Splenic abscesses in a returning traveler

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Abstract

Burkholderia, an aerobic gram-negative rod, is the causative organism behind melioidosis and is a common soil and water organism found predominantly in South-East Asia. We report the case of a 68 year-old man returning from an extended trip to the Philippines, with splenic hypodense lesions on abdominal computer tomography scan, later confirmed to be culture-positive for *Burkholderia pseudomallei*. The patient was treated with a course of intravenous ceftazidime followed by eradication therapy with oral doxycycline and trimethoprim-sulfamethoxazole. He recovered with complete resolution of symptoms at follow up. In a returning traveler from an endemic area, melioidosis should be considered as part of the differential for any febrile illness with abscesses.

Case Report

A 68 year-old man with a history of coronary artery disease, hypertension, type II diabete mellitus, and paroxysmal supraventricular tachycardia returned to the United States from a nine-month visit to his native Philippines. There, he visited family in the cities of Manila and Lucena. Five months into his time abroad, he developed a myocardial infarction and was hospitalized. He received angioplasty and placement of two stents in his coronary arteries and was subsequently discharged with appropriate medical management. Three months later, and one month before his scheduled return to the U.S., he was hospitalized for fevers and left upper quadrant abdominal pain. He did not have associated diarrhea, respiratory symptoms, or skin lesions. Diagnosis, workup, and treatment plan during his hospitalization were unknown, but the patient confirmed that he was discharged home with oral antibiotics. The patient completed the course, which resolved his fevers and abdominal pain, but was unable to recall the duration or name of the antibiotics that he took.

One month after his return to the U.S., he presented to the emergency room with progressive worsening of his left upper quadrant abdominal pain since his return. At the time of emergency department presentation, his temperature was 97.5°F (36.4°C), blood pressure 127/69 mmHg, and pulse 117 beats per minute and irregularly irregular in rhythm. Respiration rate was 27 breaths per minute and oxygen saturation was 99% on room air. Pertinent physical exam findings included tenderness in the left upper quadrant on palpation. A computer tomography (CT) scan of the abdomen and pelvis with intravenous contrast was performed, which showed multiple ill-defined hypodense lesions in the spleen (Figure 1). The patient was started empirically on oral ciprofloxacin and metronidazole, later changed to intravenous vancomycin, ceftazidime, and metronidazole after infectious disease consultation. During the hospitalization, blood cultures drawn prior to administration of antibiotics returned negative for growth. Urine culture returned positive for Group B streptococcus, initially thought to be the causative organism behind the splenic lesions. A transthoracic echocardiogram was then performed to assess endocarditis, which returned negative for both valvular vegetation and new regurgitant valvular pathology.

A CT-guided aspiration of the splenic lesion was performed on hospital day two. Culture of the aspirate eventually grew *Burkholderia pseudomallei*. After finalization of abscess culture, the patient's antibiotic regimen was changed to intravenous ceftazidime alone. The patient was discharged on this regimen for a total duration of eight weeks of induction therapy with ceftazidime, followed by 20 weeks of eradication therapy with oral doxycycline and trimethoprim-sulfamethoxazole (TMP-SMX). The patient did well on the treatment plan, and at time of follow-up had complete resolution of fever, leukocytosis, and abdominal pain. A repeat CT scan of the abdomen after completing eradication therapy showed resolution of the splenic lesions. Per protocol, the aspirate culture plate was sent to the California Department of Public Health for confirmation of diagnosis. The diagnosis was confirmed; however, the plate was destroyed before antibiotic sensitivity testing could be performed.

Discussion

Melioidosis is a common disease in tropical climates, and is endemic to regions of South-East Asia and Northern Australia, with the highest prevalence in northeast Thailand.[1] The causative organism is *B. pseudomallei*, formerly known as *Pseudomonas pseudomallei*. Similar to its better-known cousin *Pseudomonas aeruginosa*, *Burkholderia* is a saprophytic aerobic gram-negative rod present in soil and water.

Risk factors for the development of melioidosis include diabetes mellitus, hazardous alcohol abuse, immunosuppression, renal failure, and thalassemia. Occupational exposures also play a significant role in endemic regions, with rice farmers in Thailand being a particularly susceptible group.[2,3] Transmission to humans occurs through direct inoculation of the bacteria through disruptions in the skin, ingestion, and inhalation.[4] Other forms of spread are more rare, but have been documented in case reports. For example, there are reports of perinatal spread, spread via breast milk in a mother with mastitis, possible sexual transmission in a returning serviceman, and between children with cystic fibrosis. Nosocomial spread is very rare, and reported cases have eventually been linked to contaminated medical products.[5] Once established, the bacteria can cause local disease but can also disseminate hematogenously. The incubation period ranges from 1-21 days with a mean of 9 days.[2] However, there is the potential for significant latency between exposure and the subsequent development of symptoms, thought to be due to the ability of *B. pseudomallei* to survive within phagocytes.[6] This phenomenon was seen in many returning Vietnam War veterans and gave melioidosis its nickname *Vietnamese time bomb*.[4,7] As the initial inoculation may occur through multiple different mechanisms and subsequently spread to virtually any organ, the symptoms of melioidosis

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can be nonspecific. In active forms of the disease, there is fever. Pain may also be present and can help to localize the disease. Most commonly, melioidosis presents as pneumonia, but can also cause encephalitis, osteomyelitis, septic arthritis, cellulitis, and urinary infections.[2,8] The bacteria is also capable of forming abscesses in various locations in the body, most commonly in the prostate, but can also be seen in the parotid gland and spleen, among other locations.[9,10]

Diagnosis is generally made through culture. If there is high clinical suspicion of melioidosis, a clinical sample should be taken from suspected infected sites for culture. Blood, pus, semen, sputum, urine, and wound cultures can all be helpful in growing the organism. *B. pseudomallei* grows readily on commercial blood culture media. If there is particularly high suspicion and need to isolate the bacteria from background flora such as for respiratory culture, Ashdown media can be used, but otherwise provides no additional benefit in sensitivity.[11] Serological studies such as indirect hemagglutination assay are limited in utility, especially in endemic areas where most people are seropositive, due to low sensitivity of 56% for the acute disease and persistent positivity of titers after exposure or treatment.[12]

B. pseudomallei is naturally resistant to a variety of commonly used antibiotics such as narrow-spectrum cephalosporins, penicillins, and aminoglycosides. Therefore, recommended treatment regimens include a combination of intensive initial induction therapy followed by eradication therapy as a mean of consolidation. Successful induction agents used are intravenous ceftazidime and imipenem.[13,14] Duration of induction therapy varies, with a large scale Australian study recommending at least two weeks for patients who are critically ill or who have deep abscesses.[15]

Following completion of the induction phase, patients are treated in the eradication phase using oral antibiotics for at least 12 weeks.[15,16] Eradication phase treatment regimens differ between countries. In Thailand, doxycycline plus TMP-SMX is the preferred combination, while in Australia, TMP-SMX alone is used. Recently, the multi-center, double-blind randomized placebo-controlled MERTH trial compared doxycycline plus TMP-SMX (Thailand regimen) versus placebo plus TMP-SMX (Australian Regimen), for 20-week total duration. The overall conclusion was non-inferiority between the two regimens.[17] Given this finding, for patients who are unable to tolerate combined antibiotic therapy, TMP-SMX alone may be sufficient for eradication of *Burkholderia* infections. Doxycycline monotherapy was previously used as eradication therapy, but the studies from Australia and Thailand have shown that there is an unacceptably higher relapse rate than with TMP-SMX alone.[16,18] After completing proper treatment, most patients recover well and have no evidence of disease persistence. Overall relapse rates are low at 5.4-9.7%, though partial treatment and diabetes can both increase the risk.[2] For untreated infections, the mortality rate has been estimated to be above 90%.[19] In recent years, overall mortality rates have been steadily decreasing throughout the endemic regions, including Thailand as well as Australia. In Thailand, the 49% mortality rate recorded in 1997 had decreased to 40.5% in 2006.[1] In the Darwin study in Australia, initial 5 year mortality leading up to 1994 was 30%, which decreased to 9% in 5 years leading up to 2009. The authors of the Darwin study attributed the improvement over time to increasing awareness, earlier diagnosis, prompt treatment, and improved intensive care management. The difference in absolute mortality rates between the two countries is thought to be due to inequalities between the health care systems.[2] Our case highlights several unique aspects of presentation, diagnosis, and treatment of melioidosis. The patient visited an endemic country, and though he spent time predominantly in urban regions rather than rural areas with rice paddies, at some point he was likely exposed to burkholderia through the environment. It is unlikely that he acquired the infection during his first hospitalization for the myocardial infarction, as nosocomial spread of melioidosis is rare and not acknowledged as a typical form of transmission.

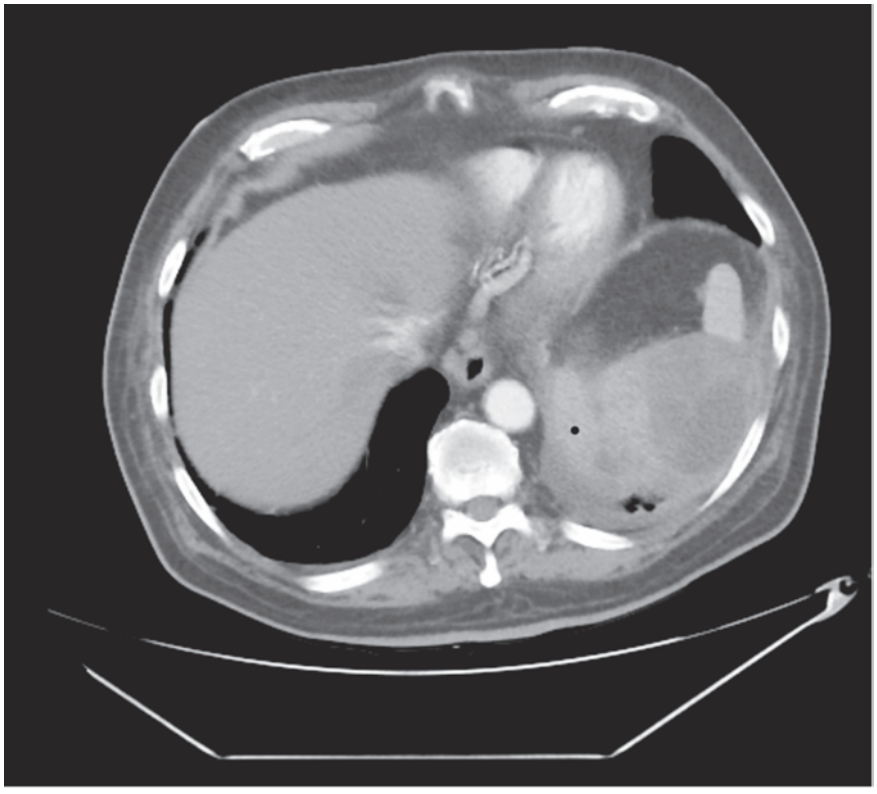

Figure 1. Multiple splenic hypodensities seen on computed tomography scan.

The patient was then hospitalized in the Philippines for a second time with fever and abdominal pain which raise the suspicion for disseminated disease and the formation of splenic abscesses. During this hospitalization, while it was unknown what the diagnosis and treatment plan was, the patient was not taking any oral antibiotics for consolidation after his return to the United States, indicating that melioidosis was either misdiagnosed or incompletely treated. This is corroborated by the fact that the patient developed a recurrence of his symptoms after returning to the U.S. Classically, melioidosis manifests as fevers and septicemia. What is therefore surprising in our case is that during his hospitalization in the U.S., the patient did not have any fevers but rather his most salient complaint was abdominal pain, presumably due to the abscess. From the long-term epidemiological study of melioidosis in Darwin, only 19 out of 540 cases over 20 years featured a soft tissue abscess as a primary focus of infection. Its location in the spleen is another interesting aspect of our case. Again from the same study, splenic abscesses, whether as a primary or secondary focus, are rare and were seen in only 5% of the cases reviewed, much less than prostatic abscesses, which were seen in 20% of

cases.[2] Curiously, blood cultures drawn prior to administration of antibiotics and throughout the hospital course were persistently negative for *Burkholderia*, and the diagnosis was only made by aspirating and culturing the abscess. The bacteria is known to be able to be easily cultured on standard commercial blood culture media, and the use of selective media such as Ashdown's is recommended for respiratory isolates where it can help in isolating the bacteria from the other respiratory flora.[11] In our case, the organism did grow on standard media when culturing the abscess aspirate, suggesting that negative blood cultures did not represent failure of the culture media but rather that any bacteremia had been suppressed by earlier antibiotic therapy and the infection remained confined to the abscess reservoir.

Conclusions

With the increase in international travel in recent decades, physicians everywhere are exposed to a greater variety of infectious diseases than ever before. Many formerly exotic infections presenting in the returning traveler may confound the practitioners who may not have encountered them. This is complicated by the fact that the U.S. is host to a large immigrant population, many of whom return to their country of origin periodically to visit friends and family, such as the above case. In comparison to tourists, this population has been shown to have greater morbidity and mortality due to various barriers to effective care, including poor pre-travel medical counseling, decreased sanitation, prolonged stays, and inadequate treatment once overseas.[20]

Melioidosis presents a challenging diagnosis for many clinicians in the U.S., given the wide spectrum of presentation and potential for a long-latency period. Even otherwise healthy travelers without risk factors for melioidosis may still be infected and can develop symptoms many months after their initial infection. Unfortunately, given the similarity in initial symptoms and the overlap of geographic prevalence for the diseases, melioidosis is sometimes mistaken for and treated as a tuberculosis infection. It is important for clinicians to distinguish these two entities, since delays in diagnosis and proper treatment of melioidosis can be catastrophic, as septicemia and shock may develop. It is also important to be aware of atypical presentations as seen in our case, especially in the setting of partial treatment with a prior regimen of antibiotics, which can obscure the salient symptoms associated with the disease. Overall, melioidosis as part of the differential diagnosis for a traveler returning from an endemic area presenting with fevers and splenic abscesses is warranted, especially one with a positive exposure history or underlying risk factors.

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