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Case Study

Expanded Leptospirosis Syndrome – An Unusual Case

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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 downward 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

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1. Introduction

Leptospirosis, caused by the spirochete bacterium Leptospira, is a zoonotic infection commonly found in low-income tropical countries. 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 (1). These diverse clinical presentations pose diagnostic and management challenges, especially with multi-organ involvement, including rare instances of pancreatic and cardiac complications (2-4). Central nervous system (CNS) complications in leptospirosis, such as aseptic meningitis or encephalitis, further contribute to clinical complexity (5). While multisystem organ involvement, including CNS, pancreas and heart, is exceptionally rare, recognizing and diagnosing such cases require keen clinical suspicion. Recently, many atypical presentations have emerged. Similar to dengue which expanded syndrome beyond typical hemorrhagic manifestation, leptospirosis can behave analogously beyond typical hepato-renal syndrome (6). In this context, we present an expanded leptospirosis case featuring acute meningoencephalitis, hepatitis, myocarditis, and pancreatitis.

2. Case Presentation

A young woman in her 20s, a farmerwith no prior known comorbidities, presented during August (rainy season) with 15 days of high-grade continuous fever (101-1020F), accompanied by chills and rigorspartially relieved by taking oral antipyretics. Concurrently, she experienced a continuousmoderate-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 developed vomiting (up to seven times a day), non-bloody and non-bilious, with mild dullaching epigastric pain. At a local hospital, fever and vomiting improved with prescribed medications. However, on the tenth day of illness, she developed hypoactive altered mental status(decreased responsiveness to commands with reduced verbal output), without abnormal body movements, up rolling of eyeballs, or focal neurological deficits. The patient was brought to the emergency.

Initial examination revealed a drowsy patient (Glasgow Coma Scale: E3V4M5) with tachycardia ,and Grade I Hypertension.

Icteric skin and conjunctival injection without suffusion were noted . Detailed neurological examination revealed bilateral mid-dilated pupilssluggishly reactive to light, neck rigidity, positive Brudzinski and Kernig's signs, exaggerated deep tendon reflexes (3+) and 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 indicated 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 normal. Electrocardiogram showed sinus tachycardia with non-specific ST segment changes. Serial cardiac biomarkers trended downward. Fundoscopy showed no papilledema. A non-contrast computed tomography (CT) scan of the head revealed cerebral edema. Cerebrospinal fluid (CSF) analysis showed elevated cell counts and proteins with a normal gram stain. Biofire PCR of CSF was negative for H. Influenza, 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 (Figures 1A-B).

Tropical fever workup was positive for leptospira by IgM ELISA, 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), mild abdominal pain and nausea developed. Abdominal ultrasound o revealed a mildly bulky hypoechoic pancreas with elevated serum amylase/ lipase levels. Magnetic resonance cholangiopancreatography (MRCP) showed diffusion restriction with low values in ADC maps of the pancreas, particularly in the tail region, along with minimal peripancreatic fat stranding ,suggesting acute pancreatitis (Figures 1C-E). Intravenous fluids and other supportive management were initiated.

Table 1. Basic and advanced laboratory reports of the patient.

Investigation	Units	Range	Day 1	Day 7	Day 10	Day 15
Hb	g/dl	13-17	14.6	10.9	13.2	12.9
TLC (x1000)	$\times 10^3$ cells/mm3	4-11	21.31	15.21	13.17	12.6
DLC (N/L/M)	%	40-70/20-40/2-8/1-6	84/8.2/7.0	72/17/6.2	65/20/8.8	64/22/7
Platelet	$\times 10^3$ cells/mm3	150 -450	768	354	553	320
TB	mg/dl	0.3 – 1.2	2.93	1.89	1.88	1.16
DB	mg/dl	0 – 0.2	1.33	0.93	1.05	0.48
SGPT	U/L	0-50	423	511	543	106
SGOT	U/L	0-50	292	312	337	65
ALP	U/L	30-120	180	303	661	306
GGT	U/L	0-55	161	354	803	383
Total Protein	g/dl	6.6-8.3	7	5.3	7.1	6.6
Albumin	g/dl	3.5-5.2	3.4	2.7	3.2	3.4
Globulin	g/dl	2.5-3.2	3.6	2.6	3.9	3.2
Urea	mg/dl	17-43	60	36	28	
Creatinine	mg/dl	0.72-1.18	0.88	0.32	0.26	
Sodium	mmol/L	136-146	155	141	138	
Potassium	mmol/L	3.5-5.1	4.4	3.6	3.08	
Chloride	mmol/L	101-109	118	104	100	
Calcium	mg/dl	8.8-10.6	10	8.5	9.9	
Uric acid	mg/dl	3.5-7.2	3.8	1.6	2.6	
Phosphorus	mg/dl	2.5-4.5	4.2	1.7	1.0	
PT/INR			15.3/1.43			
Procalcitonin	<0.5	ng/ml	0.39			
Amylase	U/L	28-100		350	220	164
Lipase	U/L	0-67		396	399	272
CPK - MB	U/L	0-24	120		44	
Troponin I	ng/ml	<0.02	2.6		0.8	
Leptospira IgM ELISA	IU/L	<14	44			66

Blood cultures (day 1 and day 7): Sterile
CSF Analysis:

Cells – 20/ mm^3
(Differential count – 85 % lymphocytes and 15% polymorphs
Sugar/
corresponding blood sugar – 127/158 mg/dl
Protein – 73 mg/dl
Gram stain and culture – Negative.
KOH and acid-fast bacilli stain – Negative
CSF CBNAAT - negative

CSF bio-fire PCR - Negative for *E. coli, H. influenzae, Listeria, Neisseria, Streptococcus pneumonia*, CMV, HSV1, HSV2, HSV 6, VZV, HPV, enterovirus, *Cryptococcus neoformans*.

Ultrasound of abdomen – mildly bulky hypoechoic pancreas.

Non-contrast Computed tomography scan of head – cerebral edema.

CEMRI BRAIN: T2/FLAIR hyperintensity is seen in the left occipital lobe. Leptomeningeal thickening and enhancement are seen predominantly in the sulcal spaces of the left parietal lobe and bilateral high frontal lobes. No restricted diffusion or increased susceptibility is seen.

MRCP - The pancreas shows diffusion restriction with low values in ADC maps. Minimal peripancreatic fat stranding is seen in the tail region.

Hb – Haemoglobin, TLC – Total Leukocyte count, DLC – differential leukocyte count, RDW – red cell distribution width, ALT – alanine transaminases, AST – aspartate transaminases, ALP – alkaline phosphate, GGT – gamma-glutamyl transferase, PT – prothrombin ratio, INR – International standardized

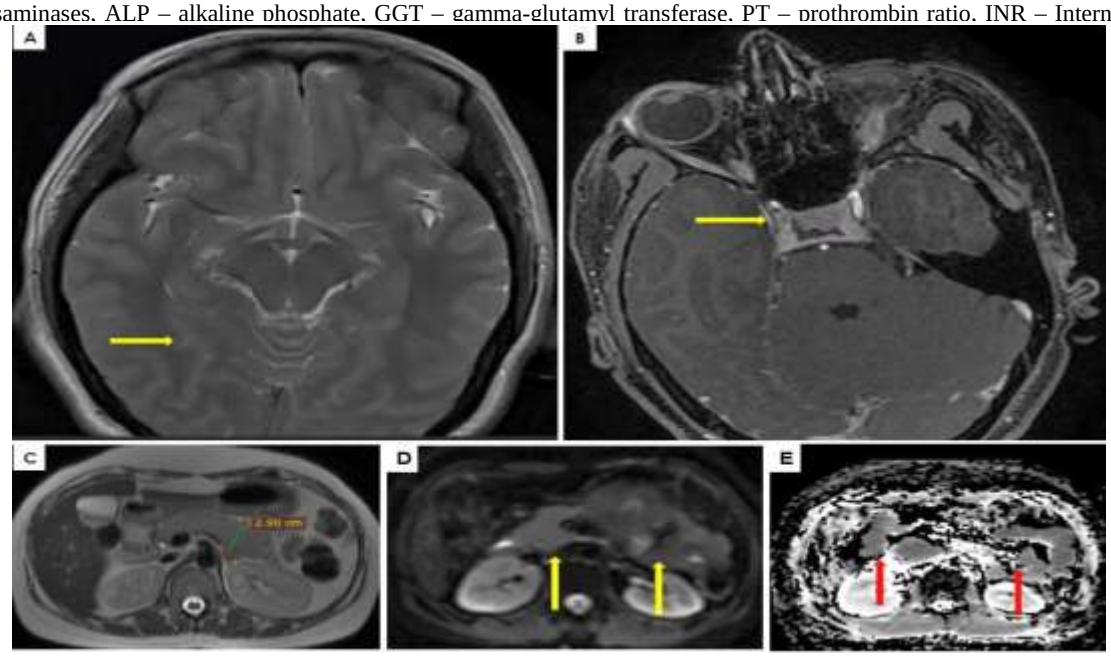

Figure 1. Radioimages of the patient. (A&B) show axial section of contrast-enhanced MRI scan of the brain with ill-defined temporal densities (arrow) and meningeal enhancement (arrow) respectively; (C) shows the axial section of MRCP having bulky pancreas (arrow); (D&E) shows the axial sections of magnetic resonance cholangiopancreatography having diffusion restriction in ADC (arrows) compared to DWI (arrows) respectively.

With clinical, epidemiological and laboratory features meeting modified Faine's criteria(score of 36 >25) and positive leptospira IgM serology, expanded leptospirosis syndrome with meningoencephalitis, hepatitis, pancreatitis and myocarditis was confirmed.

Differential diagnoses included acute bacterial meningitis, tubercular meningitis, viral encephalitis, expanded dengue syndrome, enteric fever, and cerebral malaria —all ruled out by negative investigations. .Scrub typhus and leptospirosis were considered given deranged liver biochemistry.

Twelve -hours post-admission,progressive sensorium necessitated intubation and intensive care . Provisional diagnosis of acute meningoencephalitis with probable bacterial or viral etiology led to ceftriaxone, vancomycin, acyclovir and dexamethasone. Doxycycline was added after leptospirosis confirmation. The patient was gradually weaned off from the ventilator on day 3. Acute pancreatitis was managed conservatively. She received injections of acyclovir (14 days), ceftriaxone (14 days) and doxycycline (7 days), gradually improving until discharge on day 17.

Outpatient was follow-up showed no residual neurological deficits and the patient had normal blood parameters

3. Discussion

This young lady presented with acute febrile illness progressing to expanded leptospirosis syndrome involving liver, brain, heart, and pancreas over 4 weeks. Leptospirosis, tropical zoonosis, with manifestations ranging from self-limiting febrile illness to severe life-threatening illness with multi-organ dysfunctions. Severe leptospirosis, historically was characterized 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, including meningitis, myocarditis, acute respiratory distress syndrome, and pancreatitis, challenges the traditional understanding of the disease. Additionally, hepatobiliary complications (e.g., acalculous cholecystitis) have also been documented (7).

The disease can sometimes manifest with neurological symptoms, often resembling bacterial, tuberculous, or viral meningitis leads to initial diagnostic challenges. Meningeal signs occur in 80% of neuroleptospirosis cases but leptospirosis rarely manifests as a neurological disease as the present case where neurological manifestations were the initial presentations (5). 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 (5). Acute pancreatitis is a very rare manifestation of leptospirosis, though it is an underreported complication of leptospirosis (8). 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 (4).

Diagnosis of leptospirosis remains challengingdue 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 (9, 10). 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 identified as the likely source of the disease, hence he was advised to eliminate rat and maintain improved household conditions (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 lasting 4 weeks ,a concept known as expanded leptospirosis syndrome. The presentation of

CNS, heart, and pancreatic involvement highlights the need for clinical suspicion and early diagnosis. Just as with dengue, leptospirosis now warrants consideration for its expanded clinical manifestations, prompting proactive measures for early detection and management of atypical cases.

4. Conclusions

Leptospirosis exhibits a wide range of clinical manifestations and severity, with an expanding nature similar to dengue's expanded syndrome. Neurological involvement in leptospirosis can mimic viral and bacterial meningoencephalitis. Myocarditis and pancreatitis can also be considered manifestations of expanded leptospirosis.

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Authors' Contribution

Study concept and design: S. NS, H. IV, P. KP, A. T, M. D.
Analysis and interpretation of data: S. NS, N. D, P. KP.
Drafting of the manuscript: S. NS, N. D, M. D.
Critical revision of the manuscript for important intellectual content: P. KP, A. T, M. D.
Statistical analysis: P. KP, A. T.

Ethics

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 adhered to the ethical standards of the committee responsible for human experimentation (institutional and national), and conformed to the Helsinki Declaration of 1975, 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 from the patient.

Conflict of Interest

The author or authors declare that they have no conflict of interest with respect to the author or publication of this article.

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None

Data Availability

Data are available in the manuscript; additional data can be requested from the corresponding author.

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