CASE REPORT

Parietal bone osteomyelitis in melioidosis

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SUMMARY

We report a case of a 55-year-old man with uncontrolled diabetes who presented with pneumonia. During his hospital stay his clinical status worsened and he had a focal seizure. MRI showed central nervous system involvement and parietal bone osteomyelitis. As the patient's blood culture and endotracheal aspirate grew *Burkholderia pseudomallei*, melioidosis was diagnosed. He was treated with meropenem after failure to respond to ceftazidime. He gradually improved over a period of 4 weeks and was discharged. Early diagnosis and therapy resulted in improved outcome.

BACKGROUND

Infection with *Burkholderia pseudomallei* causes melioidosis. Melioidosis is predominantly seen in northern Australia and southeast Asia, including India.¹ Common modes of transmission are percutaneous inoculation, inhalation, aspiration and ingestion. Common clinical manifestations of the disease are pneumonia and skin infection. Central nervous system (CNS) involvement is, however, rare; its manifestations are severe and diverse ranging from cerebral abscess to meningoencephalitis with flaccid paraparesis. To the best of our knowledge, only one case of parietal bone osteomyelitis has been reported in the literature.² Rarity of CNS involvement in melioidosis and raising awareness among treating physicians about the condition is the driving factor for reporting this case.

CASE PRESENTATION

A 55-year-old man with uncontrolled diabetes mellitus and hypertension presented with fever and cough with expectoration of 15 days' duration. This was associated with worsening dyspnoea for 5 days. On examination, the patient was febrile with bilateral basal crackles. He was suspected to have pneumonia and was empirically started on a third generation cephalosporin and macrolide (ceftriaxone with azithromycin). The patient's haemodynamic condition deteriorated (he developed hypotension with tachycardia) and he was shifted to the intensive care unit (ICU). He had severe respiratory distress with tachypnoea and was therefore intubated and put on ventilatory support. During his ICU stay he developed tonic clonic movements of the left upper limb, which was diagnosed as simple partial seizure, and he was started on antiepileptic medication. CT imaging of the brain was inconclusive. As the patient continued to have persistent fever and refractory seizures, MRI

of the brain was carried out. The MRI showed subdural empyema with early parietal bone osteomyelitis. Blood and endotracheal (ET) aspirate showed growth of *B. pseudomallei* on culture, which confirmed the diagnosis of melioidosis.

INVESTIGATIONS

On blood investigation, the patient's blood sugars were found to be high (fasting 320 mg/dL and postprandial 460 mg/dL) with glycosylated haemoglobin of 10.9% (normal 4–6.5%), which was suggestive of uncontrolled diabetes mellitus. Complete blood picture and other biochemical investigations were within normal limits. Chest X-ray showed bilateral lower zone non-homogenous infiltrates with air bronchograms suggestive of pneumonia. CT of the brain showed no abnormality. Cerebrospinal fluid (CSF) analysis was uninformative. MRI of the brain showed a peripherally enhancing subdural collection in right parietal convexity (figure 1) and areas of restricted diffusion in right temporal and parietal bone showing heterogeneous marrow enhancement on contrast injection, which raised the possibility of early osteomyelitic

Figure 1 Axial T1 fatsat postcontrast image showing peripherally enhancing subdural collection (empyema) along the right parietal convexity with enhancement of right parietal bone.

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changes (figure 2). Right temporal lobe and insular cortex showed areas of subtle hyperintensities with contrast enhancement, which were suggestive of early cerebritis.

Blood culture and ET aspirate grew *B. pseudomallei*.

Three samples of sputum for acid-fast bacilli were negative.

DIFFERENTIAL DIAGNOSIS

Initially, the patient was suspected to have pneumonia. Disseminated tuberculosis was also thought as a possibility in light of the persistent fever, worsening of clinical status and focal seizures. CT imaging ruled out the possibility of tuberculoma and intracranial space occupying lesion. CSF analysis did not show any evidence of herpes simplex encephalitis. Based on MRI findings and culture sensitivity, the report of infection with *B. pseudomallei* was confirmed.

TREATMENT

The patient was started on intensive therapy with intravenous ceftazidime 2 g given every 6 hours. As the patient did not respond to the therapy, he was switched after 4 days to intravenous meropenem 2 g every 8 hours. Seizures were managed with multiple antiepileptic medication (levetiracetam, phenytoin, valproate sodium and oxcarbazepine). Trimethoprim-sulfamethoxazole (TMP-SMX) was added to the intensive therapy at a dose 8/40 mg/kg orally twice daily after 2 weeks. A neurosurgical opinion was sought for drainage of subdural empyema but the patient was advised medical management. His blood glucose was managed with insulin. Eradication therapy following intensive therapy was planned for a duration of 6 months with continuation of TMP-SMX at a dose of 8/40 mg/kg orally twice daily.

Figure 2 Coronal T1-weighted postcontrast image showing extra-axial collection along the right parietal convexity with marrow enhancement of right parietal bone suggestive of early osteomyelitic changes.

OUTCOME AND FOLLOW-UP

The patient gradually improved after 2 weeks of intensive therapy. Repeat chest X-ray showed clearing of pneumonic patch and repeat blood culture showed no growth. The patient was extubated and shifted to the ward once his clinical status improved. He had no further episode of seizure and antiepileptic medication was optimised. Eight weeks of intensive therapy were planned of which 4 weeks were completed during his hospital stay. MRI of the brain, which had been performed during follow-up after 2 months of intensive therapy, showed reduction in the size of subdural empyema (figure 3) and the patient was continued on eradication therapy (TMP-SMX). He was advised to follow-up after 2 months.

DISCUSSION

Melioidosis with neurological manifestations is associated with significant morbidity and mortality. Early literature mentions inhalation as the primary route but now percutaneous inoculation is considered the main mode of transmission of disease.³ In our case, inhalation could be the primary route with haematogenous spread. Most important risk factors are diabetes, alcohol abuse and chronic kidney disease.^{4 5} The incubation period of disease is about 9–21 days.⁶ Pneumonia was found to be the most common manifestation of disease in all studies.^{1 4 7 8} Osteomyelitis as presenting symptom was seen only in 3% of patients.^{4 9–11} Osteomyelitis is a very rare manifestation of the disease, its aetiology being considered to be a disseminated infection affecting metaphysis of long bones.⁹ This case report highlights the rare presentation of early parietal bone osteomyelitis with subdural empyema associated with melioidosis. A previous study by Chadwick *et al*¹² showed cerebral abscess to be the source of infection for osteomyelitis of the parietal bone. Laboratory testing includes all available samples for culture as it is the mainstay for diagnosis. Patients presenting with neurological manifestations should be investigated with CT

Figure 3 Follow-up MRI axial T1 fatsat postcontrast image showing reduction in size of the right parietal subdural empyema.

of the brain to rule out intracranial lesions related to disease, however, CT of the brain may be normal in patients with encephalomyelitis, so MRI would be a better option. Patients diagnosed to have melioidosis should be managed with an initial intensive phase and eradication phase whether infection is mild or severe. Recommended drugs are parenteral ceftazidime 50 mg/kg (up to 2 g daily) intravenously every 6 hours or meropenem 25 mg/kg (up to 1 g daily) intravenously every 8 hours for intensive therapy followed by TMP-SMX 8/40 mg/kg (up to 320/1600) orally every 12 hours either alone or in combination with doxycycline for eradication therapy. Ceftazidime has become the drug of choice for intensive therapy based on the results of a randomised trial carried out in Thailand.¹³ In our case, the patient improved with meropenem; previous comparative studies showed better efficacy of carbapenems over ceftazidime in severe melioidosis.^{14 15} Drug penetration to the brain is considered a major concern in neurological melioidosis; ceftazidime and carbapenem both achieve appropriate concentrations in the brain during the acute phase of disease. Addition of cotrimoxazole with parenteral ceftazidime in the intensive phase has not shown additional benefit but is still considered, in view of its excellent tissue penetration in clinical conditions such as bone, joint and neurological melioidosis.^{16 17} As per the literature, the duration of the intensive phase for disseminated melioidosis is 4–8 weeks and for the eradication phase it is 3 or 6 months.¹⁸ A prospective study by Sarovich *et al*¹⁹ has demonstrated that recurrent melioidosis is no longer common and showed the shift of relapse to reinfection. This decreased relapse was attributed to better antibiotic cover and prolonged intensive phase therapy. In our case, in view of the peculiar site of the osteomyelitis (close to the leptomeninges), and minimal bone damage and good clinical response to antimicrobial therapy, the patient was managed conservatively.

Learning points

- Parietal bone osteomyelitis with subdural empyema is an unusual central nervous system (CNS) presentation in melioidosis.
- Aggressive management of CNS melioidosis requires intensive therapy of at least 4–8 weeks followed by eradication therapy for 6 months.
- *Burkholderia pseudomallei* should be considered in the differential diagnosis in immunocompromised patients with febrile illness and pneumonia.
- Lack of awareness about melioidosis in non-endemic regions will misdiagnose the organism.

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Competing interests None.

Patient consent Obtained.

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