Melioidosis in a returned traveller

Zain Chagla MD FRCPC¹, Natasha Aleksova MD², Jaclyn Quirt MD², Joel Emery MD²,
Christian Kraeker MD FRCPC², Shariq Haider MD FRCPC^{1,2}

Z Chagla, N Aleksova, J Quirt, J Emery, C Kraeker, S Haider. Melioidosis in a returned traveller. *Can J Infect Dis Med Microbiol* 2014;25(4):225-226.

Melioidosis is an infection endemic to Southeast Asia and Northern Australia, and is associated with significant morbidity and mortality. The present report describes a case of chronic melioidosis in a returning traveller from the Philippines. Clinical suspicion of this illness was warranted in individuals with a history of travel to endemic regions. Safety in handling clinical specimens is paramount because laboratory transmission has been described.

Key Words: Laboratory safety; Melioidosis; Travel medicine; Tropical medicine

CASE PRESENTATION

A 64-year-old man presented to the emergency room with fever and acute ankle pain. His medical history was significant for warm autoimmune hemolytic anemia, Sjogren's syndrome, type II diabetes, chronic kidney disease, bacterial pneumonia, previously treated schistosomiasis and Stevens-Johnson syndrome following administration of amoxicillin. He had also been evaluated for a previous active tuberculosis contact but had negative skin testing at the time. His medications included prednisone, hydroxychloroquine, diamicon, metformin, atorvastatin and esomeprazole.

The patient was a Canadian resident who had emigrated from the Philippines several years ago. Approximately one year before his inpatient presentation, he returned from a six-month trip to the Philippines. While abroad he spent time working on his family's farm and recalled abrasions on his bare feet. Within weeks of returning to Canada, the patient experienced eight months of recurrent nocturnal fevers responsive to acetaminophen before his presentation to the authors' inpatient unit. Blood, urine and stool cultures along with a stool ova and parasite examination were negative. Computed tomography revealed multiple microabscesses in the spleen. A two-week course of levofloxacin and metronidazole had no effect on his symptoms.

The patient presented to the emergency department after experiencing four days of acute nontraumatic left ankle pain with decreased mobility; he also continued to experience ongoing fevers. He was admitted to the general medicine unit for further investigation. On initial examination, his temperature was 38.5°C, heart rate was 139 beats/min and blood pressure was 114/67 mmHg. The pain was localized over the left lateral malleolus, with no associated radiation, warmth, effusion or redness. Splenomegaly was noted on abdominal examination, but there were no other palpable lymph nodes. An x-ray of his ankle showed no evidence of fracture. Investigations included a leukocyte count of 7.5×10^9 cells/L, sodium level of 123 mmol/L and C-reactive protein level of 159 mg/L. A chest radiograph showed atelectasis in the left lower lung zone, which was unchanged from previous images. A transthoracic echocardiogram showed no valvular vegetations suggestive

La mélioïdose chez un voyageur de retour au pays

La mélioïdose est une infection endémique en Asie du Sud-Est et en Australie occidentale. Elle s'associe à une morbidité et une mortalité importantes. Le présent rapport expose un cas de mélioïdose chronique chez un voyageur de retour des Philippines. La suspicion clinique de cette maladie s'impose chez les personnes qui ont voyagé dans des régions endémiques. Il est essentiel de respecter les règles de sécurité lors de la manipulation des échantillons cliniques, car des cas de transmission en laboratoire ont été signalés.

of infective endocarditis. A malaria screen and *Brucella* serology were negative. Three sets of blood cultures were obtained.

Three sets of blood cultures returned positive for a Gram-negative bacilli. Although this isolate was a non-glucose fermenter and oxidase positive, it did not have the typical appearance of *Pseudomonas* species. The isolate was identified as *Burkholderia pseudomallei* using the VITEK 2 system (bioMérieux, France). Molecular testing, including 16S ribosomal RNA polymerase chain reaction (PCR), open reading frame 13 (specific for *B. pseudomallei* and *Burkholderia mallei*) and specific primers for *B. pseudomallei*, were positive, with a negative PCR for a *B. mallei*-specific primer. A joint aspirate was performed on admission; however, no organisms grew in bacterial culture.

A decision was made to initiate the patient on a prolonged course of doxycycline and trimethoprim-sulfamethoxazole for three months. Given the history of Stevens-Johnson syndrome secondary to administration of amoxicillin, he did not receive intensive-phase treatment with a carbapenem or ceftazidime. His blood cultures subsequent to the diagnosis remained negative. The patient completed the duration of treatment, and his ankle pain and fevers were resolved at subsequent follow-up visits.

DISCUSSION

Melioidosis is a bacterial infection caused by the Gram-negative *B. pseudomallei*. Endemic areas of disease include Thailand and Northern Australia; however, a significant number of cases have been reported in Southeast Asian countries such as Malaysia, Singapore, Vietnam, Indonesia, China, Taiwan, Brunei, Vietnam, Laos, Cambodia and the Philippines (1). Travel-associated disease has been documented, with the most recent case published in Canada occurring in a Cambodian refugee in 1984 (2). The organism *B. pseudomallei* is a soil saprophyte and is acquired through direct inoculation, particularly by individuals working in rice paddies, where high levels may be observed in the soil (3). Inhalation and ingestion are other major routes of infection (4), and laboratory-acquired cases have also been demonstrated. The incubation period for *B. pseudomallei* ranges from one to 21 days, with a mean of approximately nine days (1).

¹Department of Infectious Diseases; ²Department of Medicine, McMaster University, Hamilton, Ontario

Correspondence: Dr Zain Chagla, Department of Infectious Diseases, McMaster University, 300-25 Charlton Avenue East, Hamilton, Ontario L8N 1Y2. Telephone 905-522-1155 ext 33998, fax 905-523-7352, e-mail zain.chagla@medportal.ca

This open-access article is distributed under the terms of the Creative Commons Attribution Non-Commercial License (CC BY-NC) (<http://creativecommons.org/licenses/by-nc/4.0/>), which permits reuse, distribution and reproduction of the article, provided that the original work is properly cited and the reuse is restricted to noncommercial purposes. For commercial reuse, contact support@pulsus.com

On infection, the organism assumes a predominantly intracellular location within phagocytes and macrophages. A number of virulence factors, such as quorum sensing, type III and VI secretion systems, and lipopolysaccharide, have been implicated in bacterial survival and disease pathogenesis (1). However, host risk factors, particularly those with impaired neutrophil function, appear to correlate more with the development of disease. At-risk individuals include those with diabetes, alcohol abuse, chronic kidney disease, chronic lung disease, rheumatic heart disease, congestive heart failure, malignancy, immunosuppression and chronic kava use (5). The peak incidence is seen among individuals 40 to 60 years of age. In the present case, the presence of diabetes, chronic kidney disease and corticosteroid use predisposed the patient to this infection.

In the majority of immunocompetent individuals, melioidosis leads to limited disease; however, among those with underlying risk factors, it may progress to severe sepsis and death. The most common clinical presentation is pneumonia, either as a primary lobar pneumonia or as secondary hematogenous spread from infectious foci (4). Other disease manifestations include skin and soft tissue infections, bone and joint infections, hepatosplenic abscesses and isolated bacteremia. Suppurative parotitis is a common manifestation in Thailand, but is rarely observed in Australia. Furthermore, prostatic abscesses are observed in up to 20% of male patients in Australia. Central nervous system disease can include brainstem encephalitis, cranial nerve palsies or flaccid myelitis. Chronic infections (>2 months) can be a primary manifestation of disease, with symptoms very similar to active tuberculosis, including fever, weight loss, hemoptysis and upper lobe cavitary lesions (1).

The diagnosis is typically made through microbiological testing, but relies on clinical suspicion with corresponding epidemiological exposure. On Gram stain, the organism is a small Gram-negative bacilli, often with a bipolar staining. *B pseudomallei* grows readily on blood agar and MacConkey media, with colonies having a dry, wrinkled appearance. The organism is an oxidase-positive non-glucose fermenter and can be frequently confused with *Pseudomonas* species. Commercial blood culture systems as well as phenotypic identification systems readily

identify isolates. Selective agar, such as Ashdown's media containing gentamicin, crystal violet and neutral red, can aid in the isolation of *B pseudomallei* from nonsterile sites (3). PCR techniques can also be used to identify the organism, and may be particularly helpful in rapid diagnosis as well as distinguishing from *B mallei* (1).

Treatment of melioidosis includes an intensive phase for two weeks or longer for deeper foci/severe disease with intravenous ceftazidime (2 g every 6 h to 8 h), meropenem (1 g every 8 h) or imipenem (1 g every 6 h). This is followed by a prolonged eradication phase, with oral trimethoprim-sulfamethoxazole for three to six months (4). Some eradication therapies also include adjunctive doxycycline for three to six months (6).

Laboratory safety is paramount in the diagnostic processing of samples of *B pseudomallei*. Two laboratory-acquired cases have been described in the literature. One individual was exposed to aerosolized organism after a centrifuge spill (7) and another individual was exposed while performing sensitivity testing on a positive sample (8). Both individuals developed symptoms of disseminated infection and were successfully treated with antimicrobial therapy to clinical cure. Samples should be handled in a biosafety level 3 laboratory, in a biosafety cabinet, using gloves and sealed containers. Any processing involving aerosolization should be handled with respiratory barrier protection. Finally, accidental exposures, particularly those with aerosol exposure, may benefit from chemoprophylaxis with trimethoprim-sulfamethoxazole, doxycycline or amoxicillin-clavulanic acid (9).

CONCLUSION

We present a case of travel-related *B pseudomallei* infection. The patient's nonspecific, chronic presentation highlights the need for physician awareness of this tropical infection in the context of increasing Canadian global travel and immigration. Clinicians need to consider this organism in the evaluation and treatment of patients with sepsis or other febrile illnesses returning from Southeast Asia and Northern Australia, with an emphasis for laboratory safety in handling potentially infectious samples.

REFERENCES

- Currie BJ. *Burkholderia pseudomallei* and *Burkholderia mallei*: Melioidosis and glanders. In: Mandell GL, Bennett JE, Dolin R, eds. *Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases*. Philadelphia: Churchill Livingstone, 2009:2869-80.
- Chan CK, Hyland RH, Leers WD, Hutcheon MA, Chang D. Pleuropulmonary melioidosis in a Cambodian refugee. *Can Med Assoc J* 1984;131:1365-7.
- White NJ. Melioidosis. *Lancet* 2003;361:1715-22.
- Wiersinga WJ, Currie BJ, Peacock SJ. Melioidosis. *N Engl J Med* 2012;367:1035-44.
- Currie BJ, Ward L, Cheng AC. The epidemiology and clinical spectrum of melioidosis: 540 cases from the 20 year Darwin prospective study. *PLoS Negl Trop Dis* 2010;4:e900.
- Limmathurotsakul D, Peacock SJ. Melioidosis: A clinical overview. *Br Med Bull* 2011;99:125-39.
- Green RN, Tuffnell PG. Laboratory acquired melioidosis. *Am J Med* 1968;44:599-605.
- Schlech WF, Turchik JB, Westlake RE, Klein GC, Band JD, Weaver RE. Laboratory-acquired infection with *Pseudomonas pseudomallei* (melioidosis). *N Engl J Med* 1981;305:1133-5.
- Peacock SJ, Schweizer HP, Dance DA, et al. Management of accidental laboratory exposure to *Burkholderia pseudomallei* and *B. mallei*. *Emerg Infect Dis* 2008;14:e2.