Case Report

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Tuberculous meningitis leading to stroke: a case report

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Introduction: Tuberculosis is a major public health issue in developing countries. Vasculitis, resulting from tubercular meningitis, can lead to stroke.

Case presentation: A 33-year-old male presented to the Emergency Department with relapsing-remitting fever with an evening rise in temperature for 1 month, personality changes (aggression and mutism) for 2 weeks, followed by difficulty in moving his lower limbs, and bowel and bladder incontinence. Neck rigidity, a positive Kernig's sign, bilateral mute plantar responses, and 0/5 power in bilateral lower limbs were noted on examinations. MRI of the brain was suggestive of tubercular meningitis and showed an infarct with hemorrhagic transformation in the relatively uncommon, right basifrontal lobe. Gene Xpert test done on cerebrospinal fluid confirmed the diagnosis.

Discussion: Tuberculous meningitis leading to infarct is a challenging diagnosis due to nonspecific symptoms and variable cerebrospinal fluid AFB staining results. Radiological imaging with MRI helps in suggesting the diagnosis and Gene Xpert confirms the diagnosis. Antitubercular therapy, steroids, physiotherapy, and supportive care are part of management.

Conclusion: This case highlights the importance of considering tubercular meningitis-related cerebral infarction despite initial negative CSF AFB stain. Radiological investigation may help in guiding the clinician towards a diagnosis of tuberculous meningitis with vasculitis.

Keywords: stroke, tubercular meningitis, vasculitis

Introduction

Tuberculosis (TB) caused by *Mycobacterium*, a leading cause of death in Nepal, is a major public health issue[1]. Despite contributing to a mere 1–10% of all active TB cases, tubercular meningitis (TBM) is a lethal manifestation of the disease, with prognosis worsening with delay in diagnosis and initiation of treatment[2–4].

TBM remains elusive to treat with nonspecific manifestations and often presents with an array of complications that include tuberculomas, hydrocephalus, cranial nerve involvement, and vasculitis[1,5]. It is generally accepted that vasculitis is the common cause of stroke in tubercular meningitis[6]. Although vasculitis has no clear pathogenesis, it may result due to a combination of morphological changes, chemically medicated vasospasm, or immunologic attack of the vessel wall by tubercular protein and may lead to infarction[7].

Here, we are reporting the case of a 33-year-old male with tuberculous meningitis complicated with cerebral infarct with hemorrhagic transformation.

HIGHLIGHTS

- Patients with tuberculous meningitis can present with stroke.
- Radiological investigation like MRI could help in guiding clinician towards the diagnosis of tubercular meningitis especially when CSF AFB stain is negative.
- Antitubercular therapy, corticosteroid are important in managing tubercular meningitis with infarction.

Case description

A 33-year-old male presented to the Emergency Room with chief complaints of relapsing-remitting fever for 1 month. The maximum temperature recorded was 101°F (38.3°C) and was associated with an evening rise. The patient also had abrupt personality changes involving aggression and mutism 2 weeks before presentation to the

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hospital. It was followed by difficulty moving his lower limbs, and bowel and bladder incontinence. He had no cough, chest pain, abdominal discomfort, or burning micturition. Furthermore, he had no significant weight loss during the previous year. He denied previous medical illness or surgical interventions. He was a nonsmoker and had no history of substance abuse. He was a migrant worker in Malaysia, who lived with a group of individuals, sharing a common room. However, there was no history of similar illness in his roommates. Additionally, he had no previous contact with a known case of tuberculosis.

On presentation to the emergency department, he showed an eye-opening response to the speech, was confused, and could localize pain (Glasgow Coma Scale - 12/15). His pupils were 2 mm and reactive to light bilaterally. His temperature was 100°F (37.7°C), blood pressure was 100/70 mmHg, and oxygen saturation was maintained at 96% in room air. He had no pallor, icterus, lymphadenopathy, dehydration, or skin rashes.

On neurological examination, neck rigidity was present, and Kernig's sign was positive. He had a focal neurological deficit involving bilateral lower limbs with a muscle power of 0/5. However, his bilateral upper limb muscle power was normal (5/5). The extensor plantar response was mute bilaterally. His systemic examination revealed normal findings.

On investigation, his blood parameters revealed elevated Erythrocyte Sedimentation Rate (ESR) (55 mm/h), sodium (120 mEq/l), and potassium (3.9 mEq/l). Serum Glutamic Pyruvic Transaminase (SGPT) was 70 U/l (normal range: 7–45 U/l), Serum Glutamic-Oxaloacetic Transaminase (SGOT) 60 U/l (normal range: 8–48 U/l), and Alkaline Phosphatase (ALP) - 79 U/l (normal range: 45–115 U/l). His chest radiograph at the time of admission was normal. MRI findings were present as described in the Figures 1–4.

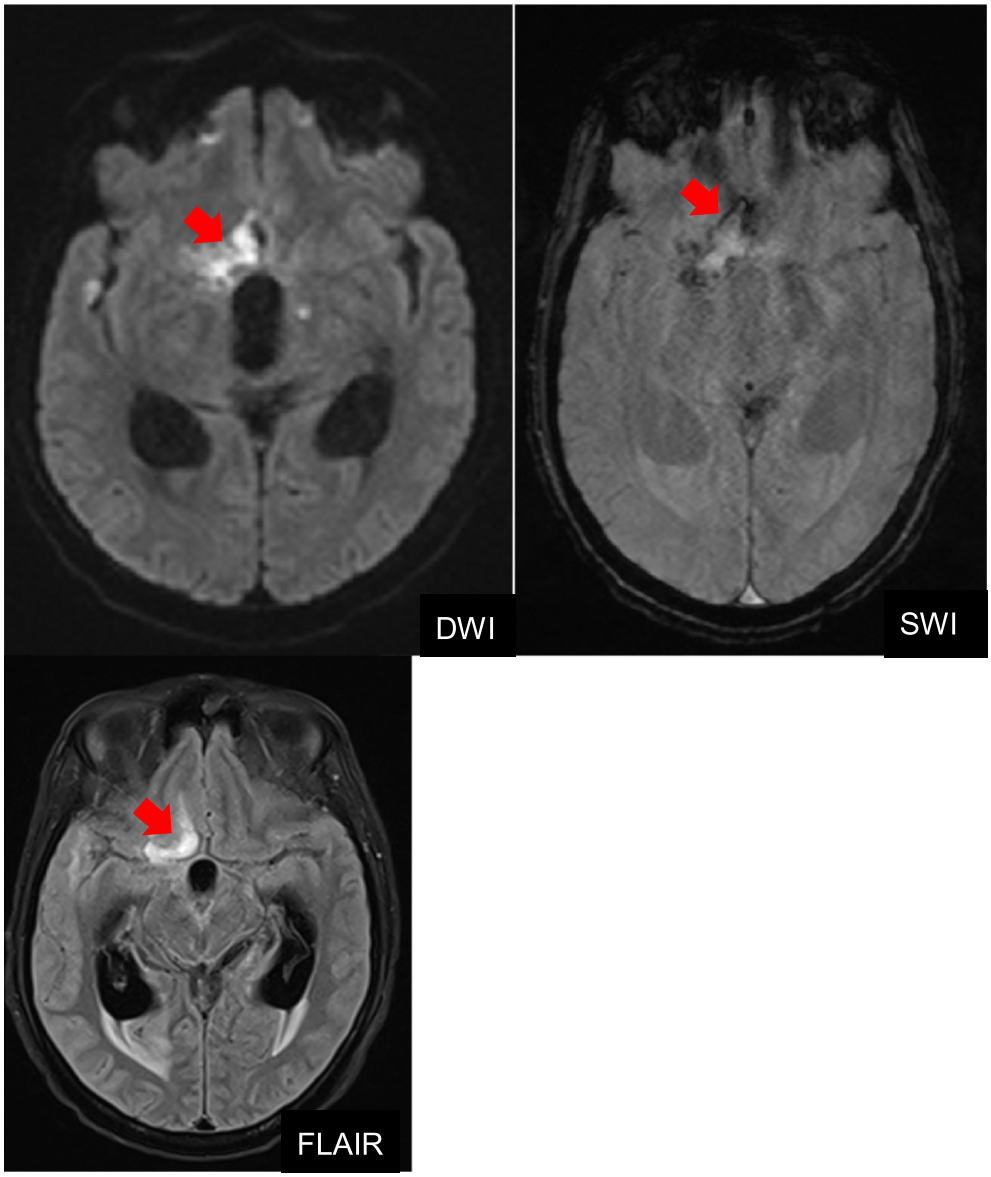

Figure 1. FLAIR hyperintensity with restriction of diffusion and blooming on SWI to suggest infarction with hemorrhagic transformation in the right basifrontal lobe (secondary to vasculitis). Dilated ventricles are suggestive of hydrocephalus.

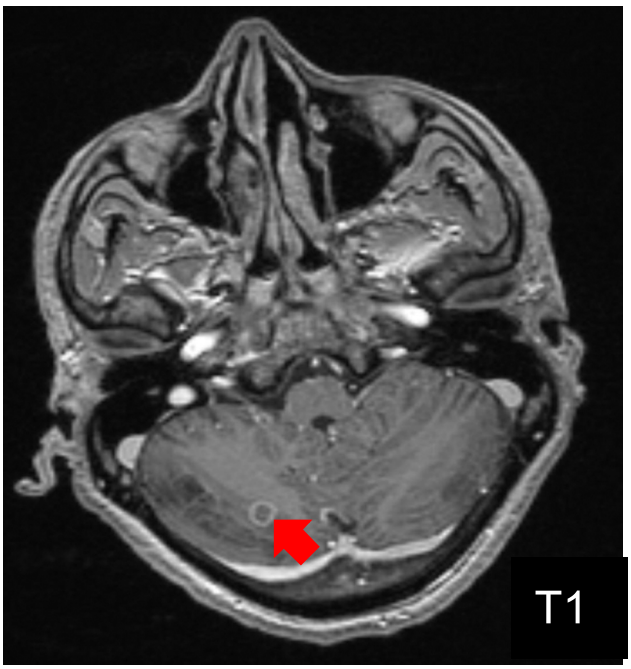

Figure 2. T1 postcontrast hypointense lesion is present on the right cerebellar hemisphere, showing ring enhancement suggestive of granuloma.

Lumbar puncture with routine cerebrospinal fluid (CSF) analysis showed protein -1062 mg/dl (normal range: 15–60 mg/dl), sugar 42 mg/dl (normal range: 50–80 mg/dl), and lymphocyte: 84 (normal range:0–5/mm^3). Gram stain, acid-fast bacilli, and India Ink test were all negative.

Considering probable tubercular meningitis with infarction, we started antitubercular medication as per the country guideline against tubercular meningitis which included 2 months of Isoniazid (H), Rifampicin(R), Pyrazinamide (Z), Ethambutol (E) to determine the response to treatment. There was an increment in SGOT and SGPT on the 7th day of admission as shown in Table 1, which hinted towards drug-induced hepatitis for which we held the medicine for 7 days and reintroduced the medication with continual observation of liver enzymes.

A whole list of investigations including coagulation profile, Renal Function Test (RFT), urinalysis, human immunodeficiency virus test, echocardiography, antinuclear antibodies, ds-DNA, rheumatoid factor, venereal disease research laboratory, hepatitis B surface antigen, C-reactive protein, antineutrophil cytoplasmic antibodies, lupus anticoagulant, and antiphospholipid antibody tests were noncontributory. No vascular anomalies were detected in Carotid vessels through carotid Doppler.

Gene X-pert detected Mycobacterial Tuberculous bacilli without resistance to Rifampicin. TB-Polymerase Chain Reaction (TB-PCR) also detected Mycobacterial Tuberculous bacilli in the CSF sample which confirmed the diagnosis of TB meningitis. We admitted the patient, and he had a gradual improvement in symptoms. Based on MRI finding suggestive of intracerebral hemorrhage, we considered this to be secondary to TB meningitis causing vasculitis.

On his 4th day of admission to the ICU, he complained of severe abdominal pain. CT scan of the abdomen was done, which showed short segmental abrupt narrowing in the distal ileum, resulting in upstream dilatation of the remaining ileal and jejunal structures suggestive of intestinal obstruction secondary to strictures. Similarly, mild peritoneal thickening and nodular enhancement were seen at the left hypochondrium/lumbar region suggestive of possible peritoneal tuberculosis. We offered a colonic endoscopy to retrieve a biopsy sample, but the procedure was refused by the patient. In addition, MRI whole spine screening was offered to the patient during his hospital stay, which was refused as well.

During the hospital stay, the patient was treated for hyponatremia, urinary incontinence, and urinary tract infection. His serum electrolyte level is shown in Table 2. On further evaluation of hyponatremia, we found the serum osmolality was 250 mOsm/kg urine osmolality 110 mosm/kg, and urine sodium 50 meq/l suggesting SIADH. For this, sodium level was monitored, fluid was restricted, and Inj 3% NaCl (when needed, over 4 h) was administered. Besides antitubercular treatment) syrup lactulose (30 ml po tds), pyridoxine (100 mg po od), tab ursodeoxycholic acid (500 mg po bd), inj fondaparinux (2.5 mg sc od), and inj dexamethasone (4 mg iv tds). Noncontrast CT was done to see for changes and showed no increase in the size of infarct hemorrhage, or hydrocephalus, and aspirin (75 mg OD) was commenced.

In addition to pharmacological treatments, he also received physiotherapy and special care was given to his nutritional requirements. There was a gradual improvement in his neurological examinations. At the time of discharge, the muscle power over the left lower limb improved to 2/5 and 3/5 in the right lower limb while 5/5 in bilateral upper limbs, and his GCS improved to 15/15 and a Modified Rankin Scale of 4/6. He was subsequently discharged with advice to take antitubercular drugs according to the directly observed therapy short course program, dexamethasone in tapering dose, and aspirin.

The patient presented for a follow-up in a month and was compliant with medication and physiotherapy. He was found to be improving with a power of 3/5 in bilateral lower limbs and a 3/6 score on the Modified Rankin Scale.

Discussion

The incidence of stroke is 13–57% in tubercular meningitis patients, which can cause poor clinical outcomes[6]. TB cerebral vasculitis, a complication of TB meningitis, can lead to the manifestation of stroke.

Tubercular cerebral vasculitis should be particularly suspected of any neurological deterioration arising from the course of tuberculosis. Vasculitis-associated strokes could be asymptomatic in ~25% patients, while others could present with fever, decreased consciousness, abnormal behavior, focal weakness, headache, unsteady gait, clumsiness, diplopia either alone or in combination, as reported by Chan *et al*.[8].

Various other etiologies like systemic vasculitides (takayasu arteritis, polyarteritis nodosa, and giant-cell arteritis), systemic autoimmune diseases (systemic lupus erythematosus, Sjögren's syndrome, and antiphospholipid syndrome), neoplasia (lymphomas), drug-induced vasculitides (narcotics and amphetamines), infectious vasculitides (syphilis, HIV)[9] could present with the similar feature as TB vasculitis and should be excluded.

In our study, the CSF study revealed leukocytosis with predominance of lymphocytes along with increased protein, while AFB staining was negative staining, which could create a dilemma

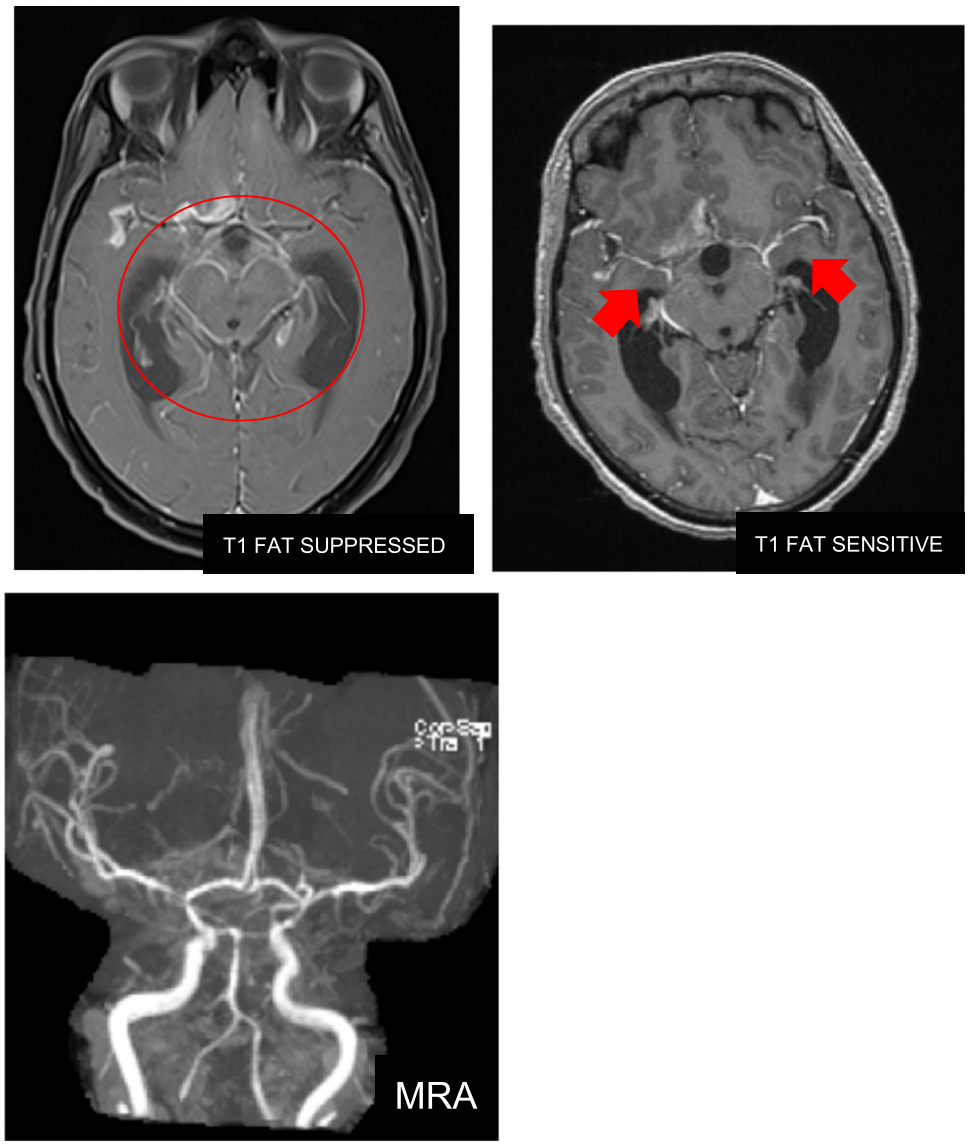

Figure 3. Diffuse leptomeningeal enhancement is noted in contrast T1 sequence in bilateral sylvian fissures (arrows), cortical sulci, suprasellar cisterns, perimesencephalic cisterns (ambient interpeduncular and quadrigeminal), prepontine and perimedullary cisterns (encircled). No significant abnormality was noted on MRA.

for clinicians regarding the diagnosis. A systemic review shows that AFB is not a very sensitive test in the diagnosis of MTB[10]. Diagnosis of 'probable tubercular meningitis' can still be made based on clinical findings, CSF study, and radiological findings in MRI or CT in accordance with the consensus of tuberculous meningitis diagnosis[11]. Neuroimaging such as MRI and CT may reveal intense basal enhancement after intravenous contrast administration, communicating or noncommunicating hydro cephalus, cerebral infarcts, parenchymatous tuberculomas, or a combination of two or more of these features as seen in our case[7]. The DWI sequence is helpful to detect acute cerebral infarcts and T2 is particularly better at demonstrating brainstem pathology. MRI is better at demonstrating complications asso ciated with TB meningitis as it is superior to CT for evaluating the brainstem and spine[12]. The cerebral infarction pattern in cere bral meningitis is mainly perforators and terminal branches[13].

The sensitivity to diagnose a case of cerebral vasculitis from MRA ranges from 59 to 90% but has a low specificity for determination of etiology such as systemic vasculitis, systemic autoimmune diseases, drug-induced vasculitides, infectious vas culitides, and reversible brain angiopathy[14]. Vasculitis can involve large, medium, and small arteries and veins. In a cross-sectional study involving 90 patients, MRA abnormality was seen in 43% of the cases[15]. MRA in vasculitis classically shows seg mental and arterial narrowing, parietal irregularities, and some times obstruction[9]. In our case, MRA was normal and MRI revealed findings as described in Figures 1–4. MRI suggestive of intracerebral hemorrhage can be due to bleeding secondary to vasculitis of the cerebral vessels[16]. The most common location of tubercular meningitis-related stroke is thalamus, basal ganglia[13] while in our case right basifrontal lobe was affected.

Based on probable diagnosis of tubercular meningitis, we instituted antitubercular medication, and dexamethasone.

The choice of a confirmatory diagnostic tool depends on the available resources. However, MTB determination from the CSF culture is the gold standard[17]. Here, in our case study, the Gene

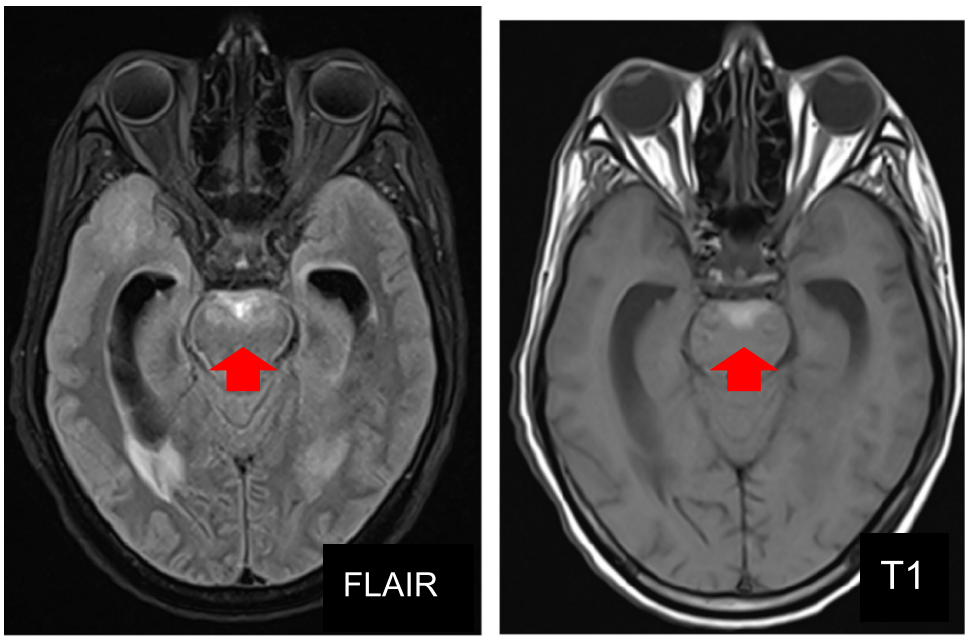

Figure 4. T1 and FLAIR hyperintensity is noted at the interpenduncular cistern to suggest basal exudates.

Xpert/RIF and CSF-PCR were positive for *Mycobacteriam Tuberculosis*, which made of a definitive diagnosis of tubercular meningitis we continued treatment with the first line of Anti Tubercular Treatment as per National Tuberculosis Management Guideline along with Dexamethasone[1]. Some reports suggest on using dexamethasone as an adjunct treatment improves survival in patients with TB meningitis[18]. Though the recommended guidelines include ATT, Dexamethasone, and supportive care, the prognosis can still be bad even with the best of care[3]. Although the literature on the role of aspirin use after hemorrhagic transformation of ischemic stroke in tubercular meningitis is limited, observational study has shown that low dose aspirin in case of intracranial hemorrhage (ICH) is not associated with an increased risk of recurrent intracranial hemorrhage in patient with ICH[19]. In our case, a noncontrast CT scan was done, which showed no hemorrhagic changes or expansion, and aspirin was commenced as a study has shown aspirin reduces the risk of new infarctions in patients with tuber culous meningitis but does not affect the mortality[20]. Early administration of aspirin, corticosteroid has shown to reduce morbidity, which was rationale for adding aspirin and organizing a scheduled follow-up for the patient[6]. In addition, patient developed drug-induced hepatitis for which antitubercular medi cation was held for few days and reinstated. Other report also mentions that the same antitubercular medications could be safely introduced in 80–90% of patients without recurrence of antitubercular-induced liver injury in patients[21].

Our patient presented with paraparesis, which could be because of pathological spinal tuberculosis, including Potts spine, tuberculoma, and encasing arachnoiditis with compression, vasculitis of the spinal cord vessels, and tuberculous radiculopathy[22,23]. Although X-ray lumbosacral spine revealed normal findings, MRI spine screening was refused by the patient which could be because of financial constraints as prime reason, especially since there would be no significant alteration in management despite further investigation, which would be natural course of treatment.

The prognosis of TB meningitis depends on neurological presentation at the time of hospital presentation and initiation of antitubercular medication[3]. Along with infarct, our patient also

Table 1

Liver function test (LFT)

Day from the date of admission	SGOT (U/l) (Normal: 8–48 U/l)	SGPT (U/l) (Normal: 7–45 U/l)	ALP (U/l) (Normal: 45–115 U/l)	Total bilirubin (mg/dl) (Normal: 0.1–1.2 mg/dl)	Direct bilirubin(mg/dl) (normal:0.0–0.2 mg/dl)
1st day	60	70	69	0.9	0.1
7th day	132	138	82	1.7	1.0
8th day	110	120	66	1.4	0.8
9th day	98	90	77	1.3	0.7
11th day	82	68	84	1.3	0.5
12th day	64	68	96	0.9	0.4
14th day	45	56	98	0.8	0.4
15th day	41	54	86	1.0	0.2
16th day	47	54	88	0.8	0.2

Table 2
Serum electrolyte level

Day from date of admission	Sodium/Potassium (mEq/l)
1st day	120/3.9
2nd day	126/3.8
3rd day	130/3.7
7th day	134/3.8
9th day	132/3.7
11th day	137/3.6
14th day	137/3.8

Normal range- Sodium: 135–145 mEq/l; Potassium: 3.5–5 mEq/l.

had hyponatremia and hydrocephalus. Hyponatremia is a common incidence in cerebral insults including TB meningitis and is primarily due to SIADH and cerebral salt wasting syndrome or a combination of both[24]. Hydrocephalus occurs in ⅔ of the patients with TB meningitis and has an unfavorable prognosis. Hydrocephalus in early-stage TB meningitis, however, are repor ted to resolve[25].

The strength of our case report is the patient presented to the tertiary care referral center for neurological and allied sciences and underwent all the investigations required to diagnose stroke. The limitation of the case report is that we could not do an endoscopy for the patient to establish primary source for tuberculous meningitis and MRI spine screening to investigate for paraparesis which could be due to financial constraints.

Conclusion

This case highlights the importance of considering tuberculous meningitis-related infarction as a differential diagnosis of stroke despite initial negative AFB smear. Radiological investigation could guide the clinician towards the diagnosis of tubercular meningitis with vasculitis.

Ethical approval

This is a case report, therefore, it did not require ethical approval from ethics committee.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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The study did not receive any grant from funding agencies in the public, commercial, or not-for-profit sectors.

Author contribution

E.A.: conceptualization, literature review, original draft preparation, supervision, visualization, data curation, writing – review, and editing; A.A.: conceptualization, data collection, data curation, literature review, original draft preparation, and data curation; A.A.: literature review, original draft preparation, writing – review, and editing; A.P.: literature review, original draft preparation, writing – review, and editing; D.B., S.S., K.D., A.S., and N.J.R.: literature review, writing – review and editing; M.R.D.: conceptualization of the study, literature review and editing, radiological interpretation, supervision, writing – review, and draft. All the authors read and approved the final manuscript.

Conflicts of interest disclosure

The authors declare no conflicts of interest.

Research registration unique identifying number (UIN)

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Guarantor

Egesh Aryal and Aayam Adhikari.

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Provenance and peer review

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