

Case Report

Neurologic melioidosis presented as encephalomyelitis and subdural collection in two male labourers in India

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Abstract

Two distinct and potentially deceitful cases of neurologic melioidosis are reported.

Case 1: A 39-year-old alcoholic and uncontrolled diabetic male presented with cough, fever, and left focal seizures with secondary generalization. A magnetic resonance imaging (MRI) brain scan revealed a small peripherally enhancing subdural collection along the interhemispheric fissure suggestive of minimal subdural empyema. Blood culture grew *Burkholderia pseudomallei*. Patient was diagnosed with disseminated bacteraemic melioidosis with subdural empyema. He was successfully treated with ceftazidime-cotrimoxazole-doxycycline.

Case 2: A 45-year-old male presented with left lower limb weakness, difficulty in passing urine and stool, and back pain radiating to lower limbs. Neurological examination revealed flaccid left lower limb with absent deep tendon reflexes and plantar reflex. Spinal MRI showed T2 hyperintensity from D9 to L1 suggestive of demyelination. Patient was treated with high dose methylprednisolone. By day 3 of steroid treatment, lower limb weakness progressed. Subsequent MRI showed extensive cord hyperintensity on T2 weighted sequence extending from C5 to conus medullaris consistent with demyelination. Cerebrospinal fluid (CSF) culture grew *B. pseudomallei*, and the patient was given meropenem-cotrimoxazole. After three weeks of parenteral treatment, the lower limbs remained paralyzed. Patient was discharged on oral cotrimoxazole-doxycycline.

Conclusions: Melioidosis should be considered as a differential in focal suppurative central nervous system (CNS) lesions, meningoencephalitis, or encephalomyelitis in endemic areas. CNS infections must be ruled out prior to steroid administration. The role of corticosteroids in demyelinating CNS melioidosis has been refuted. This is a rare documentation of effect of unintentional corticosteroid treatment in melioidosis.

Key words: melioidosis; *Burkholderia* infection; neurologic melioidosis.

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Introduction

Melioidosis, a disease caused by the soil-dwelling Gram-negative bacterium *Burkholderia pseudomallei* is acquired by inhalation, percutaneous inoculation, or ingestion. The disease is endemic in South India. It can present acutely with pneumonia and septic shock or chronically with multiple visceral abscesses that commonly involve subcutaneous tissue, skeletal muscle, liver, spleen, lungs, and prostate. Neurologic involvement in melioidosis has been estimated to be up to 3% in a 20-year long-term prospective study from tropical Australia [1]. Aboriginal neurologic melioidosis cases have been reported from India as well [2,3]. Here, two different neurologic melioidosis cases, with and without fever, involving diverse

underlying neuropathological processes are presented. There has been a paucity of evidence on the use of corticosteroid treatment in melioidosis and we report here the futility of the same. Steroid is detrimental in melioidosis and it should be ruled out prior to the administration of steroids in cases of encephalomyelitis.

Case presentation

Case 1

A 39-year-old carpenter presented with cough, fever of two weeks, and three episodes of left focal seizures with secondary generalization. Examinations revealed mild right lower limb monoparesis. The patient had a history of excessive alcohol

consumption. The complete blood picture and liver and renal functions were normal. Erythrocyte sedimentation rate (ESR) was 66 mm/hour in the first hour. He had uncontrolled diabetes mellitus (fasting and postprandial blood sugar of 166 mg/dL and 316 mg/dL, respectively). A magnetic resonance imaging (MRI) brain scan revealed a small peripherally enhancing subdural collection along the interhemispheric fissure suggestive of minimal subdural empyema (Figure 1). Because infected subdural collection was suspected, he was empirically treated with ceftriaxone and tinidazole along with phenytoin sodium. Ultrasonography revealed hepatosplenomegaly. Chest X-ray showed left midzone consolidation. Blood culture grew *B. pseudomallei* sensitive to amoxicillin/clavulanic acid, ceftazidime, cotrimoxazole, doxycycline, meropenem, and ciprofloxacin but resistant to gentamicin. Identification of culture isolates and their antibiotic susceptibility was done using the VITEK 2 system (bioMérieux, Marcy l'Etoile, France). The patient was diagnosed with disseminated bacteraemic melioidosis with subdural empyema, and the antibiotic was changed to ceftazidime 2 g intravenously every 6

hours for two weeks, followed by oral cotrimoxazole 320 mg/1,600 mg, twice a day and doxycycline 100 mg every 12 hours for six months. The patient improved and his anti-epileptic drugs were discontinued after six months.

Case 2

A 45-year-old manual laborer was brought to the emergency department with left lower limb weakness of one and a half days' duration and difficulty in passing urine and stools. On enquiry, he admitted to having lower backache for two years which had increased over the last one month, requiring analgesics. The back pain had acutely increased two days prior, radiating to the thighs and legs. His vital signs were normal. Neurological examination revealed a flaccid left lower limb with grade 2/5 power proximally and grade 0/5 power distally with absent deep tendon reflexes and plantar reflex. Right lower limb and upper limbs were normal. There was no definite sensory level on examination. Review of cardiovascular, respiratory, and abdominal systems was normal except for distended urinary bladder. Urinary bladder was catheterized. Routine laboratory tests showed leukocytosis ($16,700 \text{ cells/mm}^3$) with raised ESR (18 mm/hr). Liver and kidney functions and plasma sugar were normal. Spinal MRI showed T2 hyperintensity from the level of D9 to L1 suggestive of demyelination (Figures 2 and 3).

Figure 1. Gadolinium enhanced axial T1 weighted MR image shows peripherally enhancing small subdural collection along the posterior interhemispheric fissure suggestive of subdural empyema.



Figure 2. T2 weighted sagittal image of thoracic spine shows mildly swollen spine with hyperintensity extending below the level of D9 vertebra.



Figure 3. T2 sagittal image of lumbar spine shows hyperintensity in the lower cord and conus medullaris suggestive of demyelination or transverse myelitis. The involved cord appears mildly swollen. A white arrow points to the hyperintense area.



Figure 4. Follow-up imaging after steroid treatment: T2 weighted cervical MR shows progressive disease with cord hyperintensity extending below the level of C5.

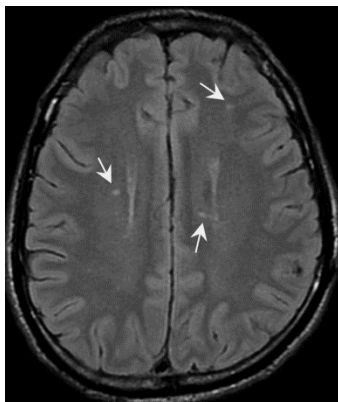


Figure 5. Follow-up imaging after steroid treatment: T2 weighted dorsal MR sequences shows extensive cord hyperintensity extending up to the conus medullaris.



The possibility of transverse myelitis was considered, and patient was treated with parenteral high-dose methyl prednisolone of 1 g/day for six days. Patient had one spike of fever of 102°F, which was attributed to the urinary tract infection and was treated with levofloxacin followed by cefoperazone/sulbactam. By the third day of steroid treatment, the patient’s lower limb weakness progressed to grade 0/5 power bilaterally. Repeat MRI showed progressive extensive cord hyperintensity on T2 weighted sequence extending from the C5 level up to the conus medullaris, consistent with demyelination or transverse myelitis (Figures 4 and 5). Cranial MRI was unremarkable except for few non-specific white

Figure 6. Brain sequences are unremarkable except for few non-specific white matter hyperintensity on FLAIR sequence.



matter hyperintense foci on fluid attenuation inversion recovery (FLAIR) sequence (Figure 6).

Cerebrospinal fluid examination done in view of fever showed 85 mg/dL protein, 66 mg/dL glucose, 160 white blood cells (WBC)/mm³, with 98% lymphocytes and 2% neutrophils, and adenosine deaminase of 66 U/L. Cerebrospinal fluid (CSF) culture grew *B. pseudomallei* sensitive to amoxicillin/clavulanic acid, ceftazidime, cotrimoxazole, doxycycline, meropenem, and ciprofloxacin, but resistant to gentamicin. Identification of culture isolates and their antibiotic susceptibility was done using the VITEK 2 system (bioMérieux). The patient was started on meropenem 1 g every 8 hours and oral cotrimoxazole (320 mg/1,600 mg, twice a day). There was no bacterial growth in blood and urine cultures. The patient’s deficit continued to worsen to involve left upper limb and a new onset left-sided ptosis.

After 10 days of treatment, the patient’s ptosis improved and he regained left upper limb power. After three weeks of parenteral treatment, while the lower limb remained totally paralyzed, MRI revealed reduction in the swelling of the conus with normal signal intensity. However, abnormal cord signals were persistent in the remaining cord, and the cord hyperintensity progressed cranially until cervicomedullary junction (Figures 7 and 8). The patient was discharged with a urinary catheter on oral cotrimoxazole 320 mg/1,600 mg and doxycycline 100 mg every 12 hours to be continued for six months.

Figure 7. Follow-up imaging after 3 weeks: T2 weighted MR of the thoracolumbar spine revealed reduction in the swelling of the conus with normal signal intensity. However, abnormal cord signals were persistent in the remaining cord (above D7 level).



Figure 8. Follow-up imaging after 3 weeks: T2 weighted MR of the cervical spine shows progression of cord hyperintensity cranially up to cervicomedullary junction.



Discussion

One of our previously published case series of melioidosis documented a case presenting with meningoencephalitis and liver and splenic abscesses [2]. Also, diabetes mellitus and alcoholism have previously been described as predisposing risk factors for melioidosis in the study region [4]. The two cases presented here are distinct from the above published case in that our first patient had macroscopic subdural collection and pneumonia and the second patient had encephalomyelitis, a demyelinating pathology, highlighting the two diverse presentations with variable prognosis. The first patient had diabetes and excessive consumption of alcohol as risk factors, while the second patient had none of these, but did have exposure to soil. It is noteworthy that the second patient had no history of fever, which is the usual presenting feature of melioidosis in 90% of cases, although he had a few spikes of fever after admission.

Apparently, there is a regional difference with higher incidence of neurologic melioidosis in Australia compared to Thailand. Out of the 14 cases of neurological melioidosis from Australia, ten presented with meningoencephalitis, two patients with both myelitis and cerebral abscesses each [1]. In another study from Thailand, 1.5% patients (3/191) had neurological involvement [5]. Presentations with dural venous sinus thrombosis have been described in a few reports [6,7]. The presenting neurological deficits in neurologic melioidosis have been monoparesis, paraparesis, cerebellar signs, seventh nerve palsy, bulbar palsy, peripheral motor weakness mimicking Guillain-Barre syndrome, and respiratory failure [8,9]. Encephalomyelitis is the most devastating presentation with the worst prognosis.

Melioidosis is caused by facultative Gram-negative bacteria *B. pseudomallei*, which is present in soil and fresh water in endemic countries. It is usually acquired by inoculation, inhalation, or ingestion. Neurological manifestations result from hematogenous seeding or direct neuronal spread from the nasopharynx. The route of spread from nasal mucosa through the olfactory nerve to the olfactory bulb has been demonstrated by bioluminescence monitoring in BALB/c mice [10]. In our first patient, it may have been a hematogenous spread, while in the second case, there was no bacteremia documented, favoring direct spread from the nasopharynx. The diagnosis is by culture of *B. pseudomallei* from blood, pus, urine, or CSF, and the accurate identification of raised rough pink colonies with metallic hue along with their biochemical reactions.

The CSF examination in the second case showed lymphocytic pleocytosis. In a series of 12 patients of neurological melioidosis from Australia, two patients had predominant mononuclear pleocytosis in CSF [8]. The recommended antibiotic therapy for neurologic melioidosis is parenteral ceftazidime 50 mg/kg (up to 2 g) every 6 hours or meropenem 25 mg/kg (up to 1 g) every eight hours for at least four weeks, followed by oral cotrimoxazole 40/8 mg/kg (up to 1,600/320 mg) every twelve hours and doxycycline 2 mg/kg, (up to 100 mg) every 12 hours for six months. Amoxicillin/clavulanic acid is not recommended, as its concentration in the CSF falls below the minimum inhibitory concentration (MIC) for *B. pseudomallei* [5]. The abscesses and collections need to be drained surgically as appropriate.

There was a delay in initiation of appropriate antibiotics in our second patient because melioidosis was not suspected clinically with the presenting feature of transverse myelitis in the absence of fever. Treatment with corticosteroid is considered a risk factor for melioidosis [11]. Though well established as the appropriate treatment of transverse myelitis, corticosteroid treatment is detrimental in melioidosis, as exemplified by our second case; the treatment might have contributed to the dissemination of *B. pseudomallei* within and outside the central nervous system (CNS) and to the worsening of neurological deficits. This is a rare documentation of the effects of unintentional corticosteroid treatment in melioidosis.

MRI is more sensitive for the detection of early changes, which include T2 hyperintensity and gadolinium enhancement of the affected area. Focal intracerebral edema and peripheral enhancement of abscess cavities may be seen. Macroabscess formation carries a poor prognosis [12]. Paraplegia secondary to *B. pseudomallei* myelitis has been described [13]. Our patient also showed features of transverse myelitis with extensive cord involvement and paraplegia (Figures 2–5).

Conclusions

Melioidosis has to be considered as a differential diagnosis in focal suppurative CNS lesions, meningoencephalitis, or encephalomyelitic presentations, especially in diabetic and alcoholic patients in endemic areas. As neurologic melioidosis can present acutely as transverse myelitis or encephalomyelitis with or without fever, we propose in all such patients a CSF examination and culture of CSF and blood to rule out CNS infections prior to administration of steroids. Timely, appropriate

antibiotics, aggressive supportive treatment, and prevention of secondary infection in the intensive care unit are paramount in reducing the mortality and morbidity in melioidosis.

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