Expanded leptospirosis syndrome – an unusual case

Abstract

Leptospirosis, caused by Leptospira species, is known for hepatorenal dysfunction in severe cases. Emerging evidence shows atypical manifestations, complicating diagnosis, especially in regions where it mimics other tropical illnesses like dengue or malaria. A healthy young female presented with high-grade fever, headache, malaise, vomiting, epigastric pain, and altered sensorium. Examination revealed conjunctival injection, meningeal signs, and abdominal tenderness. Liver function tests showed transaminitis with direct hyperbilirubinemia and albumin reversal, while renal function tests were normal. An ECG showed sinus tachycardia with non-specific ST segment changes. Elevated cardiac biomarkers trended down with monitoring. Fundoscopy was normal, but a CT scan revealed cerebral edema. Cerebrospinal fluid analysis indicated meningitis, and MRI confirmed meningoencephalitis. Based on clinical findings and modified Faine's criteria, leptospirosis was diagnosed. Multi-organ involvement was evident, excluding renal dysfunction. The patient responded well to treatment and was discharged in stable condition. This case highlights an unusual presentation of leptospirosis with multi-organ involvement but no renal dysfunction. Such atypical cases are increasingly recognized, similar to expanded dengue syndrome. Early recognition of these presentations is crucial for appropriate management to prevent adverse outcomes. Clinicians must know these evolving patterns for timely diagnosis and improved prognosis.

Keywords: Hepatitis, Meningoencephalitis, Myocarditis, Pancreatitis, Severe leptospirosis

Introduction

Leptospirosis, caused by the spirochete bacterium Leptospira, is a zoonotic infection commonly reported in low-income tropical countries.(1) The disease exhibits a wide range of clinical manifestations, from mild anicteric leptospirosis to severe systemic complications, often resembling other prevalent tropical infections such as dengue, scrub typhus, enteric fever, viral hepatitis, and malaria.(2) The diverse clinical presentations pose a challenge in diagnosing and managing the

disease, especially when it involves multiple organ systems, including rare instances of pancreatic and cardiac involvement.(3-5). Central nervous system (CNS) complications in leptospirosis, such as aseptic meningitis or, more rarely, encephalitis, further contribute to the complexity of the clinical picture.(6) While multisystem organ involvement, including CNS, pancreas and heart, is exceptionally rare, recognizing and diagnosing such cases demand keen clinical suspicion. However, in recent times, many atypical presentations are coming up. Like dengue expanded syndrome apart from typical hemorrhagic manifestation, leptospirosis can behave in an analogous way apart from typical hepato-renal syndrome.(7)

In this context, we present an expanded leptospirosis case having acute meningoencephalitis, hepatitis, myocarditis, and pancreatitis.

Case presentation

A young woman in her 20s, a farmer, with no prior known comorbidities, on the month of August (rainy season), presented with 15 days of high-grade continuous fever (101- 1020F), accompanied by chills and rigors, partially relieved by taking oral antipyretics. Concurrently, she experienced a continuous, moderate-intensity holocranial headache, generalized body aches, and malaise. Notably, there were no complaints of photophobia, neck stiffness, or rash at this stage. On the third day of illness, the patient had vomiting up to seven times a day, non-bloody and non-bilious, with mild, dull, aching epigastric pain. Seeking medical attention, she visited a local hospital where fever and vomiting improved with prescribed medications. However, on the tenth day of illness, she developed hypoactive altered mental status, in the form of decreased responsiveness to commands with decreased verbal output. There were no abnormal body movements, uprolling of eyeballs, or focal neurological deficits noted. The patient was brought to the emergency.

On initial examination, the patient, of average built, appeared drowsy with a Glasgow Coma Scale score of E3V4M5. Vital signs indicated tachycardia and Grade I Hypertension. General inspection revealed icteric skin and conjunctival injection without suffusion. Detailed neurological examination revealed bilateral mid-dilated pupils, sluggishly reactive to light, neck rigidity was present, both Brudzinski and Kernig’s signs were positive, deep tendon reflexes were exaggerated (3+) with bilateral plantar reflexes eliciting extensor response. Abdominal examination detected abdominal

rigidity and tenderness upon palpation, without any rebound phenomenon. Other systemic examinations were unremarkable.

Relevant investigations were conducted, and initial laboratory findings were indicative of neutrophilic leucocytosis and thrombocytosis on the hemogram (Table 1). Liver function tests indicated transaminitis with direct hyperbilirubinemia and an albumin:globulin reversal, while renal function tests remained within normal range. Electrocardiogram showed sinus tachycardia with non-specific ST segment changes. Cardiac biomarkers were positive, serial monitoring revealed a decreasing trend. Fundoscopic examination did not reveal papilledema. A non-contrast computed tomography (CT) scan of the head revealed cerebral edema. Cerebrospinal fluid (CSF) analysis demonstrated elevated cell counts and proteins, with a normal gram stain. Biofire PCR of CSF was negative for H. influenzae, Listeria, Neisseria, Streptococcus pneumonia, CMV, HSV1, HSV2, HSV6, VZV, enterovirus, and Cryptococcus neoformans. Subsequent contrast-enhanced magnetic resonance imaging (CEMRI) of the brain confirmed meningo-encephalitis (Fig 1A-B).

The tropical fever workup came out to be positive for leptospira by IgM ELISA, while peripheral smear for the malarial parasite, dengue NS1 antigen and IgM antibody, IgM ELISA for scrub typhus, and IgM ELISA for hepatitis A and E were negative. The patient was diagnosed as a probable case of leptospirosis. On day 7 of admission (day 22 of illness), the patient complained of mild abdominal pain and nausea. An ultrasound of the abdomen revealed a mildly bulky hypoechoic pancreas with elevated serum amylase and lipase levels. Magnetic resonance cholangiopancreatography (MRCP) exhibited diffusion restriction with low values in ADC maps of the pancreas, particularly in the tail region, along with minimal peripancreatic fat stranding suggestive of acute pancreatitis (Fig 1C-E). She was given intravenous fluids and other supportive management. Since her clinical, epidemiological and laboratory features were compatible with modified Faine's criteria – score of 36 (>25), with positive leptospira IgM serology, a diagnosis of expanded leptospirosis syndrome with meningoencephalitis, hepatitis, pancreatitis and myocarditis was made.

We initially kept an acute febrile illness differential diagnosis of acute bacterial meningitis, tubercular meningitis, viral encephalitis, expanded dengue syndrome, enteric fever, and cerebral malaria but relevant investigations were negative, helping to rule out these etiologies presenting with similar

manifestations. In view of deranged liver biochemistry, scrub typhus and leptospirosis were kept as a possible differentials.

Twelve hours post-admission, the patient exhibited progressive deterioration in sensorium, for which the patient was intubated and started on supportive management. The patient was admitted to the intensive care unit. Considering a provisional diagnosis of acute meningoencephalitis with probable bacterial or viral etiology, the patient was started on ceftriaxone, vancomycin, acyclovir and dexamethasone. With the diagnosis of leptospirosis, doxycycline was added. The patient was gradually weaned off from the ventilator on day 3 of admission, Further, in the course of clinical illness, the patient was diagnosed as acute pancreatitis which was managed conservatively. She received injections of acyclovir, ceftriaxone and doxycycline for 14, 14 and 7 days respectively, during the hospital course. She gradually improved and was discharged in a hemodynamically stable state on day 17 of hospitalization.

The patient was followed-up after discharge on an outpatient basis. There were no residual neurological deficits and she had normal blood parameters.

Discussion

This young lady presented with acute febrile illness, later on confirmed to be expanded leptospirosis syndrome with involvement of the liver, brain, heart, and pancreas in a progressive manner over 4 weeks of duration of illness. Leptospirosis is a widespread tropical zoonosis, which can present with a wide spectrum of manifestations from a mild, self-limiting febrile illness to severe life-threatening illness with multi-organ dysfunctions. Severe leptospirosis, historically characterised by its classical presentation of hepatorenal dysfunction in the form of Weil's disease, is now revealing a broader clinical spectrum, encompassing a diverse array of atypical manifestations.(2) This expanded spectrum may be called as expanded leptospirosis syndrome similar to dengue expanded syndrome, which often includes meningitis, myocarditis, acute respiratory distress syndrome, and pancreatitis, challenges the traditional understanding of the disease. Additionally, hepatobiliary complications, such as acalculous cholecystitis have been observed.(8)

The disease can sometimes manifest with neurological symptoms, often resembling bacterial, tuberculous, or viral meningitis, leading to initial diagnostic challenges. Meningeal signs occur in

80% of neuroleptospirosis cases but leptospirosis rarely manifests primarily as a neurological disease as seen in the present case where neurological manifestations were the initial presentation.(6) In a study conducted by Panicker et al. with 40 leptospirosis patients, 7.5 % of patients presented with meningoencephalitis, while 5% had an intracranial bleed.(6) Acute pancreatitis is a very rare manifestation of leptospirosis, though it is an under-reported complication of leptospirosis.(9) Hence, all the symptoms and signs should be carefully addressed as in this case who developed in hospital vomiting and biochemical and radiological evidence revealed pancreatitis. Concomitant myocarditis in this case was suspected with clinical evidence of tachycardia, ST-T segment changes in ECG with positive troponin I despite normal echocardiography, however literature has scarcity of this complication of leptospirosis.(5)

Diagnosis of leptospirosis remains challenging, due to the overlap of symptoms with other tropical infections and the varied clinical manifestations. While culture remains the gold standard, serological methods, including the microagglutination test and IgM enzyme-linked immunosorbent assay, are commonly employed for diagnosis, it helps to support modified Faine's criteria as presumptive evidence.(10,11) Early initiation of antimicrobial therapy is crucial in suspected cases, given the largely clinical nature of diagnosis and the potential for rapid diagnostic tests to yield negative results. Treatment typically involves antibiotics such as doxycycline or ceftriaxone, tailored to the severity of the disease.(1,2) Early recognition and start of antimicrobial therapy led to early resolution of the disease in our patient. Monitoring of patients is essential as leptospirosis can progress to severe illness if left untreated. Leptospirosis is a zoonotic disease, and humans acquire the infection from the environment after exposure to soil or water contaminated with animal urine. In our patient poor sanitary housing condition with rat inhabitations was found as the likely source of the disease, hence advised for rat elimination along with maintenance of the household condition.(3)

This case advocates for an updated understanding of leptospirosis, recognizing its potential for varied presentations and the importance of considering it in the differential diagnosis of febrile illnesses with multisystem involvement with 4 weeks of duration of illnesses as expanded leptospirosis syndrome. The presentation of CNS, heart, and pancreatic involvement highlights the need for heightened clinical suspicion and early diagnosis. Just as dengue, leptospirosis now warrants consideration for

its expanded clinical manifestations, prompting proactive measures for early detection and management of atypical cases.

Conclusions

Leptospirosis has varied clinical manifestations and severity with an expanding nature similar to dengue-expanded syndrome. Neurological involvement in leptospirosis can mimic viral and bacterial meningoencephalitis. Myocarditis and pancreatitis can be expanded leptospirosis manifestations.

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Ethics approval and consent to participate: The case study was conducted according to accepted ethical guidelines for the conduct of research on HUMANS. No Animals were used in this research. All human research procedures followed were in accordance with the ethical standards of the committee responsible for human experimentation (institutional and national), and with the Helsinki Declaration of 1975, as revised in 2008. Considering the retrospective observational single case study and de-identified nature of the case, ethical approval was not required, however, individual Written informed consent was obtained.

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