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Case Report

Melioidosis in a European traveler without comorbidities: a case report and literature review

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SUMMARY

Melioidosis is an endemic disease in Southeast Asia and northern Australia. It habitually affects immune-depressed hosts and may have a wide range of clinical manifestations. The use of positron emission tomography–computed tomography (PET-CT) has not been described previously for this disease. We report the case of a European traveler without comorbidities who developed melioidosis with pulmonary and bone marrow involvement 1 year after exposure. Antibiotic treatment was managed by taking into account the evolution on PET-CT. We review the literature and suggest the use of PET-CT for the initial evaluation of melioidosis, especially to look for a bone location, and to manage the length of antibiotic therapy.

1. Introduction

Melioidosis is an endemic disease in Southeast Asia and northern Australia, caused by a Gram-negative bacillus, *Burkholderia pseudomallei*. It may affect almost any organ in the body. Reactivation from a latent focus of melioidosis is rare but possible (5–10%) despite prolonged eradication phase treatment, especially in the case of initial bacteremia.[1]

The use of positron emission tomography–computed tomography (PET-CT) has not been described previously for this disease. We report the case of an unusual presentation of the disease and the first published use of PET-CT in melioidosis. We review the literature and suggest the use of this exam in the management of melioidosis.

2. Case report

A previously healthy 55-year-old Caucasian man presented to our hospital with a high fever of 40 °C, night sweats, weight loss of 6 kg over the previous 6 months, and right shoulder pain. His medical history was unremarkable except for alcohol weaning 5 years earlier. He had travelled to Cambodia 1 year ago, where he had led a healthy lifestyle and had had no cutaneous wounds or contact with water.

The examination was normal. Laboratory test results showed an elevated serum C-reactive protein (CRP) level at 30 mg/l, normal white blood cell count, and a negative HIV serology. Blood cultures were negative. An X-ray showed osteolytic lesions of the right arm and shoulder, confirmed by magnetic resonance imaging (MRI). An ^{18}F-fluorodeoxyglucose (18F-FDG) PET-CT revealed intense uptake in the right humerus (maximum standard uptake value (SUVmax) = 7.3) and in a pulmonary lesion (SUVmax = 1.8) identified as a small lung cavitation on CT scan (Figure 1).

A surgical bone biopsy of the right humerus showed giant-cell granuloma with necrosis. Acid-fast stains of bone and bronchial biopsies were negative, but bone marrow culture allowed the isolation of *B. pseudomallei*.

A 4-week treatment of intravenous ceftazidime (100 mg/kg/day) and oral trimethoprim–sulfamethoxazole (TMP–SMX, 50 mg–10 mg/kg/day) was started. Because of a drug-induced skin rash, TMP–SMX was switched to doxycycline (6.5 mg/kg/day) during the prolonged eradication phase, in association with amoxicillin–clavulanate (3 g–375 mg/day). Susceptibility to these antibiotics was previously assessed in vitro. The shoulder pain disappeared

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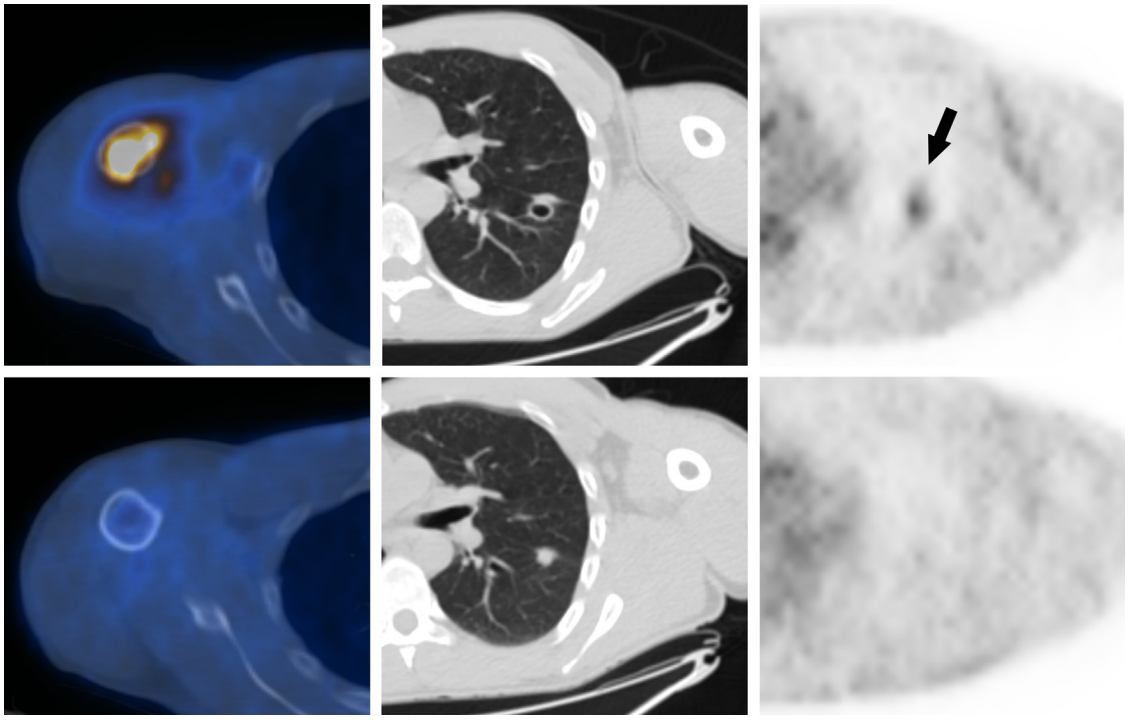

Figure 1. Top row, at diagnosis: left, osteolytic lesion of the right humerus with intense uptake of ^{18}F-FDG; middle and right, lung CT scan showing cavitary lesion in the left lower lobe; right, moderate ^{18}F-FDG uptake of the cavitary lesion. Bottom row, after 6 months of treatment: left, disappearance of ^{18}F-FDG uptake in the right humerus; middle, consolidation of the cavitary lesion; right, disappearance of ^{18}F-FDG uptake in the lung lesion.

within 2 weeks, but further MRI evaluation after 3 and 6 months of treatment showed persistent osteolytic lesions of the right humerus with gadolinium uptake. However, PET-CT performed after 6 months showed complete normalization of the humeral and pulmonary SUVmax (Figure 1), allowing discontinuation of antibiotics.

3. Discussion

B. pseudomallei, also known as Whitmore's bacillus, is a Gram-negative, aerobic, environmental bacterium found in soil and water in Southeast Asia and northern Australia. Melioidosis is usually acquired during the rainy season, by inhalation or by inoculation through non-intact skin. Although unusual, vertical transmission at birth, nosocomial transmission, zoonotic transmission, and laboratory acquired infection have been recorded.

The main risk factors for melioidosis are diabetes, alcohol use, chronic lung disease, chronic renal disease, and any situation inducing immunosuppression.

Melioidosis covers a wide spectrum of severity, ranging from chronic disease to fulminant sepsis, and may affect almost any organ in the body.[2] The acute form is the most frequent, commonly associated with lung location. Melioidosis may also present as a chronic illness, with the additional presence of internal chronic abscesses. In one of the most important prospective cohorts published to date, which included 540 patients with culture-confirmed melioidosis, the most common manifestations were pneumonia (51%), genito-urinary infection (14%), skin infection (13%), and sepsis without a clinical focus (13%).[1] Bone or joint locations concerned 4% of cases. Mortality varies greatly from 50% in Cambodia and Thailand[3] to 9% in Australia,[1] and increases with age (≥50 years), and the presence of at least one risk factor as pulmonary location of melioidosis, septic shock (occurring in about 21% of all cases), or bacteremia.[1–4]

B. pseudomallei is usually identified by conventional techniques, including Gram stain and aerobic culture on agar media. For non-sterile specimens, Ashdown's selective medium is preferred, if available. Bacteremia is identified in more than half of cases,[1] and melioidosis represents about 10% of blood stream infections and 10% of acute lower respiratory infections of bacteriological etiology in Cambodia.[3,4] Even though the performance of serological tests has improved recently, their use is limited to areas with a low prevalence, since most of the population is seropositive in endemic areas.

B. pseudomallei shows natural resistance to a large number of antimicrobial agents, including all narrow-spectrum cephalosporins, most penicillins, macrolides, all aminoglycosides, and polymyxins. However, it is generally susceptible to chloramphenicol, TMP–SMX, tetracyclines, third-generation cephalosporins, ureidopenicillins, carbapenems, and amoxicillin–clavulanate. Although a proportion of *B. pseudomallei* isolates are susceptible to fluoroquinolones by in vitro testing, clinical evidence indicates that fluoroquinolones are not effective.

Antimicrobial therapy for melioidosis is divided into acute and eradication phases. One of the current recommendations for the acute phase, used in the largest Australian cohort, is a combination of parenteral antimicrobial agents for at least 14 days with ceftazidime (50 mg/kg, up to 2 g, 6-hourly) or meropenem (25 mg/kg, up to 1 g, 8-hourly).[5] In cases of deep-seated infections (e.g., central nervous system infection or osteomyelitis), TMP–SMX may be added because of its high tissue penetration. For the eradication phase, TMP–SMX alone with folic acid supplements for at least 12 weeks may be sufficient, even if a four-drug regimen (chloramphenicol, doxycycline, and TMP–SMX) is commonly used in Thailand. Doxycycline should not be considered alone, and its addition to TMP–SMX for the eradication phase remains debatable.[5]

Our observation is unusual regarding the occurrence of melioidosis in a European traveler without comorbidities, about 1 year after exposure. This case shows that melioidosis must be

considered in the event of an acute or chronic febrile illness after returning from an endemic area like Southeast Asia or northern Australia, especially when tuberculosis has been ruled out.

We also suggest that PET-CT may be useful for the initial assessment of melioidosis locations, especially to look for asymptomatic ones (e.g., the pulmonary cavitation in our case), and to guide the duration of antibiotics in the eradication phase. In the presented case, PET-CT showed complete healing more accurately than MRI, which displayed chronic abnormalities related to bone marrow remodeling after osteomyelitis.

Conflict of interest: No conflict of interest to declare.

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