Case Report

Central Nervous System Melioidosis, the Mimic of Cerebral Tuberculosis

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The central nervous system (CNS) melioidosis is uncommon. The authors report a case of melioidosis brain abscess who presented with a 5-month history of seizures and right leg weakness. The presentation, neuroimages, and pathology mimicked tuberculous granuloma or abscess. The diagnosis was finally made by the culture of subdural tissue. The authors advise that the CNS melioidosis should be suspected if a patient presenting with CNS granuloma or abscess lives in the endemic area of melioidosis and has any of its risk factors. Prompt diagnosis and treatment remain crucial due to its high mortality rate.

Keywords: *Central nervous system, Neurological, Melioidosis*

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Melioidosis is an infectious disease caused by the gram-negative bacterium, *Burkholderia pseudomallei*. The regions which are considered to be endemic include Southeast Asia, northern Australia, South Asia (including India), and China. Melioidosis can present with various clinical manifestations of any organs. However, central nervous system (CNS) involvement is unusual and sometimes difficult to establish the diagnosis. From the prospective study in northern Australia, only five percent of melioidosis cases were documented as neurological melioidosis[1]. The aim of this article is to report a case of CNS melioidosis in which presentation, neuroimages, and pathology mimics CNS tuberculosis. The following content will include case presentation, investigations, treatment and clinical course.

Case Report

A 55-year-old car mechanic man who lives in eastern Thailand presented with gradually progressive weakness and transient clonic movement of the right leg for 5 months. He had been well until, 5 months prior to admission; he developed 2 episodes of seizure 1 week apart. Each attack began with a tonic-clonic movement of the right leg, arm and face evolving to the whole body. He also had a loss of consciousness for 5 minutes followed by 10-minute confusion before the recovery. He went to a general hospital at the time and was diagnosed with alcoholic withdrawal seizures. Three months later, a clonic movement of the right leg recurred but not spreading to other body parts. After that, his right leg had progressively been weak and numb causing him difficult to walk. He reported neither headache nor fever. A history of previous seizures and a family history of epilepsy were denied. He had a history of head injury without loss of consciousness 7 months ago. His head was hit by a soil-contaminated machine at the time leading to a small laceration wound. The medical history included type 2 diabetes mellitus and dyslipidemia which were treated by diet control. No medication was currently used. He quit alcohol drinking 2 months ago after everyday consuming liquor equally to 47.4 grams ethanol per day for 15 years. The general examination was unremarkable including body temperature. No chronic liver stigmata were observed. Neurological examination revealed motor weakness (MRC grade IV) of the right leg, decreased pinprick sensation of the right foot and hyperreflexia of the right knee and ankle jerks. The Babinski sign showed extensor plantar response of the right foot.

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Investigations

The patient's symptoms compatible with focal motor seizures and the clinical right leg weakness strongly suggested focal lesion at the left frontal parasagittal area. Thus, a contrasted magnetic resonance imaging (MRI) of the brain was done showing multiple rim-enhancing hypointense T1 and hyperintense T2 lesions with restricted diffusion at the left frontoparietal lobe, ranging from 0.5 cm to 1.9x4.1cm in size (Fig. 1). Perilesional vasogenic edema was seen. There was an area of focal dural thickening with enhancement at the left parietal region and the left parietal bone also showed hypointense T1 change of the inner table. Lumbar puncture was not done. The Anti-HIV antibody was negative, and chest radiography was normal. Plasma glucose level was 184 mg per dL. Liver function test demonstrated minimally elevated liver enzymes.

The insidious clinical onset and the MRI result which showed rim-enhancing parenchymal lesions with dural involvement suggested that the central nervous system tuberculosis should be the most likely diagnosis. However, these features could be a brain abscess caused by other organisms such as low-virulent bacteria, fungus or even brain tumors. Therefore, we consulted a neurosurgeon with the patient's consent for brain tissue biopsy. A craniotomy was done, and the operative finding revealed a soft, yellowish-white mass confined in subdural, subarachnoid and intraparenchymal regions over the left motor area. Subdural tissue biopsy was carried out, and its pathology demonstrated granulomatous inflammation with necrosis. Acid fast bacilli stains and polymerase chain reaction for tuberculosis were both negative. Burkholderia pseudomallei were identified from the aerobic bacterial culture of the subdural tissue swab. Susceptibility testing showed the organism is sensitive to amoxicillin/clavulanic acid, ceftazidime, cefoperazone/sulbactam, meropenem, ciprofloxacin, trimethoprim/sulfamethoxazole (TMP/SMX) and tetracycline. Blood culture for bacteria was reported as no growth. Melioidosis titer was 1: 1,280. Diagnosis of CNS melioidosis was finally established.

Treatment, outcome, and follow-up

At first, we decided to treat the patient as CNS tuberculosis before the subdural tissue culture was revealed. However, intravenous ceftazidime and TMP/SMX were given along with oral phenytoin for controlling seizures when the CNS melioidosis was diagnosed. The symptoms of weakness and numbness subsequently improved and the seizures did not recur. Three months later, follow-up MRI revealed decreased size and numbers of multiple rim-enhancing lesions at left superior frontoparietal lobe (Fig. 2). As a result, the antibiotics were switched to oral TMP/SMX and doxycycline. The clinical symptoms continuously improved and the serial follow-up MRI had shown a consistent reduction in size and number of lesions until final resolution (Fig. 2). The whole course of oral TMP/SMX and doxycycline administration lasted 24 months and 8 months respectively. Finally, the patient still had mild weakness of the right iliopsoas muscle (MRC grade IV+).

Discussion

The prospective study at Royal Darwin Hospital had documented 12 cases of CNS melioidosis over 9 years out of 232 melioidosis cases[1]. A variety of neurological syndromes has been reported including encephalomyelitis[1,2], meningitis[3,4], brain abscess[5,6], epidural abscess and subdural empyema[5,7]. The

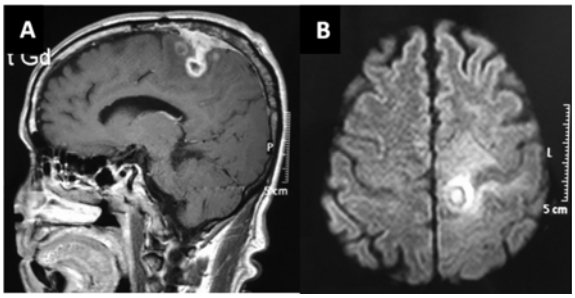

Fig. 1 Gadolinium-enhanced T1W sagittal image shows multiple rim-enhancing lesions and focal dural thickening with enhancement at the left frontoparietal lobe. Hypointense T1 change of the inner table of the left parietal bone is also observed (A). Axial DWI image demonstrates restricted diffusion of the same brain lesions (B).

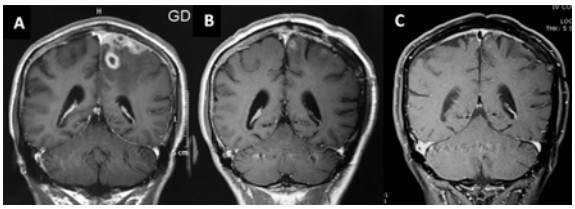

Fig. 2 Serial gadolinium-enhanced T1W coronal images show the subsequent reduction in size and number of rim-enhancing lesions at left frontoparietal lobe: before treatment (A), 3 months after treatment (B), and 27 months after treatment (C).

encephalomyelitis appears to be geographically restricted to the northern region of Australia while the other forms of CNS melioidosis do not. We report a case of CNS melioidosis in the form of brain abscess. The patient had an underlying diabetes mellitus and heavy alcoholic drinking which were the major risk factors of melioidosis. He presented with seizures and motor weakness without headache or fever, which was the most common clinical feature of the neurological melioidosis. To our knowledge, the 5-month clinical onset of this patient was longer than the longest duration previously reported[8]. Both the clinical features without headache or fever and the very long clinical onset would reflect the chronic disease process without systemic inflammatory response. The MRI brain finding of our case showed multiple rim-enhancing lesions accompanying with restricted diffusion in DWI that favored abscess rather than tumor. Adjacent dural inflammation and osteomyelitis of the skull without other organs involvement indicate the infectious mechanism of local invasion rather than hematogenous spreading. This locally invasive pathology could be a consequence of preceding microorganism infiltration via the cranial laceration wound. The pathology of subdural tissue revealed granulomatous inflammation with necrosis which is the pathologic hallmark of tuberculosis; however, few reports described such pathologic finding in the cases of CNS melioidosis[9,10]. The features including long clinical onset, MRI findings, and histopathology made us take the decision to treat the case as CNS tuberculosis at first unless the culture was positive for *Burkholderia pseudomallei*. There has been no standard treatment regimen for the CNS melioidosis due to its rarity. In general principle of melioidosis treatment, ceftazidime, imipenem or meropenem is the mainstay of intensive therapy while TMP/SMX is the critical drug for eradication therapy[11]. Because of the excellent tissue penetration, an addition of TMP/SMX in the intensive therapy is recommended by some centers. The Darwin melioidosis guideline recommends at least 8-week duration of intensive phase followed by the 6-month period of eradication phase for CNS melioidosis[12]. We treated our patient with intravenous ceftazidime plus TMP/SMX for 12 weeks, and then oral TMP/SMX plus doxycycline for 8 months and finally oral TMP/SMX alone for 16 months. Our decisions to stop treatment depended on clinical and radiological remissions. Our patient finally had a good outcome; however, data from the previous study suggested that the CNS melioidosis had a poor prognosis with the death rate of 25 percent[1].

Conclusion

The CNS melioidosis is uncommon. Encephalomyelitis and brain abscess are among the most frequent disease forms. Its presentation, neuroimages or even pathology can mimic other diseases such as CNS tuberculosis. Thus, the particular disease should always be suspected if a patient presenting with CNS infection lives in the endemic area and has any risk factors of melioidosis. Prompt diagnosis, especially with tissue culture, and early treatment, remain crucial due to its high mortality rate.

What is already known on this topic?

The neurological melioidosis is rare. There are 2 disease forms which are mainly reported including encephalomyelitis and brain abscess. Headache and fever are among the most common clinical features of the disease. MRI brain is the neuroimaging of choice due to its high sensitivity. The prognosis of the CNS melioidosis is poor owing to its high mortality rate.

What this study adds?

The brain abscess from melioidosis can present without the symptoms of headache or fever. The disease can be presented with a very long clinical onset up to 5 months as our case. The CNS melioidosis should be considered as a differential diagnosis if the brain tissue pathology shows the granulomatous inflammation with necrosis in a patient with risk factors.

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Potential conflicts of interest

None.

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โรคเมลิออยด์ในระบบประสาทกลาง, ผู้ล้อเลียนวัณโรคสมอง

มณฑล ว่องวันดี, ไกรยศ เกียรติสุนทร, พัชรสาร ลีนะสมิต

โรคเมลิออยด์ในระบบประสาทกลางพบได้ไม่บ่อย ผู้นิพนธ์รายงานผู้ป่วยโรคฝีในสมองจากเมลิออยด์ ซึ่งมาด้วยประวัติชักและขาขวาอ่อนแรงมานาน 5 เดือน ทั้งอาการนำ ภาพถ่ายระบบประสาท และพยาธิสภาพ มีลักษณะคล้ายวัณโรคสมอง ท้ายที่สุดการวินิจฉัยโรคทำได้โดยการเพาะเชื้อของเนื้อเยื่อใต้เยื่อหุ้มสมองชั้นดูรา ผู้นิพนธ์แนะนำว่าควรสงสัยโรคเมลิออยด์ในระบบประสาทกลาง ถ้าผู้ป่วยซึ่งมาด้วยการติดเชื้อระบบประสาทกลางที่มีลักษณะของฝีหรือแกรนูโลมา อาศัยอยู่ในบริเวณที่มีการระบาดของโรคเมลิออยด์ และมีปัจจัยเสี่ยงอย่างหนึ่งอย่างใด การวินิจฉัยและรักษาอย่างทันท่วงทียังคงมีความสำคัญอย่างยิ่งเนื่องจากโรคนี้มีอัตราการเสียชีวิตที่สูง
