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A Rare Presentation of Central Nervous System Melioidosis

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Abstract

We report a case of an 18-year-old army man who was diagnosed with cerebral melioidosis with disseminated abscesses. The patient presented with fever and focal neurological signs with positive cerebral imaging findings followed by a positive blood culture for *Burkholderia pseudomallei*. Further imaging of other sites also revealed multiple abscesses. He responded well to an intensive course of antibiotic therapy of eight-week duration followed by 6 months of eradication therapy. The repeat cerebral imaging showed complete resolution of basal ganglia abscess at the end of intensive antibiotic therapy.

Subject Areas

Infectious Diseases

Keywords

Melioidosis, Basal Ganglia, Abscess, Antibiotic

1. Introduction

Melioidosis is endemic in Southeast Asia and northern Australia and it is caused by *Burkholderia pseudomallei* [1]. It gains entry to the human host through skin abrasion, inhalation or ingestion. The clinical manifestations of melioidosis are variable and it commonly involves the lungs, visceral organs and occasionally musculoskeletal system with cerebral involvement being a rare presentation. The definite diagnosis is made by positive culture of the organism from blood or tissue biopsy. In endemic areas where the *B. pseudomallei* is detected in the blood culture or biopsy, the suspicion for systemic melioidosis should be raised.

Cerebral melioidosis are rarely reported and cases with disease presentations secondary to cranial abscesses are exceedingly rare [2]. The radiological features

of cerebral melioidosis are variable and usually present as encephalitis or abscesses. Basal ganglia abscess is reported to be rare in central nervous system melioidosis. The duration of treatment depends on the site and extent of the infection. Prolonged intravenous (IV) therapy for four to eight weeks is needed for complicated infections such as cerebral melioidosis followed by eradication therapy.

2. Case Presentation

An 18-year-old army man presented with intermittent fever for one week, associated with headache, chills and occasional dry cough. He was not known to have any previous medical illness. On physical examination, his Glasgow Coma Scale (GCS) score was full. However he appeared lethargic. He was febrile with a temperature of 38.7 degree Celsius. There was no significant abnormality detected on the cardiovascular, respiratory and abdominal examination. Neurological examination revealed upper motor neuron signs on the left lower limb with hypertonia, brisk knee and ankle reflexes, decreased in motor power to 4- (moving against slight resistance) with sustained ankle clonus and positive Babinski response. Neck stiffness and positive Brudzinski's sign were present. Preliminary blood investigations showed leukocytosis, white cell count of 12.7 × 10^3/UL; and mild elevation of liver enzymes, aspartate aminotransferase of 250 u/L and alanine aminotransferase of 171 u/L (**Table 1**). The renal function test was within normal limits and blood and urine cultures sent for cultures. The chest radiograph was reported to be normal. In view of the history of fever with significant neurological deficit, an urgent plain computed tomography (CT) brain was done.

Immediate CT brain showed an ill-defined hypodense lesion at the right basal ganglia (**Figure 1**). He was then treated as for meningitis with IV ceftriaxone and IV acyclovir. Lumbar puncture (LP) was performed and the cerebrospinal fluid (CSF) sent for analysis. The CSF was reported acellular, clear in appearance with elevated protein level and low glucose level suggestive of bacterial meningitis. The CSF culture and gram staining showed no organisms. Magnetic resonance Imaging (MRI) of the brain with gadolinium contrast was done which showed a ring-enhancing lesion in the right basal ganglia with subdural effusion (**Figure 2**). Viral screening including Hepatitis B, C and Human-immunodeficiency Virus (HIV) were all non-reactive. He remained febrile on day 4 of admission and the blood culture grew *Burkholderia pseudomallei*. Bedside ultrasound of the abdomen revealed splenic micro-abscesses (**Figure 3**). A subsequent contrast enhanced CT of the thorax, abdomen and pelvis showed airspace opacities in the right lung, left lung consolidation and multiple splenic micro-abscesses (**Figure 4**).

The therapy was switched to the recommended antibiotic regime according to the Royal Darwin Melioidosis Guideline [3] that includes eight weeks of intensive phase of IV meropenem followed by six months of eradication therapy with trimethoprim-sulfamethoxazole and folic acid. At the end of the treatment, he

Table 1. Laboratory investigations.

Variables	Normal range	On admission	After 2-weeks interval
Hematocrit	40% - 54%	28.2	36.9
Hemoglobin	10 - 18 g/dL	9.3	12.4
White-cell count	4-11 × 10^3/UL	12.7	6.9
Differential count			
Neutrophils	(2.9 - 7.9) × 10^3/UL	8.7	3.3
Lymphocytes	(1.8 - 4.0) × 10^3/UL	1.3	2.6
Monocytes	(0.0 - 80.0) × 10^3/UL	0.7	0.4
Eosinophils	(0.4 - 2.1) × 10^3/UL	0.0	0.48
Basophils	(0.0 - 0.2) × 10^3/UL	0.0	0.0
Platelet count	(150 - 400) × 10^3/UL	220	396
C-reactive protein	0.0 - 5.0 mg/L	218.2	1.70
Potassium	3.5 - 5.0 mmol/L	3.4	3.6
Urea	1.7 - 8.3 mmol/L	5.0	3.5
Creatinine	62 - 106 μmol/L	69	89
Glucose	3.1 - 6.4 mmol/L	4.4	
Bilirubin	<17 μmol/L	37	7
Direct	0 - 5 μmol/L	22	1
Protein	66 - 87 g/L	60	85
Albumin	34 - 48 g/L	17	40
Aspartate aminotransferase	0 - 38 u/L	250	21
Alanine aminotransferase	<41 u/L	171	42
Alkaline phosphatase	0 - 129 u/L	153	100
Lactate Dehydrogenase	313 - 512 u/L	1548	
Creatine Kinase	39 - 308 u/L	1748	
HbA1C		5.8	
CSF Biochemistry			
Appearance		Clear	
CSF Glucose	2.22 - 3.90 mmol/L	2.10	
CSF Protein	0.15 - 0.45 g/L	0.45	
CSF Albumin	g/L	0.19	
CSF Culture		No growth	
CSF Cell count	Wbc/mL	Nil	
CSF Gram stain		No organism seen	
CSF Acid Fast Bacilli culture		Negative	
CSF Herpes Simplex Polymerase Chain Reaction		Not detected	
CSF Toxoplasma antibody IgM		Not detected	
CSF Toxoplasma antibody IgG		Reactive	
CSF Mycobacterium Tuberculosis PCR		Not detected	

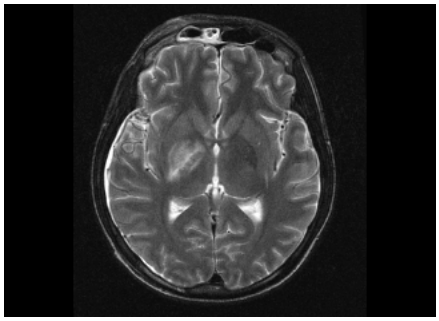

Figure 1. Non-enhanced CT brain shows hypodense lesion in the right basal ganglion.

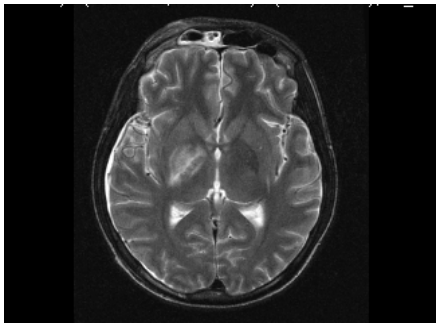

Figure 2. Axial T2WI: High signal changes in the right basal ganglion with right subdural effusion.

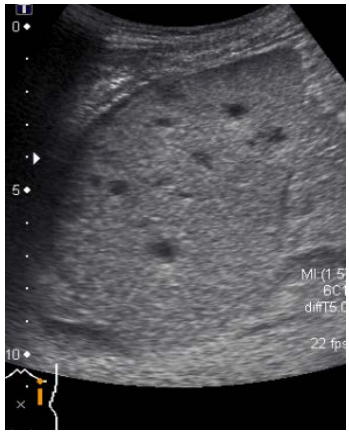

Figure 3. Splenic micro-abscesses on abdomen ultrasound.

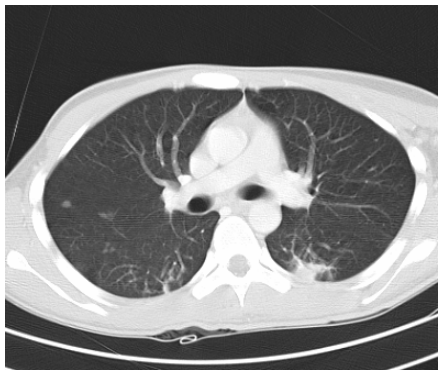

Figure 4. CT Thorax in lung setting showed air space opacities in the right lung with consolidation in the left lower lobe of the lung.

had gained full neurological recovery and the repeated CT scan after eight weeks of treatment showed complete resolution of the previous basal ganglion lesion and subdural effusion.

3. Discussion

Melioidosis is an infectious disease caused by *Burkholderia pseudomallei*, which is endemic in the tropics [4]. It is a Gram-negative aerobic bacillus that gains entry to human host through skin abrasion, inhalation and ingestion. It has a predilection for multi-organ involvement and frequently involves the lungs, visceral organs, skin or soft tissue and rarely, meninges and the cerebrum. It has a variable clinical manifestation with non-specific radiological features and it requires a high index of clinical suspicion. The definitive diagnosis is made by presence of positive culture of the organism from blood or tissue [5]. Nevertheless, advanced imaging plays a pivotal role in establishing the extent of the disease, characterizing the lesion, making management decision, as well as following up on the disease progression.

The initial plain CT scan in this patient revealed a hypodense lesion in the right basal ganglion, leading to a possible diagnosis of encephalitis. MRI with gadolinium contrast was used to further delineate the lesion and revealed a solitary ring-enhancing lesion in the right basal ganglia with surrounding edema (**Figure 5**). Diffusion weighted imaging with apparent diffusion coefficient (ADP) mapping showed a central core of restricted diffusion, which is suggestive of an abscess (**Figure 6** and **Figure 7**) [6]. MR Imaging is sensitive in delineating the high signal changes of the cortex, basal ganglia, thalamus, cerebellum and midbrain while to rule out demyelination, abscess or tumour. Central nervous system melioidosis is rarely reported and mostly presents as meningoencephalitis with cerebral abscesses and brain stem involvement which can present as cranial nerve palsies, or flaccid paraparesis alone [7]. The biochemistry findings of the CSF from the LP and the presence of *Burkholderia pseudomallei* in serial blood cultures confirm the diagnosis of cerebral melioidosis with disseminated infection. The CSF analysis from patients with cerebral melioidosis often shows no organism on Gram staining, leukocytosis with mononuclear cell predominance, high protein level, and normal glucose level [8] [9].

Basal ganglia are rare location for abscess formation. In adults, hematogenous brain abscesses usually occur at areas supplied by middle cerebral artery and very occasionally, in the deep tissues, such as basal ganglia and thalamus [10]. Streptococci and anaerobes are the most commonly encountered microorganisms in basal ganglia and thalamic abscesses [11]. Among the immunocompromised patients, basal ganglia is more commonly affected by toxoplasmosis and tuberculosis. Other differential diagnosis of a ring-enhancing lesion in the basal ganglia include glioblastoma, metastasis, and pyogenic abscess, subacute ischemic infarction, resolving hematoma, and demyelinating disease [12].

Cerebral melioidosis is a rare manifestation of the infection and associated with melioidosis at other sites in up to 10% of cases [8]. Therefore, the findings

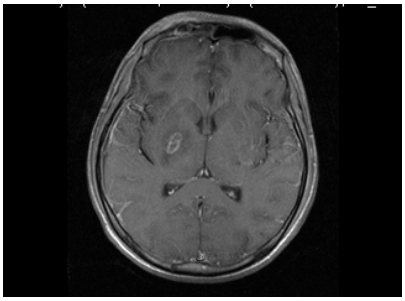

Figure 5. Post Gadolinium axial T1WI ring-enhancing lesion in the right basal ganglion.

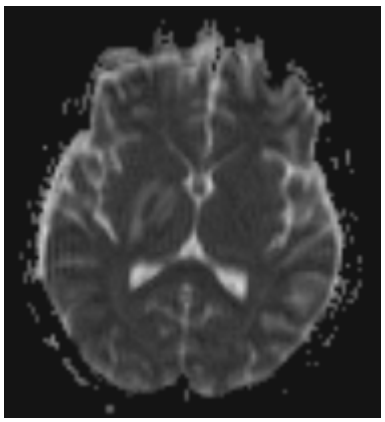

Figure 6. Diffusion weighted image (4100/119, b value of 1000 s/mm^2) shows high signal intensity, with low signal on ADC map represent restricted diffusion of the abscess core.

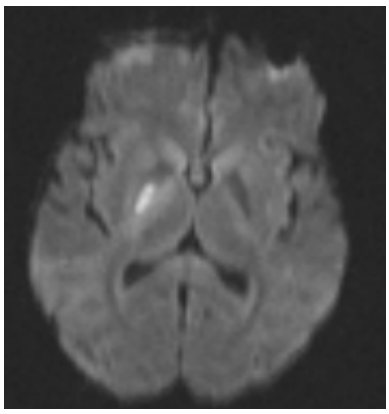

Figure 7. Diffusion weighted image (4100/119, b value of 1000 s/mm^2) shows high signal intensity, with low signal on ADC map represent restricted diffusion of the abscess core.

of cerebral melioidosis should prompt the clinicians and radiologists to look for other foci of infection. The ultrasound is sensitive in detection of visceral microabscesses but whole body CT scan provides a good information on the extent of the disease. The CT thorax is more sensitive and shows various manifestations of melioidosis infection in the lungs, from air space opacities and nodules, to cavitating lesions and consolidation, which may not be seen on the chest X ray.

In this case illustration, the patient presented with symptoms of meningoencephalitis initially. The subsequent discovery of *Burkholderia pseudomallei* in the blood culture prompted the clinicians to look for disseminated abscesses in

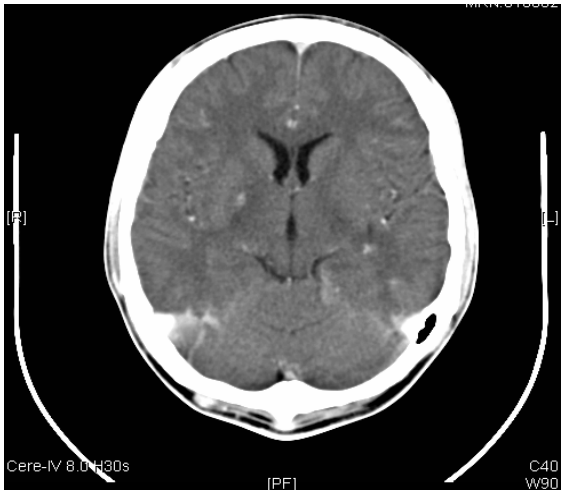

Figure 8. Post treatment CECT brain at 3-month interval: Smaller ring enhancing lesion (2.3 mm × 3.7 mm) with reducing edema.

other organs. Our patient responded well to eight-weeks duration of IV meropenem followed by recommended eradication therapy, which include six months of trimethoprim-sulfamethoxazole and folic acid. Repeated brain imaging at three-month interval showed a partial resolution of the basal ganglion abscess (**Figure 8**) while the repeated brain imaging at six-month intervals showed complete resolution of the ring enhancing lesion in the right basal ganglion and splenic micro- abscesses (image not shown) with full recovery of neurological deficits suggest of good treatment response. His basal ganglion abscess and subdural effusion were not drained as recommended by the neurosurgery team due to its location and difficulty in surgical approach. He is currently under our outpatient follow up for the surveillance of reactivation of the disease.

4. Learning Points

The common clinical manifestations of melioidosis infection are pneumonia and localized skin involvement. Culture remains the mainstay of the diagnosis with Gram stain revealing gram-negative bacilli of *B. pseudomallei.* Melioidosis presenting as cerebral abscesses carries a high mortality rate. When encephalomyelitis or brain abscesses are suspected, MRI brain is helpful to delineate the CNS involvement [9]. Prolonged course of antibiotic treatment is indicated in complicated infection and eradication therapy is needed as *B. pseudomallei* have the potential to reactivate, with a latent period that can last up to decades.

5. Patient's Consent

Explicit consent from the patient illustrated in this case had been obtained for the medical details and radiographic images to be used for publication purposes.

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