Variable Presentation of Neurological Melioidosis in Northeast Thailand

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Abstract. We describe three instructive cases of neurologic melioidosis that demonstrate the variable nature of clinical manifestations and disease pathology. The appropriate duration and choice of parenteral and oral antimicrobial therapy for neurologic melioidosis are also discussed.

INTRODUCTION

Melioidosis, the infection caused by Burkholderia pseudomallei, is most commonly reported from Northeast Thailand and Northern Australia. Manifestations of disease are extremely broad-ranging. A specific syndrome of meningitis with flaccid paraparesis or peripheral motor weakness occurs in 5% of cases in Northern Australia, and cerebral abscess is occasionally reported. We prospectively evaluated 191 melioidosis cases presenting to Sappasithiprasong Hospital, Ubon Ratchathani, Northeast Thailand, during 2005 to define the frequency and manifestations of neurologic melioidosis in this setting. Three adult cases were defined with variable presenting features and disease pathology. These cases provide a framework for the discussion of appropriate antimicrobial therapy of neurologic melioidosis.

CASE REPORTS

Patient 1, a 68-year-old male rice farmer with a history of chronic kidney disease associated with renal calculi and a left lithotomy 2 years previously, presented with a 7-day history of fever. Parenteral ceftriaxone was prescribed for suspected acute pyelonephritis, but on day 3 he developed a left hemiparesis (grade I) with a left upper motor neuron facial palsy; his Glasgow coma score (GCS) was 14. A random plasma glucose was 25 mmol/L. Three blood cultures were negative. Throat swab and urine were culture-negative for B. pseudomallei. Computer tomography (CT) showed hypodensity in the right frontoparietal lobe (Figure 1–A). He was treated with ceftazidime for 14 days, followed by meropenem for 2 weeks. Follow-up CT showed almost complete resolution of the abnormality. He made a full neurologic recovery and remained well for 5 months, after which he presented with recurrent hemiparesis (grade IV). CT showed a ring-enhancing lesion in the right frontal lobe with surrounding edema (Figure 1–B). He was treated with ceftazidime for 3 months, followed by a 1-year course of oral eradicative treatment with trimethoprim–sulfamethoxazole (80 mg/400 mg, 6 tablets/day; body weight 55 kg). He has since regained full neurologic function.

Patient 2, a 51-year-old female rice farmer with a history of diabetes mellitus and chronic kidney disease associated with a right nephrectomy 10 years previously, presented with a 6-day history of fever and two generalized tonic–clonic convulsions. Neurologic examination on admission was normal with a GCS of 15. A blood culture grew B. pseudomallei with a typical susceptibility pattern (susceptible to ceftazidime, meropenem, trimethoprim–sulfamethoxazole, doxycycline, and amoxicillin–clavulanic acid). He was treated with meropenem for 2 weeks followed by ceftazidime for 6 weeks; no oral antimicrobials were prescribed. He made a full neurologic recovery and remained well for 5 months, after which he presented with recurrent hemiparesis (grade IV). CT showed a ring-enhancing lesion in the right frontal lobe with surrounding edema (Figure 1–C). He was treated with ceftazidime for 3 months, followed by a 1-year course of oral eradicative treatment with trimethoprim–sulfamethoxazole (80 mg/400 mg, 6 tablets/day; body weight 55 kg). He has since regained full neurologic function.

Patient 3, a 45-year-old female rice farmer with a history of diabetes mellitus, presented with a splenic abscess. She was
treated for suspected melioidosis with parenteral amoxicillin–clavulanic acid for 9 days followed by oral amoxicillin–clavulanic acid for 4 months (amoxicillin 3 g/day and clavulanic acid 750 mg/day), and trimethoprim–sulfamethoxazole (80 mg/400 mg, 4 tablets/day; body weight 35 kg) for a month after the development of a rash. Follow-up abdominal ultrasound showed complete resolution of the splenic lesion. Eleven months after the first admission, she presented with a 1-month history of fever, chills, and a progressively enlarging skull mass. On examination, there was an 8-cm soft fluctuant parietal skull mass (Figure 1-3A). No neurologic deficit was present. Blood cultures were negative, but urine culture grew B. pseudomallei. Skull x-ray revealed two “punched-out” bone lesions in the affected area (Figure 1-3B). CT showed a cystic lesion in the scalp and an epidural abscess with bone changes consistent with osteomyelitis (Figure 1-3C). Ceftazidime was commenced 4 days prior to a craniotomy, during which the infectious process was found to involve the scalp muscle, bone, and epidural space. Craniectomy was performed, and 30 mL of yellowish pus was evacuated, which was

Antimicrobial therapy for melioidosis generally requires parenteral therapy for 10–14 days, followed by oral antimicrobials for 12–20 weeks. Recommended drugs are ceftriaxone or a carbapenem drug for parenteral therapy, followed by trimethoprim–sulfamethoxazole with or without doxycycline for oral eradication therapy. Therapy for intracerebral melioidosis requires special consideration because not all drugs used for the treatment of melioidosis achieve therapeu-tic concentrations in the brain. Ceftriaxone or a carbapenem are appropriate because they both achieve high levels in CSF. The addition of parenteral trimethoprim–sulfamethoxazole to ceftriaxone is not associated with a survival advantage in the treatment of melioidosis in general, but dual therapy should be considered for the treatment of neurologic melioidosis in general, but dual therapy should be considered for the treatment of neurologic melioidosis. Ceftazidime or a carbapenem are appropriate because they both achieve high levels in CSF. The addition of parenteral trimethoprim–sulfamethoxazole to ceftriaxone is not associated with a survival advantage in the treatment of melioidosis in general, but dual therapy should be considered for the treatment of neurologic melioidosis. Ceftazidime or a carbapenem are appropriate because they both achieve high levels in CSF. The addition of parenteral trimethoprim–sulfamethoxazole to ceftriaxone is not associated with a survival advantage in the treatment of melioidosis in general, but dual therapy should be considered for the treatment of melioidosis in general.

Doxycycline concentrations in CSF are not higher than their minimal inhibitory concentration (MIC) to B. pseudomallei but may be important for the treatment of extracerebral sites. We recommend parenteral treatment of neurologic melioidosis for a minimum of 4 weeks, followed by oral eradication therapy for a minimum of 6 months. This mirrors treatment recommendations at the Royal Darwin Hospital in Northern Australia (Professor Bart Currie, personal communication). Choice and duration of oral eradica-tive treatment are determinants of relapse. Amoxicillin–clavulanic acid has been shown to be associated with a higher rate of relapse, but the combination remains an alternative oral agent in Thailand. This is not an acceptable option, however, for treatment of neurologic melioidosis because the concentration of amoxicillin–clavulanic acid in CSF is < 10% relative to blood, which falls below the MIC for B. pseudomallei. Patient 2 had relapse while being treated with amoxicillin–clavulanic acid, and patient 3 had relapse 5 months after completing 20 weeks of oral treatment, 16 weeks of which was with amoxicillin–clavulanic acid. Options for treatment of patients with intolerance to trimethoprim–sulfamethoxazole or infected with strains resistant to trimethoprimsulfamethoxazole are limited. Prolonged parenteral therapy is impossible in resource-poor regions, where probably the best option is chloramphenicol plus doxycycline.