Melioidosis as a Rare Cause of Deep Surgical Site Infection in a Filipino Patient with Metastatic Spinal Disease: A Case Report

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Abstract

Background: Melioidosis is a potentially fatal disease caused by *Burkholderia pseudomallei*. Over a century after its discovery, there seems to be a paucity of reported cases in the Philippines relative to other countries where it is found to be endemic. This suggests that the true burden of melioidosis in the country is not well-defined. The rarity of the disease, its protean clinical manifestations, and the lack of pathognomonic features pose a great diagnostic challenge. Furthermore, the proper recognition of the organism is an extreme necessity as it is intrinsically resistant to numerous antibiotics and requires specific long-term treatment.

Case: This is a case of a 49-year-old Filipino diagnosed with a metastatic spinal disease from a primary thyroid carcinoma and underwent posterior spinal decompression and stabilization. Revision of instrumentation was done following identification of an implant loosening. During the interim, wound dehiscence and infection developed. The patient was readmitted and underwent debridement of the lumbosacral spine. Wound cultures all yielded growth of *Burkholderia pseudomallei*. The patient received meropenem and then trimethoprim-sulfamethoxazole with ciprofloxacin during the intensive and eradication phase, respectively. Erythrocyte sedimentation rate and C-reactive protein were monitored and a significant reduction in both values reflected a good therapeutic response.

Conclusion: This is a rare case of a deep surgical site infection caused by *Burkholderia pseudomallei*. It is known that melioidosis is a potentially fatal infection but is under-reported in the Philippines. At present, further epidemiological studies along with an increased level of awareness of melioidosis are greatly needed to help define the true burden of illness and optimize patient management following prompt recognition.

Keywords: melioidosis, Philippines, *Burkholderia pseudomallei*

Introduction

Burkholderia pseudomallei is a gram-negative, rod-shaped saprophytic bacterium that resides in soil and water environments of tropical and subtropical regions of the world. When introduced into the human host, typically via a dermal wound or inhalation, *B. pseudomallei* can result in a fatal disease called melioidosis, or Whitmore's disease.[1] It is geographically endemic in Southeast Asia and northern Australia, with occasional cases in countries such as India and China.[2] Melioidosis was first described in 1910 by Captain A. Whitmore and C. S. Krishnaswami in Myanmar and since then, cases have been identified and described in different Southeast Asian countries.[3]

Unlike its Southeast Asian neighbors, there was little progress apropos of the epidemiology of melioidosis in the Philippines. The first documented case occurred in 1948 in a 25-year-old American soldier who presented with weight loss and symptoms of pneumonia.[4] Subsequently, sporadic reports were identified in the literature describing melioidosis diagnosed in travelers

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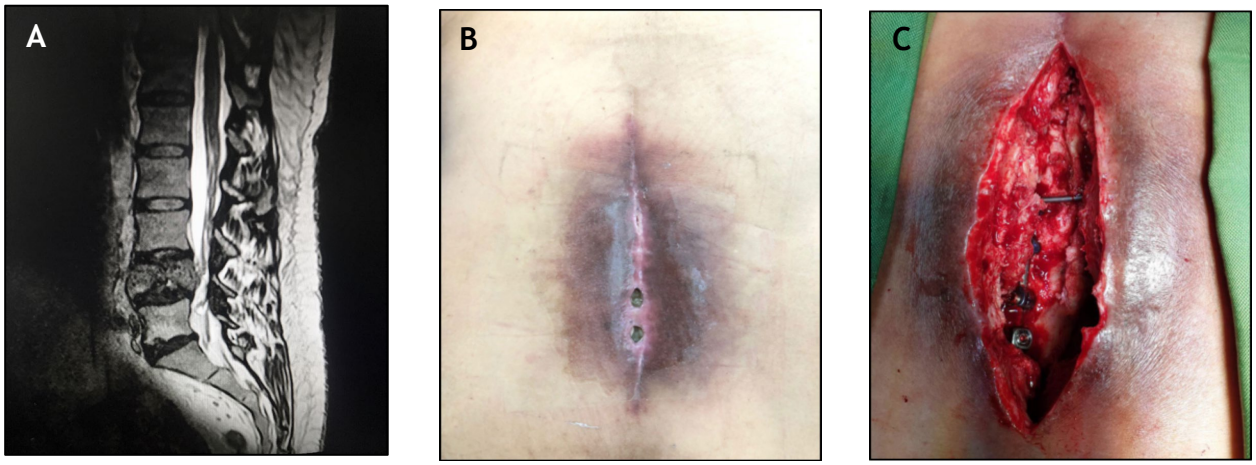

Figure 1. Magnetic resonance imaging of the lumbar spine showing a mass-like lesion within the L4 vertebral body [pointed by an arrow] (A); image of the infected wound on admission (B); intraoperative image of debridement and wound exploration (C)

but indigenous cases among Filipinos have been very rarely documented. San Martin et al collated all Philippine cases of melioidosis published internationally and locally, as well as unpublished case series and reports from different tertiary hospitals in the Philippines.[5] There were 25 papers and 41 cases identified. In the cases identified in the Philippines, only four were found to have cancer as a risk factor and none had metastatic spinal disease.

The report by San Martin et al indeed highlighted the fact that melioidosis is probably more common in the Philippines but is likely to be grossly under-reported.[5] Our case is a 49-year-old Filipino who was diagnosed with metastatic spinal disease and presented with a deep surgical site infection unexpectedly yielding growth of *Burkholderia pseudomallei*.

Case

This is a case of a 49-year-old female, Filipino, grade school teacher from Lapu-Lapu City, Cebu who presented with fever and purulent discharges over the post-operative site at the lumbosacral area. The patient was non-hypertensive, non-diabetic, and non-asthmatic.

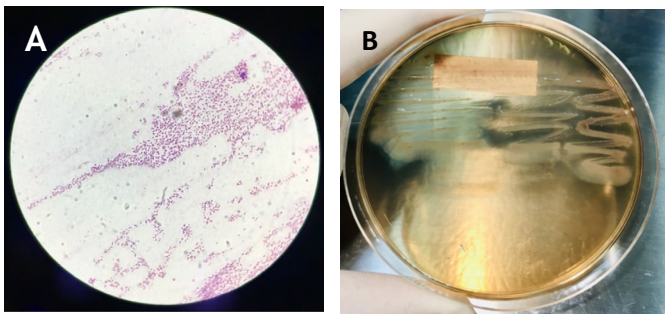

Figure 2. *Burkholderia pseudomallei* appearing as gram-negative rods on gram stain (A) and as smooth, pink to colorless colonies after 48 hours on MacConkey (MAC) agar (B)

She was a non-smoker, non-alcoholic drinker, and denies illicit drug use. Obstetric and gynecologic history was unremarkable. Heredofamilial diseases included hypertension and diabetes mellitus.

She was previously diagnosed with follicular adenoma and papillary microcarcinoma of the thyroid last 2011 and underwent a total thyroidectomy. She was maintained on thyroid hormone supplementation. Five years after the procedure, the patient complained of a sudden onset of lumbosacral pain associated with bilateral lower extremity numbness. The patient sought consult and magnetic resonance imaging of the lumbar spine showed a mass-like lesion within the L4 vertebral body suggestive of a malignant etiology (*Figure 1*). CT-scan guided percutaneous fine needle biopsy was performed and the histopathologic report was suggestive of metastatic follicular carcinoma. The patient was referred to an orthopedic surgeon and proceeded with posterior decompression of L4 and posterior stabilization of L2-S1. The patient was subsequently discharged with improved condition.

The patient then sought consult with a radiation oncologist and began receiving radiation therapy. Three years after the orthopedic procedure, the patient had persistent severe pain in the lumbosacral area. Aseptic implant loosening was entertained and removal of L5-S1 pedicle screws was done along with a revision of instrumentation and bilateral pelvic fixation. There were no complications observed thus the patient was discharged. The patient was advised home rest but had soil exposure from frequent gardening.

Two months after the instrumentation revision, wound dehiscence was noted which gradually increased in size. Two weeks later, purulent discharges were noted oozing out from the post-operative site. The condition was tolerated until four days prior to admission when undocumented fever was noted. Immediate consult was sought and the patient was advised of urgent admission.

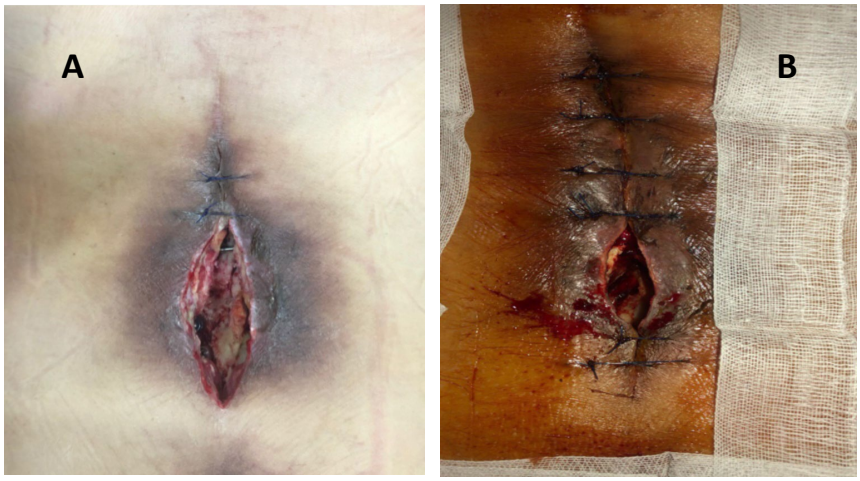

Figure 3. Repeat debridement and change of VAC dressing 5 days after the surgery (A) and 12 days after the surgery (B)

On admission, the patient was afebrile with stable vital signs. A 2-centimeter elongated dehisced wound with purulent discharge was noted on the post-operative site at the lumbosacral area (*Figure 1*). There were no motor and sensory deficits. Initial workup showed normal CBC but with significantly high erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). Surgical site infection was entertained and the patient was empirically started on piperacillin-tazobactam. Consequently, debridement and wound exploration of the lumbosacral spine with an application of vacuum-assisted closure (VAC) dressing (*Figure 1*) were done.

Necrotic tissues were identified with purulent material draining at the level of L4, and L5. Samples were collected and were sent for gram stain, culture, and sensitivity which yielded growth of *Burkholderia pseudomallei* (*Figure 2*). There are no definitive therapeutic guidelines concerning the sensitivity of this organism as per the Clinical and Laboratory Standards Institute (CLSI) but potential active agents included ceftazidime, carbapenems, trimethoprim-sulfamethoxazole, and doxycycline among others. Piperacillin-tazobactam was shifted to meropenem which was given for 2 weeks. Repeat debridement and reapplication of VAC dressing at the lumbosacral area were done on the fifth and twelfth days (*Figure 3*) after the procedure. The patient responded well clinically and was sent home with trimethoprim-sulfamethoxazole and ciprofloxacin. Evaluation of the post-operative site was done two weeks after discharge which showed a dry, well-coaptated wound with no discharges or areas of surrounding erythema. ESR and CRP were repeated on the second and fourth weeks of treatment. In both instances, a reduction in values was noted as indicative of a good therapeutic response.

Discussion

The genus *Burkholderia* is currently composed of several species, but only three are notable pathogens for humans or animals: the *B. cepacia* complex, *B. pseudomallei* (the agent of melioidosis), and *B. mallei* (the agent of equine glanders).[6] Melioidosis is a disease of humans and animals with immense clinical diversity. It is a life-threatening infectious disease of both the tropics and subtropics with high case fatality rates reaching 40% even if drugs of choice are provided and up to 80% if an inappropriate diagnosis is made.[7]

Melioidosis has been called the "Great Imitator" because it does not display any pathognomonic clinical features.[8] It has a wide array of signs and symptoms that can easily be mistaken for diseases such as tuberculosis, pneumonia, or soft tissue abscesses. There are diverse types of melioidosis, each with its own set of symptoms. The Infectious Disease Association of Thailand has summarized 345 cases in 4 categories: multifocal infection with septicemia; localized infection with septicemia; localized infection; and transient bacteremia.[9] The localized form generally presents as an ulcer or skin abscess that may result from inoculation through a break in the skin and cause fever and general muscle aches. The infection may remain localized or may progress rapidly through the bloodstream.[6] Our patient initially presented with wound dehiscence with purulent discharges suggesting a localized infection.

Although the first case of melioidosis was described more than a century ago, the disease is likely to be underreported in many parts of the world including the Philippines. San Martin et al collated all cases of melioidosis in the Philippines which were published internationally and locally.[5] They also included unpublished case series and reports from different tertiary hospitals in the Philippines. There were 41 human cases (*Figure 4I*) of culture-confirmed melioidosis in the Philippines; 18 of which involved foreign travelers and 23 were indigenous cases. Among the indigenous cases, 20 were from four different unpublished reports. The preponderance of reported cases among foreign travelers along with the paucity of indigenous cases suggests that the disease is being underreported in the country.[5]

From the collated data conducted by San Martin et al, the most common co-morbidity identified in melioidosis was diabetes mellitus followed by heart disease and cancer (*Table 1*).[5] Similarly, in other literature, diabetes is consistently the most important risk factor followed by hazardous alcohol use, chronic renal disease, and chronic lung disease.[6,10-12] In recent years, however, malignancy and immunosuppression, particularly cancer chemotherapy and dexamethasone use with

Table I. Summary of the clinical characteristics of the culture-confirmed cases of melioidosis in the Philippines[5]

Clinical Characteristic	Number of cases
Mean Age	50.2
Sex	
Male	35(85.54%)
Female	5(14.6%)
Comorbidities	
Diabetes Mellitus	24(58.5%)
Heart Disease	11(26.82%)
Cancer	4(9.76%)
Pulmonary TB	2(4.9%)
Kidney Disease	1(2.4%)
Drowning	1(2.4%)
Alcoholism	1(2.4%)
Dyslipidemia	1(2.4%)
Osteoarthritis	1(2.4%)
Organs involved	
Pulmonary	22(53.7%)
Soft tissue	12(29.3%)
Hepatic	5(12.2%)
Neurologic	4(9.76%)
Splenic	2(4.9%)
Mycotic Aneurysm	2(4.9%)
Osteomyelitis	1(2.4%)

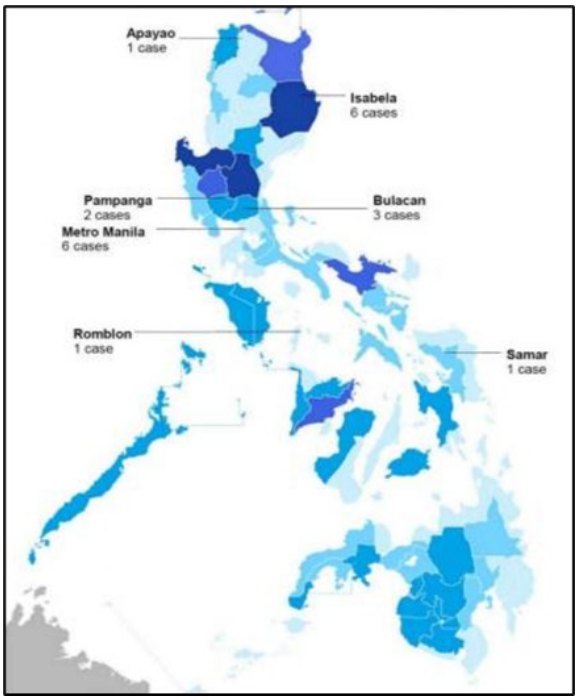

Figure 4. Geographical Distribution of Melioidosis cases in the Philippines.[5]

radiotherapy were also identified as important risk factors.[13] To the author's knowledge, this is the first known case of melioidosis with the identified risk factors being metastatic spinal disease and a history of radiotherapy. Moreover, the leading clinical diseases depicted in the study were pneumonia and soft tissue infections; which were also consistent in other literature.[14] Since melioidosis may be difficult to differentiate clinically from other respiratory tract infections, there may be a possibility that many cases treated as simple pneumonia may be pulmonary melioidosis.[5] Notably, from the figure shown (*Figure 4*), there seems to be no published case of melioidosis in Cebu, the province where the index case is residing.

Burkholderia pseudomallei is a small, gram-negative, oxidase-positive, motile, aerobic bacillus with occasional polar flagella. On gram staining, a bipolar "safety pin" pattern is seen. The organism is easily grown in a standard culture medium but may be misidentified as *B. cepacia, P. stutzeri,* or other *Pseudomonas* species.[6] Thus, any oxidase-positive, indole-negative, gram-negative rod that does not morphologically resemble *Pseudomonas aeruginosa* should be suspected as *B. pseudomallei*. Other key features include growth on MacConkey agar, no hemolysis on blood agar, susceptibility to amoxicillin-clavulanic acid, and resistance to colistin or polymyxin B.[15] The organism is present in soil and surface water in endemic regions. Humans and animals are infected by percutaneous inoculation, inhalation, or ingestion.[6] Because of its protean manifestations, the diagnosis of melioidosis heavily relies on the identification of *B. pseudomallei* in the laboratory. The diagnosis of our index case was established via growth in conventional culture and identified by *VITEK 2*™.

B. pseudomallei is intrinsically resistant to penicillin, ampicillin, first- and second-generation cephalosporins, gentamicin, tobramycin, and streptomycin.[6] There are no standardized interpretative guidelines for the susceptibility testing of *B. pseudomallei* but the main therapeutic options include ceftazidime, carbapenems, trimethoprim-sulfamethoxazole, and doxycycline.[16] Following the identified growth of *B. pseudomallei* in three different wound discharge specimens, the antibiotic regimen for this patient was shifted to meropenem. Several studies confirm that the carbapenems imipenem and meropenem have the lowest minimum inhibitory concentrations against *B. pseudomallei*. Smith et al conducted *in vitro* time-kill studies to measure the rate of bacterial killing and have shown that ceftazidime was outperformed by carbapenems in the treatment of *B. pseudomallei*.[17,18] Observational data from Australia have suggested that meropenem produces better outcomes in severe melioidosis than ceftazidime, which has led to the recommendation that meropenem is the drug of choice for melioidosis.[19]

Melioidosis has a prolonged course of illness and proves to be difficult to eradicate hence requires an extensive course of antimicrobial treatment. This typically consists of 10 to 14 days of intensive phase with IV antibiotics to prevent mortality from severe illness followed by an eradication phase with oral antibiotics for 3 to 6 months to prevent relapse.[20] Monitoring treatment compliance is crucial as it has been proposed that adherence may be the most important factor in determining recurrence.

Recurrent melioidosis occurs in 5% to 25% of cases and has a high mortality rate of 25%.[21]

The challenge in the Philippines is to promote awareness of melioidosis among physicians and laboratory staff. There is reason to believe that despite being an agricultural country, there is an underestimation of the actual cases of melioidosis in the Philippines. Some rural provinces post an additional challenge since even access to basic healthcare is another pressing issue. San Martin et al accentuated the fact that although the most common presentation of *B. pseudomallei* infection is pneumonia, the local guidelines in the Philippines do not even mention melioidosis as a differential diagnosis for community-acquired pneumonia.[5]

Conclusion and Recommendations

This reports a case of melioidosis as a rare cause of deep surgical site infection in a patient with metastatic cancer who underwent spine surgery. It is known that melioidosis is a potentially fatal emerging infection with a myriad of clinical presentations but is likely under-reported in the Philippines. Education principally highlighting the recognition and treatment of this disease should be emphasized. Capacity building in medical laboratories particularly in the rural areas where melioidosis is most likely to have the highest incidence is still a daunting task but should be highly advocated. At present, further epidemiological studies along with an increased level of awareness of melioidosis are greatly needed to help define the true burden of illness and optimize patient management following prompt recognition.

Informed Consent. Written informed consent was obtained from the patient to report her case. All patient identifiers were removed from the manuscript.

Conflict of Interest. The author declares no conflict of interest that may interfere with the review or publication of this case.

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