Clinical Case Report

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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] 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.[3] 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-

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Table 1

General laboratory investigations performed on the patient.

Laboratory test	Reference range	Test results during hospitalization				
		Day 1	Day 2	Day 3	Day 6	Day 9
White cell count, $10^3/\mu L$	4–11	14.23	-	-	10.72	11.08
Hemoglobin, g/dL	11.5–15.5	16.4	-	-	13.1	12.3
Platelet count, $10^3/\mu L$	150–400	204	-	-	160	166
Differential count (%)						
Neutrophils	40–75	50.8	-	-	-	-
Lymphocytes	20–45	37.9	-	-	-	-
Monocytes	2–10	10.9	-	-	-	-
Eosinophils	1–6	0	-	-	-	-
Basophils	<1	0.4	-	-	-	-
Prothrombin time, s	8–12	11.1	-	-	-	-
INR		1.12	-	-	-	-
APTT, s	23.9–35.5	34.3	-	-	-	-
Urea nitrogen, mg/dL	7–25	39	-	35	-	-
Creatinine, mg/dL	0.6–1.2	1.4	-	0.8	-	-
Glucose, mg/dL	70–105	136	-	-	-	-
Sodium, mmol/L	136–145	135	-	-	134	137
Potassium, mmol/L	3.5–5.1	4	-	-	5.1	4.7
Calcium, mg/dL	8.6–10.3	-	8.9	-	-	-
Phosphorus, mg/dL	2.5–5.0	-	5.4	-	-	-
AST, U/L	13–39	99	-	34	-	-
ALT, U/L	7–52	69	-	38	-	-
Total bilirubin, mg/dL	0.3–1.0	-	0.42	-	-	-
Alkaline phosphatase, U/L	34–104	-	46	-	-	-
Albumin, g/dL	3.5–5.7	-	3.4	-	-	-
Total protein, g/dL	6.4–8.9	-	6	-	-	-
Procalcitonin, mg/dL	<0.5	0.55	-	-	-	-
C-reactive protein, mg/dL	<1.0	2.75	-	-	-	-
CPK, U/L	30–223	531	-	127	-	-
CK-MB, U/L	0–20	19	-	11	-	-
Troponin I, ng/mL	<0.01	0.13	-	<0.01	-	-

ALT = alanine aminotransferase, APTT = activated partial thromboplastin time, AST = aspartate aminotransferase, CK-MB = creatine kinase-muscle/brain, CPK = creatine phosphokinase, INR = international normalized ratio.

nase, alanine transaminase, and creatine phosphokinase were noted. The complete blood, serum, and cerebrospinal fluid (CSF) laboratory results are presented in Tables 1 and 2.

Because the laboratory results raised concerns of NMS or a central nervous system (CNS) infection, sulpiride, alprazolam, and trazodone were discontinued due to clinically suspicious NMS. Contrast magnetic resonance imaging of the brain revealed abnormalities consistent with those of diffuse meningitis. A CSF sample demonstrated pleocytosis with neutrophil predominance, a high protein level, and a low glucose level (Table 2). The CSF culture yielded *B pseudomallei*. Accordingly, intravenous ceftazidime (2 g/8 h for 3 weeks) was administered, which resolved the symptoms. In-hospital treatment was followed by co-trimoxazole and minocycline outpatient treatment.

3. Discussion

Several risk factors have been established as associated with melioidosis, including diabetes, chronic kidney disease, malignancy, and alcohol consumption.[4] Occasionally, as in our patient who denied any prior systemic diseases, the risk factors may be absent.[3] Although melioidosis can affect any organ in the body, the 2 most common clinical manifestations are pneumonia and bacteremia.[5] 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%.[3] Previous studies have reported that approximately 1.5% to 2% of the patients with melioidosis in Southeast Asia exhibit neurological involvement.[6,7] In another study in Taiwan, male predominance was noted (male:female = 4:1), and CNS involvement was identified in 1.7% of melioidosis cases.[1]

Our patient presented with the symptoms of an altered level of consciousness, high fever, muscle rigidity, and dysautonomia, which mimicked 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.[8,9] Of 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.[10] 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.[11] 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/CO)	Nonreactive (<0.05)	Nonreactive (0.00)
anti-HCV Ab (S/CO)	Nonreactive (<1.00)	Nonreactive (0.04)
Free T4, ng/dL	0.7–1.48	0.79
TSH, μIU/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		Negative (<1:80)
CSF analysis	**Reference range**	**Test results**
Glucose-CSF, mg/dL	50–75	12
Total protein-CSF, mg/dL	15– 45	140
White cell count, /μL	0–5	1248
Red cell count, /μL		45
Differential count (%)		
Neutrophils		60
Lymphocytes		40

Ab = antibody, ANA = antinuclear antibody, CSF = cerebrospinal fluid, HBsAg = hepatitis B surface antigen, HCV = hepatitis C virus, HIV = human immunodeficiency virus, RF = rheumatoid factor, S/CO = signal to cut-off ratio RPR/VDRL = rapid plasma reagin/Venereal Disease Research Laboratory, T4 = free thyroxine, TPPA/TPHA = *Treponema pallidum* particle agglutination assay/*Treponema pallidum* hemagglutination assay, TSH = thyroid-stimulating hormone.

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.[12] 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.[13] 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.[14] 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.[15] 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.[16] 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 mimicker 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.[1,2] 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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Author contributions

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