Case Report

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Leptospirosis with a Rare Presentation of Acute Multiple Cerebral Infarcts: A Case Report

Internal Medicine Section

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ABSTRACT

Leptospirosis is a zoonotic disease that can manifest as an asymptomatic infection or as a fulminant, fatal illness. According to published literature, neurological manifestations can be observed in 10-15% of cases. Here is a case of a 65-year-old female patient who presented with a history of fever lasting six days, followed by seizures and loss of consciousness. *Leptospira* IgM was found to be positive, and Magnetic Resonance Imaging (MRI) of the brain showed multiple acute cerebral infarcts. The patient was treated with intravenous antibiotics, antiepileptics and other symptomatic treatments. During her hospital stay, the patient improved symptomatically. Neurological manifestations of leptospirosis may result from immune-mediated reactions, leading to cerebral arteritis. This makes it a potential differential diagnosis for fever with acute cerebrovascular accidents in tropical and endemic regions.

Keywords: Immune phase, Neuroleptospirosis, Neurological manifestations

CASE REPORT

A 65-year-old female patient, who was a resident of South India and a housewife belonging to a lower socio-economic status, was brought to the medical casualty by her attendants with a history of high-grade fever lasting for six days, accompanied by myalgia and headache. The patient's attendants reported multiple episodes of non projectile vomiting on the third day of fever and two to three episodes of seizures on the fifth day, which were generalised tonic-clonic seizures that lasted for a few seconds without regaining consciousness between episodes. After the last seizure activity, the patient developed altered sensorium and progressed to loss of consciousness within one day. There was no history of trauma, cough, breathlessness, chest pain, or previous infections reported. The patient revealed no history of any co-morbidities in the past and was not on any medications.

On examination, the patient's Glasgow Coma Scale score was E1V1M4. She was febrile, and tachypnoea and tachycardia were noted. Blood pressure was within the normal range. No rashes or eschar was observed on any part of the body. Upon examination of the respiratory system, bilateral normal vesicular breath sounds were heard with no adventitious sounds, and on cardiovascular examination, normal heart sounds were noted. Abdominal examination revealed mild hepatomegaly.

A detailed Central Nervous System (CNS) examination showed signs of raised Intracranial Tension (ICT), with neck stiffness present, and both Kernig's and Brudzinski's signs were positive. Muscle tone was increased in all four limbs, deep tendon reflexes were exaggerated, and bilateral plantar reflexes were extensor. Based on this history and examination findings, differential diagnoses of meningoencephalitis due to viral/bacterial infections, scrub typhus, leptospirosis, and cerebral malaria were considered.

Routine blood investigations, such as complete blood count, ESR, liver function tests, kidney function tests, electrolytes, and serology, were within the normal range [Table/Fig-1]. Other investigations, like Malarial Parasite Quantitative Buffy Coat (MP QBC), Dengue IgM, Chikungunya IgM, *Leptospira* IgM, Scrub Typhus IgM, Widal test, blood and urine culture, and CSF analysis, were also sent for analysis and empirical antibiotics were started with Inj. Ceftriaxone 2 g i.v. BD, Inj. Artesunate 120 mg i.v. BD, and Inj. Doxycycline 100 mg i.v. BD, and the patient was ensured adequate hydration.

Tests	Value	Normal range
Haemoglobin (gm/dL)	9.4	12-15.5
Total count (cells/µL)	7100	4000-11000
Neutrophils (%)	59	-
Lymphocytes (%)	32	
Eosinophils (%)	3	
Monocytes (%)	2	
Platelet (lacs cells/µL)	2.52	1.5-3.5
ESR (mm/hr)	40	0-20
Serum urea (mg/dL)	18	6-24
Creatinine (mg/dL)	0.8	0.7-1.4
Serum sodium (mmol/L)	136	135-146
Serum potassium (mEq/L)	3.8	3.5-5.2
Serum bilirubin (mg/dL)	1.5	0.1-1.2
SGOT (IU/L)	46	8-45
SGPT (IU/L)	32	7-56
HIV	Negative	-
HbsAg	Negative	
HCV	Negative	

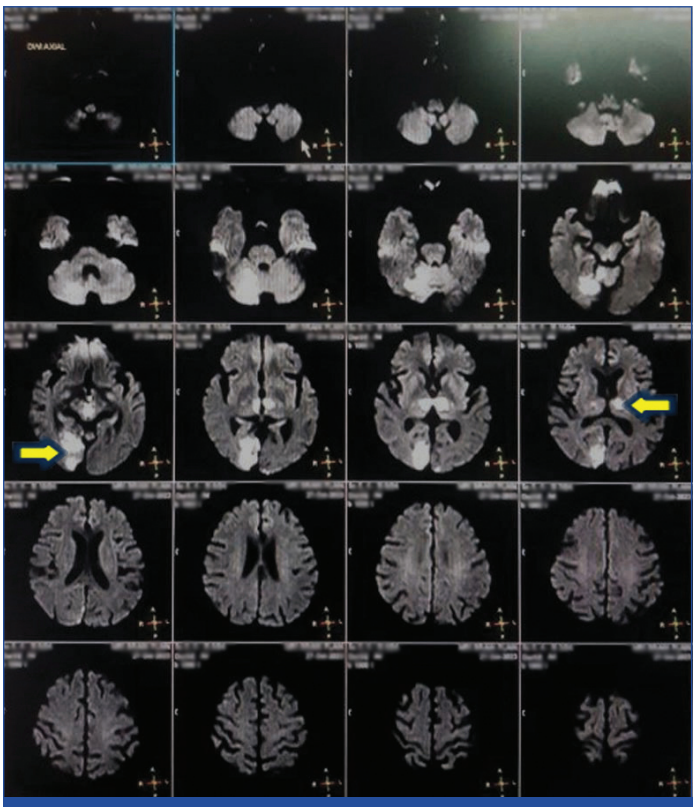
[Table/Fig-1]: Haematological and biochemical profile.
ESR: Erythrocyte sedimentation rate; SGOT: Serum glutamic oxaloacetic transaminase; SGPT: Serum glutamic pyruvic transaminase; HIV: Human immunodeficiency virus; HbsAG: Hepatitis B surface antigen; HCV: Hepatitis C virus

The chest X-ray and Electrocardiography (ECG) were normal. The abdominal ultrasound showed mild hepatomegaly without any ascites. The 2D echocardiogram was normal. The fundus examination showed no evidence of papilledema.

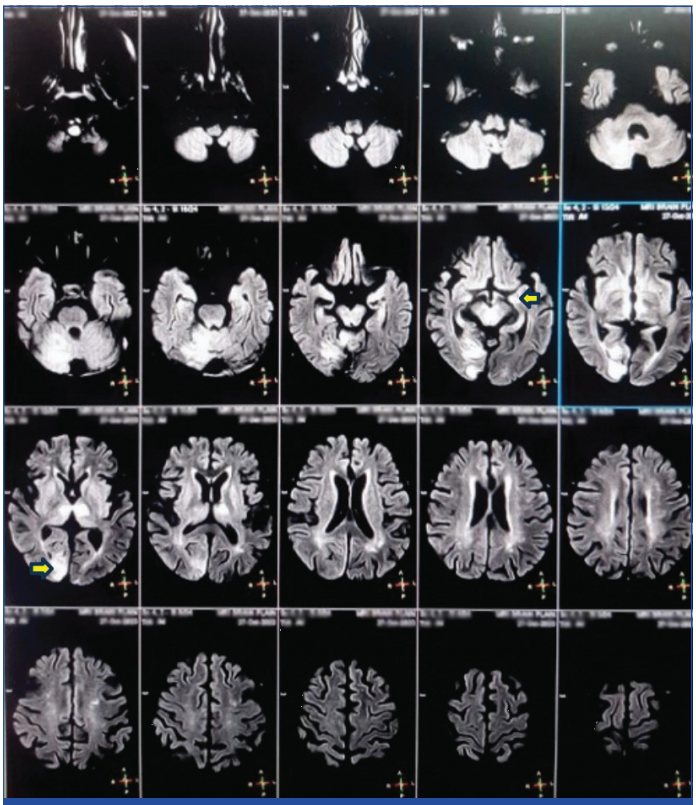
Leptospira IgM tested positive. CSF analysis showed features suggestive of aseptic meningitis. Furthermore, Malaria Parasite Quantitative Buffy Coat (MPQBC), Dengue IgM, scrub typhus IgM, Widal test, and blood and urine cultures were negative. Hence, antimalarials were stopped, and the patient was continued on Ceftriaxone 2g i.v. twice daily and Doxycycline 100 mg i.v. twice daily for 7 days, followed by oral Doxycycline 100 mg twice daily for another seven days. Symptomatic treatment with i.v. fluids, i.v. antiepileptics, and Inj. Mannitol was also administered.

CT brain scans were normal. The patient's general condition did not improve after 72 hours of admission, so an MRI of the brain

was planned. The MRI showed acute infarcts in the bilateral thalami (probably due to vasculitis and immune mediated reactions to leptospires), periaqueductal white matter, parasagittal occipital cortex, and cerebellum on the right-side [Table/Fig-2,3]. MR angiogram and venogram were normal [Table/Fig-4].

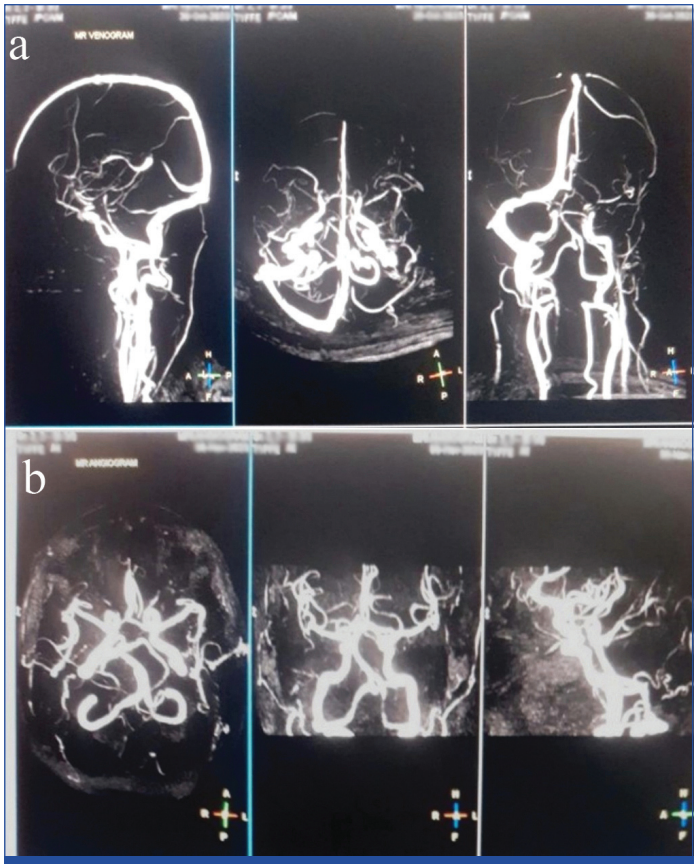


[Table/Fig-2]: MRI brain with Hyperintense signal on DWI with reversal on ADC suggestive of multiple acute infarcts on bilateral thalami, periaqueductal white matter, right occipital cortex and cerebellum (arrow).



[Table/Fig-3]: MRI brain with FLAIR hyperintensity on multiple areas suggestive of acute infarcts (arrow).

During the course of the hospital stay, the patient's general condition improved from the 5th day. She became conscious and coherent on the 10th day. On the 14th day, the patient was discharged from the hospital without any neurological manifestations. She was



[Table/Fig-4]: Normal appearing MR Venogram (4a) and MR Angiogram (4b) of brain with no evidence of vasculitic changes.

asymptomatic at the follow-up visit after one month. A repeat MRI of the brain was planned for six months later, but the patient was reluctant to attend the follow-up.

DISCUSSION

Leptospirosis is a globally important zoonotic disease caused by pathogenic *Leptospira* species. It is characterised by a broad spectrum of clinical manifestations, varying from asymptomatic infection to fulminant fatal disease [1]. Although most cases of leptospirosis can present with milder disease, the severe form can cause Acute Respiratory Distress Syndrome (ARDS), acute hepatic failure, acute kidney injury, and multiple organ dysfunction syndrome [2]. According to published literature, neurological manifestations can be seen in 10-15% of patients with leptospirosis, with the most common manifestation being aseptic meningitis [3]. Other presentations include myeloradiculopathy, myelopathy, Guillain-Barré syndrome-like presentations, intracerebral haemorrhage, cerebellar dysfunction, iridocyclitis, and tremor/rigidity [4]. Both cerebral and coronary arteries can be damaged by leptospirosis, but cerebral infarction due to leptospirosis is rarely reported [5].

Carriers of the disease include both wild and domestic animals, such as rodents, cattle, pigs, and dogs. Spirochetes colonise the proximal renal tubules of infected animals. The bacteria are shed in the urine from reservoir animals and can survive in contaminated soil and water for extended periods. Transmission to humans occurs through mucosal exposure or breaks in the skin [6]. Risk factors for exposure include occupational exposure, recreational activities, and household environmental factors [7].

Leptospirosis is classically described as a biphasic illness with an average incubation period of 5-14 days, which can range from 2 to 30 days [8]. It consists of an initial leptospiraemic phase (lasting 3-7 days) followed by an immune phase (lasting 4 to 30 days). The first phase corresponds to the multiplication and spread of the organism throughout the body, while the second phase is characterised by the development of circulating antibodies and the detection of leptospires in the urine. In the second phase, the

clinical signs of leptospirosis are more organ-specific, which include haemoptysis, dyspnea, oliguria, jaundice and uveitis [9].

Neurological manifestations may occur due to the effect of leptospires on the CNS or as a result of an immune-mediated response to the bacterium. Leptospirosis is responsible for 5-13% of all cases of aseptic meningitis. According to Panicker JN et al., 40 patients admitted to a general medical ward over a three-year period with acute neurological disease were found to have leptospirosis [3]. Other manifestations include encephalitis with altered sensorium, psychosis, seizures, stroke, intracranial haemorrhage, movement disorders and cerebellitis. According to OH Del Brutto, postmortem studies of leptospirosis cases showed cerebral arteritis involving large arteries at the base of the brain, especially the middle and anterior cerebral arteries [10]. Furthermore, it can damage not only cerebral arteries but also coronary arteries. Nervous system involvement is primarily immune-mediated, and gross changes include exudates, leptomeningeal oedema and congestion and haemorrhage in the brain and spinal cord. Microscopically, perivascular round cell infiltration of small and medium-sized blood vessels, along with patchy demyelination are prominent features [11].

A definitive diagnosis of leptospirosis is based on the isolation of the organism from the patient, a positive Polymerase Chain Reaction (PCR) result, or seroconversion evidenced by a rise in antibody titer. The Microscopic Agglutination Test (MAT), which uses a battery of live leptospiral strains, and the Enzyme Linked Immuno Sorbent Assay (ELISA), which uses broadly reacting antigens, is the standard serologic procedures. Considering the laborious nature of the test procedure and the low sensitivity during the acute stage, the utility of MAT as a reference test seems imprudent. However, ELISA also needs to be validated, as there can be many cross-reactions with other infections [12].

Mild leptospirosis can be treated with oral doxycycline or amoxicillin. Moderate to severe leptospirosis is treated with penicillin (1.5 million units i.v. or IM every 6 hours), ceftriaxone (2g/day i.v.), or doxycycline (100 mg i.v. every 12 hours). The role of steroids in the treatment of leptospirosis is controversial.

In this case, the patient presented with neurological manifestations after one week of fever history, likely in the immune phase of the disease. The ensuing neurological disease depends on the virulence of the strains and the development of an inflammatory response. The prognosis of neuroleptospirosis is largely unknown. Most studies report mortality rates for systemic leptospirosis varying from 5 to 15%. Altered sensorium, seizures and raised CSF protein levels were found to correlate with a worse prognosis [13].

CONCLUSION(S)

Leptospirosis is a global zoonotic disease that can present with variable clinical manifestations. It can be a differential diagnosis for fever accompanied by acute cerebrovascular accidents in patients from tropical and endemic regions. Although, it is a rare manifestation, it should not be ignored.

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