Melioidotic Osteomyelitis of the Femur Occurring in a Traveler

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_Burkholderia pseudomallei_ is a gram-negative bacillus mainly distributed in South Asia, northern Australia and Iran. However, its incidence is probably greatly underestimated in other regions of the tropical world due to the lack of diagnostic microbiology facilities. Multiple clinical presentations of _B. pseudomallei_ have been reported ranging from localized, benign infection to fulminant sepsis. Relapse of the infection is frequent even among those completing a full course of antibiotic treatment. Septic arthritis and osteomyelitis are an uncommon presentation of the disease; 14 cases have been reported during the last 10 years. The optimal treatment remains elusive. We describe a case of melioidotic osteomyelitis treated with an imipenem and doxycycline regimen.

A 46-year-old Englishman, who had a 3-week history of traveling in Thailand and jungle tracking at Perhentian Island, Malaysia, presented with a 10-day history of fever, chills, rigors, and right thigh pain and was admitted to Kuala Terengganu Hospital in Malaysia. On examination, he was febrile with temperature of 39.6°C. The right thigh was painful with some limitation of range of movement. A full blood count demonstrated a white cell count of 11.7 × 10⁹/L with predominant neutrophilia and an erythrocyte sedimentation rate (ESR) of 106 mm/h. Blood cultures grew _B. pseudomallei_ and he was started with intravenous ceftazidime and amoxicillin-clavulanate. Seven days later he was repatriated to France, where he used to live, and therefore was admitted to our infectious disease unit. Physical examination revealed an afebrile patient still suffering from pain at his right thigh. Laboratory studies disclosed the following: a white cell count of 10.6 × 10⁹/L with a normal neutrophil cell count, an ESR of 70 mm/h, and a C-reactive protein level of 138 mg/L. X-ray of the right femur was normal. Gallium-technetium scintigraphy demonstrated an infectious localization of the right proximal femur consistent with osteomyelitis. Ceftazidime and amoxicillin-clavulanate were stopped and he was started on intravenous imipenem and doxycycline for 3 weeks, followed by subcutaneous imipenem and oral doxycycline for 3 months. The patient remained afebrile, right thigh pain completely disappeared and a subsequent gallium-technetium scintigraphy at 3 months showed full resolution of the osteomyelitis. The patient is asymptomatic after 1 year of follow-up.

Since the late 1980s, and a randomized clinical trial conducted by White et al., ceftazidime has become the therapy of choice in acute melioidosis. Recently, imipenem has been shown to be as effective as ceftazidime when comparing mortality among patients with severe melioidosis. Treatment of localized melioidotic osteomyelitis remains problematic because no clinical trials have been reported. A carbapenem or a ceftazidime-containing regimen may be proposed. Carbapenems are the most active antibiotics against _B. pseudomallei_, with a minimal inhibitory concentration that inhibits 90% of strains tested (MIC₉₀) of 0.5 µg/mL, and have demonstrated a postantibiotic effect against _B. pseudomallei_ whereas ceftazidime does not. They have a high ability to penetrate into the bone. Thirty to 120 minutes after administration of 1 g of imipenem, the mean concentration in bone has been estimated at 2.6 µg/mL, which is above the MIC₉₀ of _B. pseudomallei_. In addition, carbapenems may be administrated twice a day and are available in both subcutaneous and intramuscular (IM) forms, which is of great importance for the patients’ quality of life given the length of the treatment. However, _B. pseudomallei_ has the ability to survive within phagocytic cells. Since β-lactams do not penetrate intracellular sites and kill nonmultiplying bacteria, therapy with β-lactams may fail to prevent future relapse of melioidosis. Therefore, we decided to combine carbapenems with an antibiotic capable of penetrating phagocytic cells, although this association has never been reported in the...
past for this localization of \textit{B. pseudomallei}. Tetracyclines and fluoroquinolones can penetrate phagocytic cells, can penetrate bone, and may be effective against \textit{B. pseudomallei}. Because antimicrobial resistance to fluoroquinolones was not tested for our strain, we instituted doxycycline.

An increasing number of people from industrialized countries travel to developing countries. Like our patient, travelers to developing countries are exposed to the risk of acquiring melioidosis and opportunities exist for this disease to spread from established endemic areas to developed countries. Clinicians in developed countries should be educated on how to recognize and treat melioidosis.

References