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Case Report

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Neuroleptospirosis Complicated by Cerebral Venous Sinus Thrombosis

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Abstract

Leptospirosis is an acute infectious disease that manifests as a biphasic sickness with an initial leptospiraemic and a subsequent immunological phase. It is caused by a spirochete belonging to the genus *Leptospira*. Leptospirosis seldom manifests clinically as a primary neurological impairment. We report a case of a middle-aged man who was initially diagnosed with leptospirosis and subsequently complicated by development of cerebral venous sinus thrombosis. This intriguing case study emphasises the importance of identifying uncommon leptospirosis symptoms in endemic regions such as Malaysia.

Keywords: Neuroleptospirosis; complications; cerebral venous sinus thrombosis,

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INTRODUCTION

Leptospirosis, a globally prevalent zoonotic disease caused by pathogenic *Leptospira* bacteria, poses a significant challenge to clinicians and researchers due to its substantial morbidity and mortality rates. The World Health Organisation (WHO) estimates over 500,000 severe cases annually worldwide, with rodents as the primary reservoirs.[1] This disease is often associated with occupational exposure and is prevalent in areas with inadequate sanitation. Transmission occurs through dermal contact with infected animal urine, and clinical presentations vary widely, ranging from mild febrile illness to severe manifestations like Weil's disease.

Central nervous system involvement is rare, with severe complications leading to diverse neurological issues such as cerebral venous sinus thrombosis (CVST), cerebrovascular accidents, and meningitis.[2] We present a case of a young man with mild leptospirosis complicated by development of CVST with the patient's clinical course.

CASE REPORT

A previously healthy middle-aged farmer from rural area presented to the district hospital with a three-day history of high-grade fever, accompanied by non-projectile vomiting, diarrhoea, myalgia, and intermittent headaches. He reported multiple recent exposures to potentially contaminated water in his paddy fields within the week prior to symptom onset.

He was admitted with initial suspicion of leptospirosis and started on treatment. However, three days after hospitalisation, his condition worsened with severe headaches, recurrent projectile vomiting, and a dysphasic. He did not have seizures, neurological deficits, shortness of breath, jaundice, or dark urine. Vital signs remained stable. Given the suspicion of neuroleptospirosis and the anticipated complexity of his management, he was promptly referred to a tertiary centre for further evaluation and treatment.

Upon arrival, the patient appeared confused and disorientated to people, time, and place. His best Glasgow Coma Scale (GCS) was 12/15, indicating moderate impairment (eye response = 3, verbal response = 4, motor response = 5). He was febrile, with a temperature of 38.5°C. Vital signs: blood pressure at 152/90 mmHg, pulse rate at 95 beats per minute, respiratory rate at 20 breaths per minute, and oxygen saturation at 98% on room air. Examination revealed mild conjunctival suffusion of the sclera. Meningeal irritation was evident, as he exhibited neck stiffness and positive Kernig's and Brudzinski's signs. There were no other focal neurological signs. Cardiorespiratory and abdominal examinations showed no abnormalities.

Complete blood count revealed white blood cell counts of 16×10^9/L (normal: 7-12 x10^9/L) with neutrophil count of 87% (40-60%). Haemoglobin was 13.7 g/dL (11-15 g/dL), and platelets were178×10^9/L (150-450x10^9/L). Renal and liver function tests were normal. Inflammatory markers were elevated: C-reactive protein (CRP) at 85 mg/L (<10mg/L) and an erythrocyte sedimentation rate (ESR) at 56 mm/hour (<15 mm/hour). Coagulation profile, including the international normalised ratio (INR), was normal. Blood and urine cultures and sensitivity were negative for any microorganisms. However, serum samples tested positive for *Leptospira* DNA via real-time polymerase chain reaction (PCR).

An urgent non-contrast computed tomography (NCCT) scan of the brain revealed a left temporal intracerebral haematoma (ICH) compressing the ipsilateral ventricle (**Figure 1**). The haematoma was estimated at 30 ml in size, causing a midline shift of more than 5 mm. Additionally, a maximum intensity projection (MIP) image of the CT venogram (CTV) showed that the left transverse sinus, left sigmoid sinus and right transverse sinus were patent. while there was still a defect seen over the right sigmoid sinus (**Figure 2**).

Based on the clinical presentation, biochemical results, and radiological findings, a provisional diagnosis of CVST secondary to severe neuroleptospirosis was made. Differential diagnoses, including dengue, malaria, typhoid fever, and scrub typhus, were ruled out through negative serological tests.

Upon referral to our tertiary center, the patient was started on intravenous ceftriaxone 2g every 12 hours for 14 days continued until discharge 20 days later. Given the presence of CVST with concomitant neurological deficits, an urgent left decompressive craniectomy and clot evacuation were performed.

During the surgery, the patient experienced a significant blood loss of approximately 1.2 litres, necessitating the transfusion of three pints of packed cells. The brain appeared relaxed but mildly oedematous. Haemodynamic support was provided through a low-dose noradrenaline infusion to sustain mean arterial pressure of ≥ 75mmHg. Postoperatively, the patient was admitted to the neurosurgical intensive care unit for close monitoring and cerebral resuscitation. Sedation was managed with propofol and fentanyl infusions at the rate of 60-100mg/hour and 30-50 mcg/hour, respectively, to achieve a Richmond Agitation and Sedation Score of negative 1 to zero. A follow-up NCCT brain scan performed 24 hours later showed small ICH with mild cerebral oedema (**Figure 3**).

Sedation was tapered over 48 hours, with the patient's GCS improving to E3, V4, and M4 (11/15). Three days postoperatively, with no surgical site bleeding, stable platelets and INR values, subcutaneous low-molecular-weight-heparin (LMWH) 40mg twice daily was initiated to treat CVST. Anticoagulation therapy with warfarin was monitored to maintain an INR of 2 to 3, with close observation for neurological deterioration or bleeding.

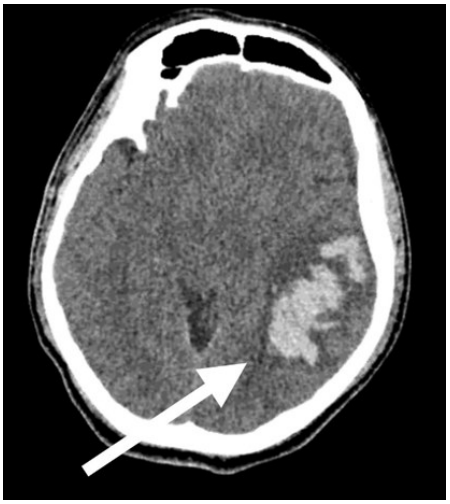

Figure 1: Pre-operative axial non-contrast CT scan of the brain showed left temporal ICH with mass effect (arrow).

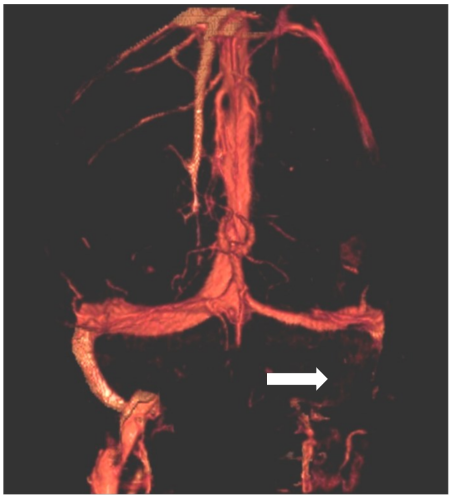

Figure 2: Maximum Intensity Projection (MIP) of the Computed Tomography Venogram (CTV) imaging showed that the left transverse sinus, left sigmoid sinus and right transverse sinus were patent. while there was still a defect seen over the right sigmoid sinus (arrow).

One week post-decompressive craniectomy, the patient was transitioned from LMWH to oral apixaban, a factor Xa inhibitor, 10 mg twice daily for seven days, which was well tolerated, without any bleeding tendencies. Concurrently, he began chest and limb physiotherapies to aid his recovery.

The patient was discharged home on post-operative day 22 with a GCS of 14/15, right-sided motor strength of 4/5 of the right hand and leg and 5/5 on the left side, and no sensory deficit. He continued on oral apixaban at a maintenance dose of 5 mg twice daily. At neurological follow-up three weeks later, he was well with a GCS 14/15 and full motor strength (5/5) in all four limbs. Compliance with the apixaban regimen was confirmed, with no bleeding and repeated CTV showed improvement, with residual filling defects in the sigmoid and transverse sinuses.

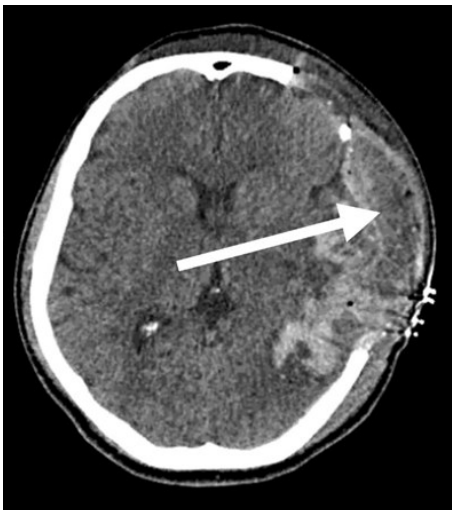

Figure 3: Post-operative axial view non-contrast CT scan of the brain showed slight reduction of the left temporal ICH (arrow) after the craniectomy and clot evacuation.

DISCUSSION

The zoonotic illness leptospirosis, caused by pathogenic spirochetes of the genus *Leptospira*, is found in tropical and subtropical climates worldwide; it is endemic in many areas, including Malaysia. Due to frequent monsoon rains, Malaysia suffers from leptospirosis when there is a greater danger of exposure to contaminated water due to high rainfall and flooding.[3,4] Malaysia has about 1.08 cases per 100,000 people, with higher rates in Selangor, Kelantan, and Sarawak.[3,4] Mortality ranges vary from 5% to 25%.[1,5]

The disease is biphasic, leptospiraemic followed by immunological phase, and can present with mild to to severe symptoms. Rare neurological complications include CVST, meningitis, encephalitis, and stroke.[5] The proposed pathophysiology of CVST includes cerebral vasculitis and endothelial injury, which leads to intravascular thrombosis.[6] A Brazilian study found CVST in five out of 30 patients (incidence rate of 16.7%) with severe leptospirosis.[7] A lesser incidence was noted in different research from Thailand, where CVST was reported in two out of 282 leptospirosis

patients (0.7%).[8]

Leptospirosis is diagnosed using PCR, serology, and culture on blood, urine, and CSF samples. In our patient, PCR on day 3 of illness confirmed leptospirosis. PCR sensitivity depends on sample timing and ranges from 40–60%, with >95% specificity.[1,5]

Neurosurgical intervention may be considered in neuro-leptospirosis with CVST.[9] Our patient underwent a left decompressive craniectomy and clot evacuation due to worsening GCS and CTV findings. He avoided complications (bleeding, post-operative infection, stroke, and death), possibly due to early recognition, prompt intervention, and being young with no comorbidities.

To prevent recurrence, current guidelines suggest treating CVST with either LMWH or unfractionated heparin (UFH) for 3-12 months, followed by oral vitamin K antagonist (VKA) should be used with an INR of 2 to 3. A meta-analysis showed that VKAs had a greater likelihood of cerebral venous recanalisation, but use of direct oral anticoagulants (DOAC) in CVST has comparable effectiveness and safety, as well as more effective in preventing recurrent CVST compared to LMWH. DOAC, such as Apixaban, which was used in our patient, was safe in the treatment of CVST, and it is recommended for patients with CVST for up to six months.[6,10]

Neuro-leptospirosis has an unclear prognosis. Systemic leptospirosis has 5–15% fatality rate,[1,5,7] with pulmonary involvement being the primary cause of death, a mortality rate of 24.1%.[2,9] A study by Heath *et al.* showed that with neurological and non-neurological symptoms, the mortality rate was 7%.[1] The higher rate may be attributed to delayed management from delayed referral.

CONCLUSION

Early recognition of leptospirosis and its neurological complications is crucial. In endemic areas, clinicians should maintain a high index of suspicion to ensure timely diagnosis and treatment, thereby preventing complications.

Take Home Message

- Neuroleptospirosis can present with rare but severe complications such as CVST, which may require urgent neurosurgical intervention.
- Early recognition and diagnosis using PCR testing for Leptospira DNA are critical, especially in endemic areas with relevant exposure histories.
- Prompt multidisciplinary management—including antibiotics, neurosurgical decompression, and anticoagulation therapy—can significantly improve outcomes in severe neuroleptospirosis cases.
- DOACs such as apixaban, are a safe and effective long-term treatment option for CVST, offering comparable efficacy to traditional regimens.
- Clinicians in endemic regions must maintain a high index of suspicion for atypical presentations of leptospirosis to prevent delays in diagnosis and treatment

Abbreviations

CVST	cerebral venous sinus thrombosis
GCS	Glasgow Coma Scale
CRP	C-reactive protein
ESR	Erythrocyte sedimentation rate
INR	International normalised ratio
PCR	Polymerase chain reaction
NCCT	Non-contrast computed tomography
ICH	Intracerebral haematoma
MIP	Maximum intensity projection
CTV	CT venogram
LMWH	Low-molecular-weight0heparin
VKA	Vitamin K antagonist
UFH	Unfractionated heparin
DOAC	Direct oral anticoagulant

Declarations

Patient Consent

Patient consent has been obtained.

Disclosure and Conflict of Interest

The authors declare that they have no conflicts of interest and no financial disclosures relevant to this case report.

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