Neurological melioidosis (*Burkholderia pseudomallei*) in a chronic psychotic patient treated with antipsychotics

A case report

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Abstract

**Rationale:** Neurological melioidosis, an extremely rare condition, is caused by the gram-negative bacterium *Burkholderia pseudomallei*. If treatment is suboptimal or delayed, this infection can produce diverse clinical symptoms and result in death.

**Patient concerns:** A healthy 65-year-old female who had been treated with antipsychotic medication for neurotic depression for over 2 years presented with acute-onset fever, headache, lead-pipe rigidity of all limbs, and delirium.

**Diagnoses:** Melioidosis meningitis was diagnosed by performing blood examinations and cerebrospinal fluid analysis and cultures.

**Interventions:** Intravenous ceftazidime (2 g/8 h for 3 weeks) was administered in-hospital and 240 mg trimethoprim/1200 mg sulfamethoxazole and 100 mg minocycline twice daily administered out-hospital.

**Outcomes:** The patient fully recovered after antibiotic therapy without cognitive deficits and associated neurological complications.

**Lessons:** Because melioidosis is endemic in Southern Taiwan and the use of antipsychotics might mask the symptoms, physicians dealing with patients from endemic areas with a medical history of antipsychotics should always consider the possibility of neurological melioidosis and provide prompt empirical management to suspicious cases.

**Abbreviations:** CNS = central nervous system, CSF = cerebrospinal fluid, EPS = extrapyramidal symptoms, GCS = Glasgow Coma Scale, NMS = neuroleptic malignant syndrome.

**Keywords:** *Burkholderia pseudomallei*, neuroleptic malignant syndrome, neurological melioidosis

1. Introduction

Melioidosis, a clinically infectious disease caused by the gram-negative bacterium *Burkholderia pseudomallei*, is endemic in Southeast Asia and Northern Australia.\(^{[1]}\) Because of the early onset of fulminant sepsis, it is associated with a high mortality rate (20–43%\(^{[1,2]}\)),\(^{[1,2]}\) suggesting the crucial need for early diagnosis with appropriate antibiotic therapy. Although commonly presenting as a lung infection or multiple abscesses in internal organs, melioidosis is considered a great mimicker owing to its ability to affect any organ in the body.\(^{[1]}\) Herein, we report the case of a 65-year-old homemaker receiving neuroleptic medication whose symptoms resembled those of neuroleptic malignant syndrome (NMS), another life-threatening disease that is characterized by an altered state of consciousness, high fever, generalized rigidity, and dysautonomia following the use of neuroleptics. In addition, we highlight the diagnostic challenge posed by neurological melioidosis in psychotic patients.

2. Case report

A 65-year-old homemaker from Fengshan, Kaohsiung, Southern Taiwan, had been treated for over 2 years with 50 mg sulpiride and 0.5 mg alprazolam twice daily and 150 mg trazodone nightly for anorexia and depressive disorder. She had never traveled abroad and had no contact with contaminated water or soil in the 3 months before admission. Five days before admission, she developed a poor appetite, general weakness, and confusion. During evaluation in the emergency department, she reported acute-onset fever, headache, delirium, and lead-pipe rigidity of all limbs. Notably, no recent trauma, neck stiffness, diaphoresis, cough or shortness of breath, hearing loss, blurred vision, or fresh rashes were observed.

On examination, the following results were noted: body temperature, 40.5°C; blood pressure, 138/88 mm Hg; pulse, 143 beats/min; respiratory rate, 20 breaths/min; and blood oxygen saturation, 100% with the patient breathing ambient air. She was confused and disoriented, scored E3V4M5 on the Glasgow Coma Scale, and neither Kernig nor Brudzinski signs were present. Her complete blood count showed leukocytosis, and increased levels of C-reactive protein, serum aspartate transami-
neutrophils, lymphocytes, monocytes, eosinophils, basophils, and platelet count. The differential count showed a predominance of neutrophils with a normal range of 40–75%. Hemoglobin level was 11.5 g/dL. The patient presented with symptoms of an altered level of consciousness, high fever, muscle rigidity, and dysautonomia, mimicking the features of NMS. The CSF examination revealed a high protein level and a low glucose level. The CSF sample demonstrated pleocytosis with neutrophil predominance, consistent with meningitis. A CSF sample was collected for microbiological examination. B. pseudomallei was isolated from the culture of the CSF sample. In view of the clinical presentation and positive culture of B. pseudomallei, intravenous co-trimoxazole and minocycline were administered. The patient responded well to the treatment, and the symptoms resolved. In-hospital treatment was followed by outpatient treatment.

3. Discussion

Several risk factors have been established as associated with melioidosis, including diabetes, chronic kidney disease, malignancy, and alcohol consumption. Occasionally, in our patient who denied any prior systemic diseases, the risk factors may be absent. Although melioidosis can affect any organ in the body, the 2 most common clinical manifestations are pneumonia and bacteremia. Here, we reported the case of a patient with neurological melioidosis, which is relatively rare in the literature. According to the Darwin study, the incidence of CNS involvement in melioidosis is 3%. Previous studies have reported that approximately 1.5% to 2% of the patients with melioidosis in Southeast Asia exhibit neurological involvement. In another study in Taiwan, male predominance was noted (male:female = 4:1), and CNS involvement was identified in 1.7% of melioidosis cases.

Our patient presented with the symptoms of an altered level of consciousness, high fever, muscle rigidity, and dysautonomia, mimicking the features of NMS. However, these conditions could also present in many other clinical situations, including thyrotoxicosis or CNS infection. Although NMS is most often associated with first-generation antipsychotics such as haloperidol or fluphenazine, cases involving low-potency and second-generation antipsychotic drugs have also been reported. NMS is most often diagnosed in young adult males in the majority of studies, and note, age and sex are not risk factors of NMS. While NMS is mostly diagnosed in young adult males in the majority of studies, it is related to the population distribution of the exposure to neuroleptic agents. Although the possibility of developing NMS 30 days after the initiation of neuroleptic medication is less likely, it was observed in 4% cases by Caroff and Mann. Our patient was medicated with sulpiride, a low-potency antipsychotic drug, for over 2 years. She had not previously presented with any NMS symptoms, and NMS was unlikely based on the time course of her medical history. Moreover, a series of examinations resulted in the diagnosis of acute bacterial meningitis upon the positive culture of B pseudomallei from CSF.
Table 2
Serum and cerebrospinal fluid analysis performed on the patient.

| Blood analysis | Reference range | Test results |
|----------------|-----------------|--------------|
| Vitamin B12, pg/mL | 180–914 | 463 |
| Folic acid, ng/mL | >4 | 6.13 |
| HBsAg (S/C0) | Nonreactive (<0.05) | Nonreactive (0.00) |
| anti-HEV Ab (S/C0) | Nonreactive (<1.00) | Nonreactive (0.04) |
| Free T4, ng/dL | 0.7–1.48 | 0.79 |
| TSH, µU/mL | 0.35–4.94 | 0.3077 |
| RF, IU/mL | <11 | <11 |
| ANA | <1:20 | <1:20 |
| Anti-HIV test (S/CO) | Nonreactive (<1.00) | Nonreactive (0.09) |
| RPR/VDRL test | Reactive (1:16) | |
| TPPA/TPHA | Reactive (1:40) | |
| Vitamin B12, pg/mL | 180–914 | 463 |
| Red cell count, /µL | 5–45 | 140 |
| White cell count, /µL | 0–5 | 1248 |
| Hemoglobin, g/dL | >12 | 14.2 |
| Hematocrit, % | 25–45 | 38.6 |
| Platelet count, /µL | 150–400 | 264 |
| Differential count (%) | | |
| Neutrophils | 60 | |
| Lymphocytes | 40 | |

CSF analysis

| Reference range | Test results |
|-----------------|--------------|
| Glucose-CSF, mg/dL | 50–75 | 12 |
| Total protein-CSF, mg/dL | 15–45 | 60 |
| White cell count, /µL | 0–5 | 1248 |
| Red cell count, /µL | 5–45 | 45 |
| Differential count (%) | | |
| Neutrophils | 60 | |
| Lymphocytes | 40 | |

On the basis of a Dutch study, 95% of patients with meningitis displayed at least 2 of the following 4 symptoms: fever, headache, neck stiffness, and altered mental status. In the Darwin Prospective Melioidosis Study, headache was prominent on admission in the majority of cases. Furthermore, of the patients who developed neurological complications, approximately 50% demonstrated some evidence of neck stiffness. Our patient presented with an altered level of consciousness, high fever, and headache, which are 3 of the 4 characteristic symptoms of bacterial meningitis. However, she also presented with generalized muscle rigidity, a rarity in neurological melioidosis. Muscle rigidity is a characteristic sign of extrapyramidal symptoms (EPS), which are drug-induced disorders caused by a dopamine blockade or depletion in the basal ganglia, frequently resulting from antipsychotic usage. In patients with long-term antipsychotic treatment, EPS might mislead or affect the physicians’ clinical ability to identify neck rigidity as a potential harbinger of meningitis. In addition, to the best of our knowledge, to date, there has only been 1 reported case of EPS following melioidosis in a patient who was not using antipsychotics, with the conclusion that the pathophysiological mechanism appeared to be secondary to the immunological response rather than as the result of direct CNS infiltration. Therefore, meningitis should not be dismissed in patients with fever of an unknown origin and undergoing long-term antipsychotic treatment because they may not present with the cardinal features of bacterial meningitis. This case highlights the diagnostic challenge posed by melioidosis in patients treated with antipsychotics because it is a great mimic of other diseases, manifesting as miscellaneous clinical symptoms and causing a potentially fatal outcome. From 2000 to 2005, the mortality rates regionally varied, with 22%, 33% to 65%, 9.5%, and 14% in Southern Taiwan, the Southeast Asia region, India, and Northern Australia, respectively. Furthermore, 16% to 19% of patients with inappropriate empirical therapy died before the confirmatory diagnosis of melioidosis, Melioidosis is endemic to Southern Taiwan, and antipsychotic use might mask its symptoms. Therefore, physicians dealing with patients from an endemic area with a medical history of antipsychotics should always consider the possibility of neurological melioidosis and provide suspicious cases with prompt empirical management.

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