (conjugated fraction being 15 mg/dL). The infective etiological work up showed positive Leptospira IgM ELISA (Panbio Pty. Ltd., Queensland, Australia), which was confirmed by positive PCR for Leptospira in urine. Other infective etiology work up was negative (Malaria antigen test, peripheral smear for malaria antigen, Dengue NS1 and IgM serology, Scrub typhus IgM ELISA, IgM ELISA for Hepatitis A and E, HBsAg, Anti-HCV, HIV serology as well as SARS CoV2 Xpert test). Repeat ultrasound on day 5 showed 10 × 7 cm partially liquefied acute necrotic collection in lesser sac.

Over the next 4 days, the patient worsened with multi-organ dysfunction. He was given hemodialysis daily for the persistent acute kidney injury with hyperkalemia and was continued on mechanical ventilation for persistent ARDS. Intravenous meropenem was added in place of piperacillin/tazobactum and doxycycline was continued. The percutaneous drainage of acute necrotic collection was done with 12 Fr pig tail catheter, which drained only 50 mL of necrotic fluid with altered blood. Despite these measures, the patient developed refractory shock and had cardiac arrest and died after 7 days of admission. He was diagnosed as a case of severe acute pancreatitis, acute respiratory distress syndrome, acral gangrene and disseminated intravascular coagulopathy with multiorgan dysfunction (MOD) due to leptospirosis.

3. Discussion

Here, we report a patient of leptospirosis having rare presentations of pancreatitis, acute respiratory distress syndrome, Disseminated Intravascular Coagulopathy and acral gangrene. In this patient the source of leptospirosis could not be elicited. Leptospirosis, a neglected zoonotic

| S. No | Case, Country | Diagnosis of leptospirosis | ICU/operation | Antibiotic treatment given | Patient outcome |
|-------|---------------|---------------------------|--------------|---------------------------|----------------|
| 1     | Present case, 2020 | IgM ELISA n PCR with urine PCR positive | Yes/No | Piperacillin/tazobactam, doxycycline & meropenem | Death in 7 days |
| 2     | Gomes PEAC; Rev Inst Med Trop Sao Paulo. 2019, Brazil [7] | Microscopic agglutination Test (MAT) | No/No | Ampicillin/sulbactam & ceftriaxone | Death in 4 days |
| 3     | Maier A; BMC Infect Dis. 2019, Greece | IgG n IgM ELISA n PCR (negative) | Yes/no | Meropenem | Discharge after 18 days |
| 4     | Mazhar M; Hawaii J Med Public Health. 2016, Hawaii | IgM (ELISA) | Yes/no | doxycycline, ceftriaxone, and metronidazole | Discharge |
| 5     | N J Herath; BMC Infe 2016, Sri Lanka | MAT | Yes/not reported | Penicillin, cefotaxime & doxycycline | One death, discharge in rest 5 days |
| 6     | Yew KL; J Formos Med Assoc. 2015, Malaysia | IgM by latex agglutination test | Yes/No | ceftriaxone | Discharge |
| 7     | Lim SM; J Pak Med Assoc. 2014, Malaysia | IgM | Not reported/not reported | Imipenem & ceftriaxone | Discharge after 2 weeks |
| 8     | Panagopoulos P; J Med Case Rep. 2014; Greece/Congo | IgM, rapid agglutination test | Yes/no abdominal operation | Piperacillin/tazobactam, penicillin, meropenem & vancomycin | Discharge after 16 weeks |
| 9     | Jain AK, Indian J Surg. 2013, India | ELISA | Not reported | Death | Death after 75 days |
| 10    | Popa D. J Med Life. 2013; Romania | “test for leptospirosis” | Yes/yes laparotomy | Imipenem, Teicoplanin, rifampicin & moxifloxacin | Discharge |
| 11    | Ranakawa N, BMC Infect Dis 2013, Sri Lanka | IgM & MAT | Yes/not reported | Meropenem & penicillin G | Discharge |
| 12    | Silva AP, Braz J Infect Dis. 2011; Brazil | IgM ELISA | Not reported/not reported | Ceftriazone & Penicillin | Discharge after 22 days |
| 13    | Simon F, J Travel Med. 2012; France | IgM ELISA, MAT & PCR | No/No | Ceftriazone | Discharge after 10 days |
| 14    | Baburaj P, J Assoc Physicians India. 2008, India | IgM (ELISA) | Not reported/not reported | Penicillin | Discharge |
| 15    | Dalamaga M, J Med. 2004, Greece | IgM (ELISA), Microscopic Agglutination Test (MAT), dark-field microscopy of urine | Not reported/not reported | Doxycycline | Discharge |
| 16    | Chong VH, Ann Acad Med Singap. 2007, Singapore | IgM ELISA | Not reported/not reported | Ceftriazone | Death |
| 17    | Spichler A, Am J Trop Med Hyg. 2007, Brazil | IgM & IgG (ELISA) | Yes/no | Ceftriazone & Ciprofloxacin | Death |
| 18    | Kaya E, World J Gastroenterol. 2005, Turkey | Microagglutination test, dark-field microscopy | Yes/laporatomy | Penicillin G, Ampicillin/sulbactam | One died n one discharge |
| 19    | Wang NC, J Microbiol Immunol Infect. 2003, Taiwan | Piperacillin & ceftriaxone | Doxycycline & ceftriaxone | Discharge |
| 20    | Pai ND, J Assoc Physicians India. 2002 | IgM ELISA | Not reported/not reported | Penicillin G | Discharge |
| 21    | Casella G, Am J Gastroenterol. 2000, Italy | ELISA | No/No | Ampicillin | Discharge x 30 days |
| 22    | Monno S, J Clin Gastroenterol. 1993, Japan | ELISA and MAT | Not reported/not reported | Streptomycin, clindamycin and piperacillin | Discharge |

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**Fig. 1.** Figure showing bilateral peripheral acral gangrene.
waterborne tropical infection, presents with diverse clinical manifestations and pancreatitis with acral gangrene are very rare manifestations of the disease. Upon review of literature, it was seen that a few case reports are published from across the globe of leptospirosis presenting with acute pancreatitis as given in Table 1 taken as a modification of table of Maier et al. [3]. Serology was the mainstay of diagnosis in most of the case reports except Germany in 2019 [3] in which PCR was negative from both urine and plasma. In our case, the serology as well as PCR urine were positive. Only two cases of peripheral gangrene with leptospirosis have been reported in literature till date [4,5]. First was reported in 1979 [5] while in the second one [4] was reported in 2014 where diagnosis was based on both microscopic agglutination test as well as IgM ELISA.

Leptospirosis has been seen to be associated with vasculitis which could be due to direct invasion of the infectious agent or due to immune mechanisms such as formation of autoantibodies or immune complex deposition or cell mediated immunity [3]. The presence of vasculitis could lead to peripheral gangrene in the fingers or toes. The etiology of pancreatitis remains unclear but could be due to autoimmune activation of proteolytic enzymes and auto-digestion causing ischemic injury and vasculitis [6]. Careful microbiological investigations helped reach a diagnosis in this first report of pancreatitis, acral gangrene with MODS due to leptospirosis in a COVID-19 negative patient.

Consent

Informed consent was obtained from the patient’s relative.

Author contribution

Priyam Batra: Study Conceptualisation and methodology.
Srikanth Gopi: Data curation.
E.V. Vinayraj: Test performance and validation.
K.V.P. Saikiran: Test performance and validation.
Jawed Ahmed: Test performance and validation.
Piyush Pathak: Data curation.

Deepak Gunjan: Data curation.
Kiran Bala: Test performance and validation.
Urvashi B. Singh: Test performance and validation.
Rama Chaudhry: Study Conceptualisation and methodology.

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Declaration of competing interest

All the authors have read the manuscript and have contributed equally in the formation of the manuscript. There is no conflict of interest between the authors including financial, consultant, institutional and other relationships.

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