CASE REPORT

A Rare Case of Neuromelioidosis Presenting As Brain Abscess in Patient Complaining of Long Standing Headache

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ABSTRACT

Melioidosis is a rare disease caused by *Burkholderia pseudomallei*, which may manifest with varying degrees of organ involvement, ranging from isolated organ to multi-systemic impairment. Patients with melioidosis may exhibit a wide spectrum of symptoms, from asymptomatic to severely ill. While there have been reported cases of melioidosis affecting various organs, there is limited information available on its neural involvement. In this unique case, we present a patient with no specific symptoms other than a persistent headache, who possesses only type 2 diabetes mellitus and old age as potential risk factors. Notably, the patient has no history of trauma or surgery that might have contributed to the infection. Upon MRI examination, multiple abscesses were discovered in the left parieto-occipito-temporal region. Subsequent culturing of these abscesses confirmed the presence of *B. pseudomallei*. The patient underwent a 4-week treatment regimen involving intravenous ceftazidime and oral double-strength co-trimoxazole. At the two-week mark of this therapy, the patient returned for a scheduled follow-up and exhibited no symptoms, remaining in good health ever since.
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INTRODUCTION

Burkholderia pseudomallei is a gram-negative bacillus that is primarily found as a soil saprophyte. Previously classified as Pseudomonas pseudomallei, it has been identified as the causative agent of melioidosis, a complex multisystemic disease that can affect various parts of the body. Melioidosis is characterized by the potential for extensive organ involvement, making it a potentially life-threatening condition. Interestingly, it is often challenging to pinpoint specific symptoms that are characteristic of melioidosis, contributing to the complexity of its diagnosis. This formidable infectious disease is endemic to certain regions, notably Southeast Asia, Northern Australia, South Asia, and parts of China (1). Several risk factors have been associated with an increased susceptibility to melioidosis, including diabetes, thalassemia, male gender, renal disease, excessive alcohol consumption, chronic lung disease, and the use of glucocorticoids. These risk factors underscore the importance of understanding and managing melioidosis, especially in at-risk populations. In rare instances, melioidosis can extend its reach into the central nervous system, leading to a condition known as neuromelioidosis. The clinical presentation of neuromelioidosis can vary widely, ranging from severe, life-threatening conditions to more subtle symptoms like chronic headaches. Unlike other neurological disorders that may have characteristic radiological signs, neuromelioidosis often presents with findings resembling encephalitis, meningitis, or brain abscess (1). Therefore, the definitive diagnosis of neuromelioidosis primarily relies on culture examination, which underscores the need for a high degree of suspicion. Given the rarity of melioidosis, it is important to acknowledge that knowledge about its diverse presentations, including its potential to affect the central nervous system, remains limited in many healthcare settings. This lack of awareness can lead to misdiagnoses or the underdiagnosis of melioidosis, further emphasizing the importance of enhancing our understanding of this infectious disease. Despite the endemic nature of melioidosis in Southeast Asia, comprehensive studies regarding the disease and its manifestations, particularly neuromelioidosis, remain limited in this region. Therefore, the case report

presented here aims to contribute additional data on neuromelioidosis, offering insights into its clinical presentation and the treatment approaches employed. The comparison between recommended guidelines and current treatment strategies is also explored, all within the context of a patient who presented with neuromelioidosis, with a long-standing headache as the sole symptom, providing valuable clinical insights into this complex and underdiagnosed condition.

CASE REPORT

A 60-year-old male patient visited the clinic, presenting a recurring and persistent headache as his chief complaint. He denied experiencing other symptoms such as nausea, alterations in behaviour, speech difficulties, or motor dysfunction. There was no history of prior seizures or brain-related illnesses. Initial vital sign assessments revealed normal readings, and physical examinations detected no motor, sensory, or cranial nerve abnormalities. However, MRI scan disclosed (Fig. 1): multiple ring-enhanced lesions located within the left parieto-temporal lobe. These lesions were associated with perifocal edema, which extended to neighbouring structures, including the left thalamus, posterior crus of the left internal capsule, left lentiform nucleus, left external capsule and left parieto-temporo-occipital lobe. The lesions also led to the obliteration of the left lateral ventricle, causing a rightward midline shift and mild right lateral ventricle dilation. Additionally, sub-cuticular empyema was observed in the left parieto-temporal region. Based on these findings, a tentative diagnosis of a Space-Occupying Lesion of the Left Parieto-temporal Lobe with suspicion of a Brain Abscess was made. As a result, the patient was promptly scheduled for a craniotomy and subsequently admitted to the hospital. Laboratory results indicated signs of infection, notably an elevated segment neutrophil level, poorly controlled diabetes, mild hyponatremia, and mild hypokalemia. On the first day of admission, the patient received a combination of medications, including ceftriaxone, metformin, vidagliptin, ketorolac, and esomeprazole.

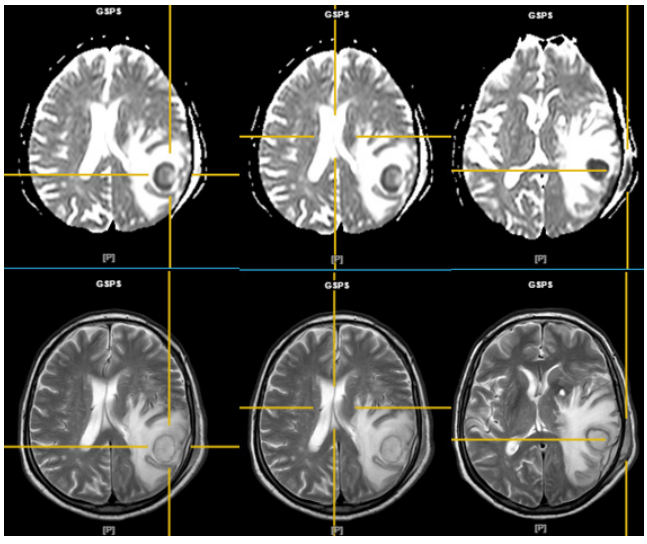

Figure 1: MRI Imagery Shows Multiple Ring Enhanced Lesion And Perifocal Edema On The Sinistral Parieto-temporal Lobe, Mass Effect Caused By Perifocal Edema Causing Midline Shift, Obliteration Of Left Lateral Ventricle And The Dilation Of The Right Ventricle, Subcuticular Empyema.

Due to the strong suspicion of a brain abscess supported by laboratory findings, the patient was referred to a microbiology pathologist. Subsequently, it was planned to initiate metronidazole while discontinuing ceftriaxone. On the second day of hospitalization, the treatment regimen was expanded to include metronidazole and vancomycin alongside the previously administered drugs. This treatment course was maintained over the following days.

On the fourth day of admission, a craniotomy was performed. Question mark incision was made at the left temporal region and upon opening of the incision, pus was discovered in the subcuticular layer. After the opening of the duramater, more pus was discovered in the subdural layer which connects to the abscess that was located in the left parieto-temporal lobe. Extracted abscess was then cultured. While awaiting culture and resistance test results, the treatment plan remained unchanged. Three days after the pus was cultured, the results revealed the presence of Burkholderia pseudomallei (Fig. 2). Notably, this pathogen exhibited resistance to cefazolin, gentamycin, amikacin, fosfomycin, and ampicillin. However, it displayed susceptibility to sulperazone, ceftizoxime, cefotaxime, ceftazidime, ceftriaxone, cefixime, tigecycline, and imipenem.

In light of these findings, the antibiotic treatment regimen was adjusted. The patient was placed on a six-week course of ceftazidime, double-strength co-trimoxazole, and doxycycline for a period of six months. After closely monitoring the patient for two days, he was discharged with instructions to return for ceftazidime injections. A follow-up appointment was scheduled for two weeks post-discharge, during which the patient reported feeling well, and his laboratory results were within acceptable parameters.

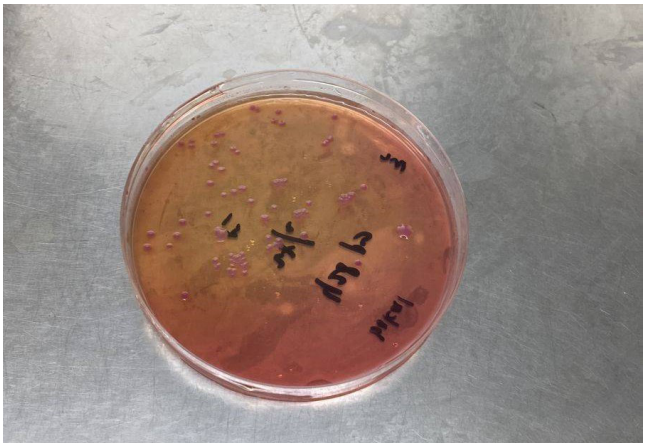

Figure 2: Culture Examination Reveals *Burkholderia pseudomallei*

DISCUSSION

Neuromelioidosis is a rare manifestation of melioidosis, which accounts for 1.5 – 5% of all reported cases (1). According to the systemic review done in 2019, Features of a patient with neuromelioidosis may present with fever (82%), headache (54%), unilateral weakness (57%) and cranial nerve deficits (52%) (2). Abscesses and perifocal edema that has predilections in the frontal and parietal lobe are described to lead towards the diagnosis of B. pseudomallei and 78% of patient's MRI will show rim enhancing patterns (2). However to achieve the certain diagnosis of B. pseudomallei, the culture examination is recommended. Up to date, there has been no reliable specific laboratory tests for to detect B. pseudomallei aside from culture. Test results such as increased CRP, neutrophil leucocytosis are common among other gram negative bacilli. Risk factors that may contribute to the infection are diabetes, thalassemia, male gender, renal disease, excessive alcohol consumption, chronic lung disease and the use of glucocorticoids. In this confirmed case of neuromelioidosis, the only presenting symptom is long standing headache while presenting risk factors such as old age and diabetes mellitus may have contributed to the infection.

Current knowledge on pathogenesis of Neuromelioidosis were not fully understood. However, there have been descriptions of molecular pathophysiology of neuromelioidosis. B. pseudomallei can spread through the central nervous system, by setting a primary focus of infection in the spleen, by infecting CD 11B+ of the spleen and causing the expression of L – selectin, enabling migration to cerebral epithelium (3).

Treatment regiment of melioidosis is divided into the intensive phase and the eradicative phase (4). Conventional regiment of the intensive phase of melioidosis consisting of chloramphenicol, co-trimoxazole and doxycycline have been used since the discovery of melioidosis in 1911 (4). However with the high mortality rate of 37.9 – 61%, trial of ceftazidime as an alternative to the conventional treatments for the intensive phase shows a drop of mortality rate by 50%, and it is because of this trial, intensive phase regiment switched to ceftazidime. In 2015 Darwin's Guideline on melioidosis, it is stated that intravenous dose of ceftazidime should be given for at least 2 weeks, however in the 2020 update of the guideline, the minimum duration is changed to 3 weeks. In sites and condition such as the CNS and the presence of organ abscess where drugs are difficult to penetrate, co-trimoxazole may enhance in tissue penetration (5).

Previous eradication phase antibiotics include chloramphenicol, co-trimoxazole and doxycycline. However through re – evaluation, there has been a high toxicity rate caused by chloramphenicol and thus removing it from the regiment (4).

Prior to culture results, the patient was treated with metronidazole and vancomycin in attempt to treat the patient empirically. The treatments were then shifted to ceftazidime and co-trimoxazole as soon as culture reveals B. pseudomallei. Intravenous ceftazidime was instructed to be given for four weeks along with oral co-trimoxazole. Administration of ceftazidime in this case mainly follows the 2020 revision of the Darwin guidelines and the susceptibility of B. pseudomallei found in the culture. Following the intensive phase of the treatment, oral co-trimoxazole is continued with the addition of oral doxycycline. Two weeks in the intensive phase during follow up, the patient improves and has been well.

CONCLUSION

Neuromelioidosis is a rare manifestation of melioidosis and is currently only diagnosable through culture examination. Treatment regiment in this case have been proven to be consistent along with prior reported cases and does not show any new pattern of antibiotic resistance. However more future case reports of neuromelioidosis are needed in order to increase the awareness of presence and possible diagnosis of the entity, also enhancing the variability and the depth of current guidelines for melioidosis. Prognosis of untreated neuromelioidosis may potentially be fatal.

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