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Case Report

Light at the End of the Tunnel- A Rare Case of Neuromelioidosis and its Imaging Findings

V Rakshith[1], Akhila Chandrasekaran[2], Ranjith Kumar Manokaran[3]

[1]Post Graduate Resident, Department of Radiology and Imaging Sciences, Sri Ramachandra Medical College, and Research Institute, Chennai, Tamil Nadu, India, [2]Senior Resident, Department of Radiology and Imaging Sciences, Sri Ramachandra Medical College, and Research Institute, Chennai, Tamil Nadu, India, [3]Associate professor, Division of Paediatric Neurology and Epileptology, Department of Neurology, Sri Ramachandra Medical College, and Research Institute, Chennai, Tamil Nadu, India

Abstract

Melioidosis, caused by *Burkholderia pseudomallei*, is a rare but serious infection with a wide spectrum of clinical manifestations, including central nervous system (CNS) involvement. Neuromelioidosis, which affects the CNS, is uncommon but carries a poor prognosis and high mortality. Here is a case of a 16-year-old girl who presented with fever, hemiparesis, and neurological deficits. Following a magnetic resonance imaging (MRI) brain, a close differential of demyelination versus infection was considered. Despite initial steroid treatment for presumed demyelination, her condition worsened. Her serial MRI brain scans showed progressively characteristic lesions, the rare "tunnel sign," which along with the clinical picture raised suspicion of an infectious etiology such as Melioidosis. Tissue sampling confirmed the diagnosis. This led to the initiation of targeted antibiotics (meropenem and co-trimoxazole) with the patient improving considerably and the follow-up MRI showing significant regression of lesions. This case highlights the diagnostic challenges of neuromelioidosis, a condition often confused with other CNS infections or autoimmune conditions. Imaging features, particularly the tunnel sign when present, along with microbiological confirmation, are crucial for diagnosis. Timely administration of appropriate antibiotics can significantly improve outcomes. This case report underscores the importance of early recognition and treatment of neuromelioidosis, especially in endemic regions.

Key words: Antibiotics, Infection, Magnetic resonance imaging, Neuromelioidosis, Steroid, Tunnel sign

INTRODUCTION

Burkholderia pseudomallei is the causative agent for Melioidosis. Melioidosis can affect numerous organs; however, involvement of the central nervous system (CNS) is uncommon. Neuromelioidosis carries a poor prognosis with high mortality.[1] Cerebral abscess is the most common magnetic resonance imaging (MRI) finding; however, isolated encephalitis, meningitis, or extra-axial collections may also be seen.[2] Adults account for most instances of CNS melioidosis when compared to the pediatric age group. According to reports, neurological involvement of patients with melioidosis is rare.[3] Consequently, our understanding of CNS melioidosis remains restricted and is based only on anecdotal data about epidemiology, clinical symptoms, laboratory results, treatment, and outcome.

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CASE REPORT

A 16-year-old girl presented with complaints of 25 days of fever and left-sided weakness for the past 3 days. She had previously been managed at another hospital for continuous fever, testing positive on the WIDAL test, and was treated with intravenous (IV) fluids, IV/intramuscular ceftriaxone, and oral azithromycin.

She then started experiencing uncontrollable hiccups, numbness in the left upper limb, and speech disturbances. On examination, diplopia, esotropia in the right eye, exaggerated deep tendon reflexes on the left side, positive plantar reflex, and Romberg's sign were observed. Hence, differentials for left-sided upper motor neuron hemiparesis with involvement of the seventh (VII) and third (III) cranial nerves were considered.

Corresponding Author: Dr. V Rakshith, Department of Radiology and Imaging Sciences, Sri Ramachandra Medical College, and Research Institute, Chennai, Tamil Nadu, India.

MRI brain [Figure 1a] showed T2 FLAIR hyperintensities in the right side of the brainstem namely, the right hemi-midbrain, the right side of the dorsal pons, the right anterior medulla along with the left posterior aspect of the medulla extending into the upper cervical spinal cord up to the C1 vertebral level. A few small areas of ring enhancement were noted within. Possibilities of demyelination and infection were considered.

Acute demyelinating encephalomyelitis was considered as a differential and the child was started on pulse methylprednisolone therapy. However, the child's sensorium worsened. On the 4th day of steroid therapy, MRI brain [Figure 1b] was repeated. It showed significant progression in size and number of the T2 hyperintense lesions along with increasing surrounding edema. In addition, there was a mild increase in the patchy areas of ring enhancement with diffusion restriction in the middle cerebral peduncle, hemipons and middle cerebellar peduncle with a fairly contiguous appearance giving rise to an appearance of "tunnel sign." New T2 hyperintensities were noted in the right gangliocapsular region. Given the worsening symptoms and progressing lesions despite treatment with steroids, infective etiology was considered. After going through the literature for these imaging characteristics, the possibility of melioidosis was considered. Following this, steroids were tapered, and parenteral meropenem and co-trimoxazole were initiated and continued for the next 20 days.

The child improved neurologically (numbness and speech) but had persistent tingling sensation over the face, slurring of speech, and non-resolving fever. A repeat MRI on the 20th day of treatment [Figure 2] showed marked progression of the previous lesions along with surrounding edema, with additional involvement of the right cerebellar hemisphere, corona radiata, and centrum semiovale. Multiple nodular and ring-enhancing T2 WI hyperintense lesions with perilesional edema scattered involving these regions. The lesions in the right centrum semiovale and corona radiata also now showed an enhancing tract-like appearance, now more typical of the "tunnel sign." Following this, lumbar puncture and cerebrospinal fluid (CSF) analysis was done which showed monocytosis with elevated protein and low glucose and negative acid-fast bacilli (AFB). The imaging and CSF analysis together raised the possibility of abscess

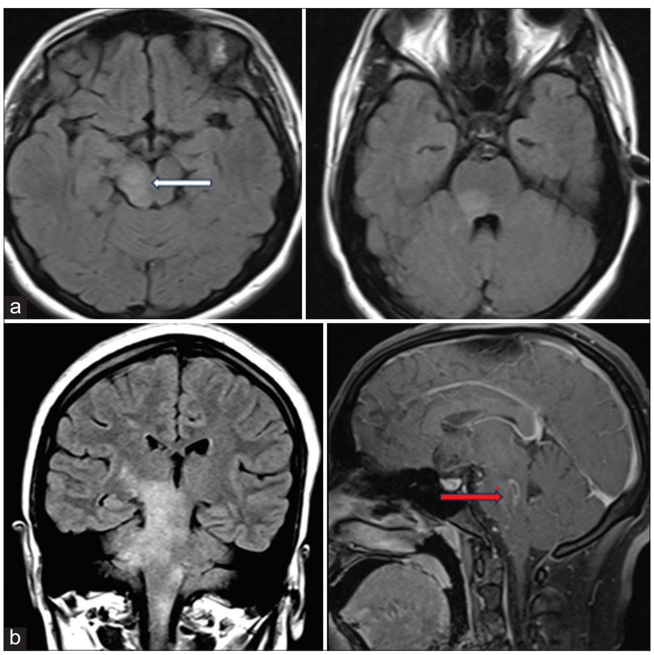

Figure 1: (a) Magnetic resonance imaging (MRI) brain: axial T2 FLAIR at level of midbrain and at the level of pons: showing T2 FLAIR hyperintensities in the right hemi-midbrain (white arrows), the right side of the dorsal pons, the right anterior, and the left posterolateral aspects of the medulla extending into the upper cervical spinal cord up to the C1 vertebral level with minimal contrast enhancement (not shown). (b) MRI brain: Coronal T2 FLAIR and Sagittal post-contrast T1 images showing the significant progression of the T2 FLAIR hyperintensities now also involving the right gangliocapsular region. Peripherally enhancing fairly contiguous lesions in the right side of the brainstem raising faint suspicion of the "tunnel sign"

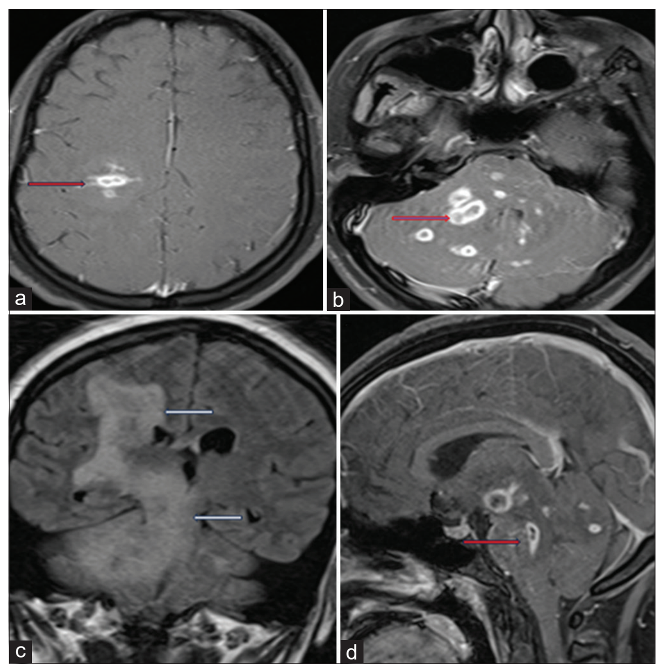

Figure 2: Magnetic resonance imaging brain contrast: axial T1+C (a and b), coronal T2 FLAIR (c), and sagittal T1+C (d) views: progression of the T2 hyperintensities adjacent to the areas of previous involvement, showed marked progression of the previous lesions along with surrounding edema, with additional involvement of the right cerebellar hemisphere, corona radiata, and centrum semiovale. Multiple nodular and ring-enhancing T2 WI hyperintense lesions with perilesional edema scattered involving these regions. The lesions in the right centrum semiovale and corona radiata also now showed an enhancing tract-like appearance, now more typical of the "tunnel sign"

and encephalitis likely secondary to Melioidosis. USG's abdomen showed no significant abnormality. A stereotactic brain biopsy with pus fluid analysis was then decided upon.

Both the pus and brain tissue culture tested positive for *B. pseudomallei*, which was sensitive to meropenem and co-trimoxazole, negative for Gram stain, AFB smear, and GeneXpert (tuberculosis). The child was continued on appropriate parenteral antibiotics.

The child is now clinically stable, experiencing no fever spikes, and tolerating nasogastric feeds while continuing chest and limb physiotherapy. A repeat MRI [Figure 3] showed significant regression in the number and size of multiple nodular and ring-enhancing lesions. The child was continued on oral co-trimoxazole for prevention of further recrudescence.

DISCUSSION

Epidemiology

B. pseudomallei (previously known as *Pseudomonas pseudomallei*) is the causative agent for Melioidosis. Whitemore and Krishnaswami recognized the first case in Burma in 1912.[1] *B. pseudomallei* is a Gram-negative aerobic bacillus with bipolar staining and is endemic in Southeast Asia, northern Australia, South Asia (including India), and China. The organism enters the human host by ingestion and inhalation or through an existing abrasion on the skin.

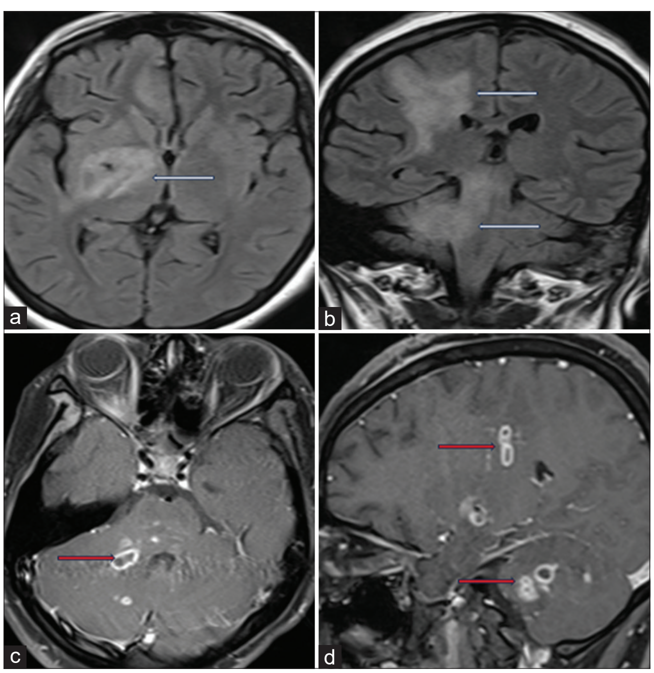

Figure 3: Magnetic resonance imaging brain contrast: axial and coronal T2 FLAIR (a and b) and axial and coronal T1+C (c and d) views: showed significant regression in the number and size of multiple nodular and ring-enhancing lesions

It lives in the water and soil of places, such as playgrounds, gardens, sewers, and farmed fields. Therefore, following natural catastrophes, such as earthquakes, cyclones, and tsunamis, an increased prevalence of melioidosis may be anticipated in endemic locations. Sexual transmission and vertical transmission during childbirth have also been reported.[2] Melioidosis was recognized to be an important problem during the Vietnam War affecting many soldiers amongst them a case of a US soldier who suffered from melioidosis meningitis 13 years ago while serving in the Vietnam War.[3] Because of this pattern of illness incidence, melioidosis is referred to as the "Vietnam time bomb."

There seems to be variation in the pathophysiology of CNS melioidosis among the patients. First, a crucial part of the illness process is the hematogenous propagation of the bacterium to the CNS. Blood is the most often isolated specimen of *B. pseudomallei*.[4] There are three ways that the circulating bacteria can get across cellular barriers, such as the blood-brain and blood-CSF barriers: transcellular, paracellular, or Trojan horse technique.[5] The latter scenario happens when the bacteria can endure within the circulating monocytes, which then migrate through L-selectin (CD62L)-mediated migration across the cerebral endothelium.[6] Second, as evidenced by animal studies, direct brainstem invasion through the nasal passage and cranial nerves is believed to be another distinguishing mechanism of CNS melioidosis, especially encephalomyelitis type.[7] Results from Wongwandee and Linasmita have found that the bacteremia rates between cases of encephalomyelitis and brain abscess were quite similar (54% vs. 58%). Finally, the pathophysiology of specific cases may be caused by a percutaneous inoculation over the scalp followed by a direct extension to the skull and brain. The fact that 25% of patients with CNS melioidosis also had contemporaneous scalp abscess or skull osteomyelitis and that some of them had a history of prior cranial injury lends credence to this.

Clinical Features

Melioidosis has enormous clinical diversity, spanning from a localized cerebral abscess, isolated encephalitis, meningitis or extra-axial collections, and spinal cord myelitis. The clinical presentation is variable and depends on the locus of infection. The most common involvement is in the lungs, which can manifest as pleural effusion or pneumonia.[8,9] In decreasing order of prevalence, other sites of involvement include the skin, circulatory, musculoskeletal, neurological, and genitourinary systems (prostatic abscesses in particular). Remarkably, neurological involvement is observed in about 5 percent of instances.[10] CNS melioidosis has been the subject of numerous case series and studies; a recent Chinese case series revealed that patients frequently presented with fever, headache, convulsions, and motor weakness.[11,12]

Fever is the most frequently occurring symptom of neuromelioidosis, while it can also occur in other infectious disorders. It is characterized by focal neurological impairments, particularly cranial nerve palsies, with lesions primarily found in the brainstem (48%). The most affected cranial nerves are the sixth, seventh, ninth, and tenth. These cranial nerve deficits can be found in the encephalitis of the brainstem due to other causes as well including *Listeria monocytogenes*, herpes simplex virus type 1, and *Mycobacterium tuberculosis*.[13-15] For brain abscess type, focal neurological deficit, i.e., unilateral weakness is the most common feature; however, cranial nerve palsies occur infrequently. Clinical features of melioidosis meningitis remain like other meningitis syndromes, which encompass fever, headache, and neck stiffness. Isolated extra-axial collection of melioidosis has not been reported in children so far.

Diagnosis

Microbiological

Few studies showed Dry wrinkled colonies on Blood Agar and pinkish rugose colonies with metallic sheen on MacConkey Agar. Gram staining of the isolates revealed Gram-negative bacilli with a typical "Safety pin appearance."[16] Culture is the usual diagnostic technique for *B. pseudomallei*. Nonetheless, there is always a chance that it will be mistakenly identified as a different species or contaminant. It is always advised that urine and throat swabs be cultured in selective media together with concurrent blood culture and biopsy specimens in suspected instances of melioidosis for improved isolation. Numerous commercially available technologies, including VITEK (BioMieux), Phoenix (Becton, Dickinson and Company), and API 20NE, can be used to further identify the species. Based on the polymerase chain reaction, Lateral Flow Immunoassay, and Immunofluorescence Assay, several new direct diagnostic techniques have been created. As a "point of care" test for early diagnosis, the Active Melioidosis Detect Lateral Flow immunoassay (InBios Inc., Seattle, WA, USA) has demonstrated encouraging results among these tests.[17]

The CSF profile of CNS melioidosis, which commonly shows pleocytosis with mononuclear cell predominance, is comparable to tuberculous or viral meningitis. Nevertheless, tuberculous meningitis typically shows a lower CSF glucose level and higher CSF protein concentration. The CSF polymorphonuclear cell predominance can be demonstrated in one-third of CNS melioidosis patients. This variable characteristic of cell dominance is also shown on the *Listeria* meningoencephalitis.[11]

Imaging

Neuromelioidosis usually appears as a hypodense mass effect and a pyogenic abscess, Microabscess cavity formation may be difficult to discern, on CT and MRI appears as either a single or several ring-enhancing lesions, surrounding vasogenic edema, and mass effect. These usually exhibit restricted diffusion on diffusion-weighted imaging and are T2 hyperintense and T1 hypointense on MRI.[12] Lesions can have a range of shapes and patterns of amplification; they might be nodular, cystic, linear, or merging to produce a "Tunnel Sign."[18] It has also been observed that the spread conforms to cranial nerve routes and white matter tracts.[12] The lesions should resemble typical pyogenic abscesses on magnetic resonance spectroscopy, with low levels of choline and N-acetyl-aspartate and lipid (0.8–1.2 ppm), lactate (1.3 ppm), and amino acid (0.9 ppm) peaks.[20] Nevertheless, an unusual melioidosis case without the previously stated peaks and strangely having an elevated choline-to-NAA ratio has been documented.[19] Macroabscess formation carries a poor prognosis.[20] Multiple studies have described the areas of predominant involvement were the occipital lobes, with extension across the midline.

Treatment

Melioidosis is a challenging infection to treat because of the bacterium's resistance to a wide range of antibiotics, including aminoglycosides, penicillin, and rifamycin. Ceftazidime and meropenem are the medications of choice for intensive-phase therapy, whereas the use of medications including co-trimoxazole, chloramphenicol, and amoxicillin-clavulanate is part of eradication-phase regimens.[10] Some drugs including chloramphenicol and doxycycline were utilized in intensive-phase therapy in some CNS melioidosis cases; nevertheless, they are not effective and thus should be avoided. The treatment time is also vital to success for 8 weeks and 6 months are the minimal duration for intensive- and eradication-phase therapy, respectively.[21]

The use of steroids in case of neuromelioidosis can further cause progression of the underlying condition by causing profound bacteremia as neutropenia is not an important immunity impairment cause of melioidosis.[22]

Differential Diagnoses

Subcortical or deep white matter ring-enhancing lesions in the brain are known to present with a wide range of differential diagnoses, including demyelinating illness, typical pyogenic abscesses, metastases, and gliomas.[23] However, to the best of our knowledge, multiple abscess conglomerating into a tubular or a linear fashion – the" tunnel sign" – has been described in very few pathologies. We have found that it may also be demonstrated in cerebral melioidosis, as this case illustrates, as well as in cerebral listeriosis.[13] A differential of tubercular abscess was also considered due to the endemicity in India.[15] The tunnel sign, if seen, should raise suspicion for these three etiologic agents.

CONCLUSION

Melioidosis, caused by *B. pseudomallei* (a gram-negative bacillus), can enter the body through inhalation, ingestion, or through skin abrasions, often in contaminated environments. Neuromelioidosis, its infection of the CNS, is rare but severe, presenting as brain abscesses, encephalitis, meningitis, or spinal cord myelitis. Diagnosis is challenging due to non-specific symptoms and the potential for misidentification of the pathogen. Imaging techniques, such as MRI and CT, alongside microbiological and molecular diagnostics, are crucial.

Treatment is difficult due to the bacterium's resistance to many antibiotics. Ceftazidime and meropenem are preferred for initial therapy, followed by eradication-phase regimens with co-trimoxazole or amoxicillin-clavulanate. Prolonged treatment is essential to prevent relapse. Awareness of melioidosis, particularly in endemic areas or post-natural disasters, is critical, as early diagnosis and appropriate therapy are keys to improving outcomes. Distinctive imaging features, such as the "tunnel sign" can aid in diagnosis.

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STATEMENT

The manuscript has been read and approved by all the authors, the requirements for authorship in this document have been met, and each author believes that the manuscript represents honest work and information is not provided in another form.

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