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# Aetiology and management of chronic granulomatous osteomyelitis: look before you leap

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## ABSTRACT

**We report a rare difficult-to-manage case of chronic granulomatous osteomyelitis due to *Burkholderia pseudomallei*, the category two organism with atypical sensitivity pattern. The patient was a 29-year-old who presented with a history of dull aching pain in the left thigh region for one year. Local examination revealed a diffuse swelling and tenderness. Any similar presentation should therefore always be supported by microbiological opinion to prevent prolonged morbidity, especially in immunocompromised patients.**


**Keywords: *Burkholderia pseudomallei*, chronic granulomatous osteomyelitis, melioidosis, osteomyelitis**

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## INTRODUCTION

Granulomatous infection of the bone is one of the most common orthopaedic problems in third world countries, including India.[1] *Burkholderia pseudomallei (B. pseudomallei)*, the causative organism of melioidosis, is a very rare isolate from chronic granulomatous osteomyelitis. It is often resistant to antibiotics chosen to treat bacterial infections as it can mimic chronic pyogenic osteomyelitis or tubercular osteomyelitis in presentation.[2] It is therefore not unlikely to assign an incorrect aetiology. Moreover, a mistaken diagnosis of this "category two" organism may lead to improper antibiotic therapy, and hence, failure of treatment. The identification of the pathogen in the microbiology set-up is the most direct and the best way to diagnose melioidosis of the bone. Most *B. pseudomallei* are susceptible to ceftazidime, amoxi-clavulanic acid, cotrimoxazole and chloramphenicol and resistant to third generation cephalosporins, aminoglycosides and polymyxin B.[3] Amoxi-clavulanic acid alone is often associated with a higher failure rate. We report a very rare presentation of melioidosis as chronic granulomatous osteomyelitis with atypical drug sensitivity pattern which alerts the clinician regarding this unusual organism causing osteomyelitis.

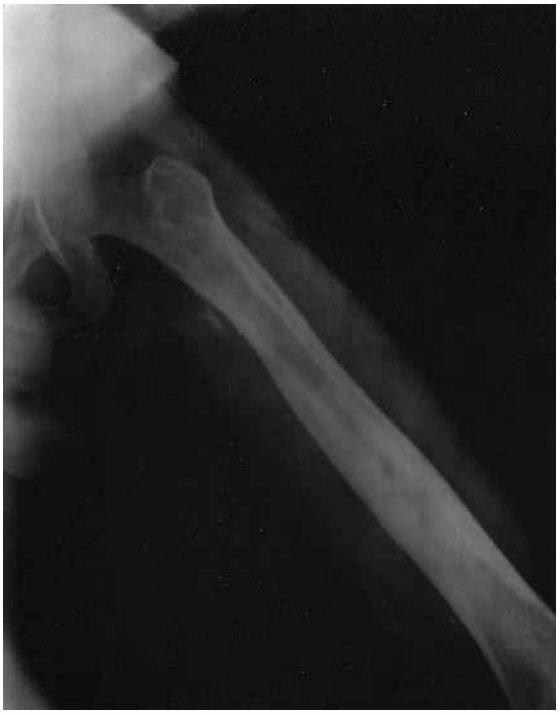

**Fig. 1** Lateral radiograph shows thickening of the cortices with widening of the mid-shaft and a few well-defined lytic lesions, surrounded by sclerosis in the shaft of the left femur.

## CASE REPORT

A 29-year-old non-diabetic and HIV seronegative businessman with no history of immunosuppression presented with a history of dull aching pain in the left thigh region for one year following a contusion a few years ago. Local examination revealed a diffuse swelling and regional tenderness. The underlying bone was thickened and tender. Movements of the left hip and knee were normal. Sclerosis in the mid-shaft of the left femur with loss of cortico-medullary differentiation was revealed on radiographs. A sequestrum was noted in the anterior aspect of the middle shaft of the left femur. Decompression of cavity and saucerisation was done. Histopathology showed chronic granulomatous osteomyelitis without any evidence of tuberculosis. Microbiological opinion regarding tissue and blood culture was negative. The patient was treated with intravenous cefotaxime (Nicholas Piramal India, Mumbai, India; 1 g BD) for two weeks

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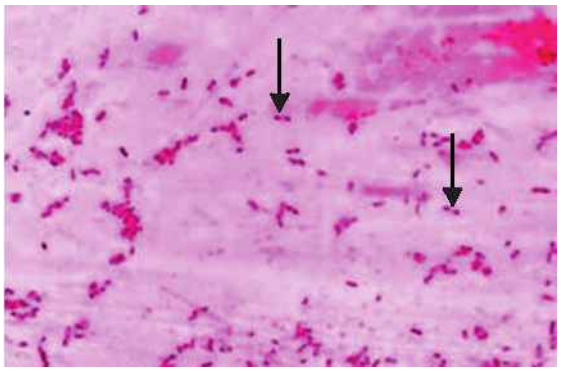

**Fig. 2** Photomicrograph of *B. pseudomallei* shows bipolar (safety pin) appearance (Gram, x1,000).

followed by oral cefixime (Unichem Lab, Mumbai, India; 200 mg BD) for four weeks, on presumption that it was a chronic pyogenic infection.

The patient revisited the orthopaedic department after six months with complaints of moderate pain in the same region with diffuse sclerosis in the middle third of the left femur on radiograph (Fig. 1). Curettage and saucerisation was redone. The curretted and debrided tissue had similar histopathological findings. An oxidase-positive Gram negative organism was grown in microbiological culture with a safety-pin appearance (Fig. 2) and was further identified as *B. pseudomallei* by a battery of tests.[4] Mycobacterial smear and culture were negative. The organism had an atypical sensitivity pattern with disc diffusion method[5] – it was sensitive to cotrimoxazole, chloramphenicol, piperacillin, ciprofloxacin, amoxi-clavulanic acid (Span Diagnostics, Surat, India), imipenem, and even gentamicin (Oxoid, Hampshire, England), and resistant to third generation cephalosporins including ceftazidime (Span Diagnostics, Surat, India) and polymyxin B (Hi Media, Mumbai, India). The patient was treated with intravenous ciprofloxacin (Ranbaxy Lab, Gurgaon, India; 200 mg BD) and amoxi-clavulanic acid (Glaxo Smithkline Pharma, Mumbai, India; 1.2 gm BD) for two weeks and discharged in a clinically improved condition with oral cotrimoxazole (Cipla, Mumbai, India; 160 mg trimethoprim and 800 mg sulfamethoxazole BD) for eight weeks.

## DISCUSSION

*B. pseudomallei*, the causative organism of melioidosis, is endemic in northern Australia and Southeast Asia, especially in Thailand[1] and the southern part of India,[2,6] where it accounts mainly for 20% of all community-acquired pneumonia. This organism is transmitted through direct contact, cutaneous inoculation, inhalation or ingestion, to cause multiple abscesses in single or multiple organs, especially in individuals with diabetes mellitus or immunosuppression.[7] Bone involvement may be part of systemic infection, or it may be the only localised focus of infection.[8,9] Our case suggests that granulomatous involvement of a bone by melioidosis may be indistinguishable from the lesions like tuberculous or staphylococcal abscess except by microbiological culture, and should always be an important differential diagnosis, especially in patients from endemic areas.[8]

The unusual drug sensitivity pattern might also be a problem in managing the patients; sensitivity to gentamicin is very rarely found in wild strains of *B. pseudomallei*.[10-13] Resistance to ceftazidime might have evolved due to therapy with third generation cephalosporin as documented previously.[14] This patient was managed successfully on the second occasion with combined therapy of ciprofloxacin and amoxi-clavulanic acid, because of a high failure rate of the latter if used alone.[3] Management strategies of melioidosis should therefore always be implemented according to the drug sensitivity pattern of the isolated organism. Increased awareness of the doctors and other healthcare workers of this "category two" organism is important, especially in this endemic area. This organism should be handled carefully and although the organism is easy to culture, it might be discarded as a contaminant in the laboratory. This case did not show the typical characteristics of melioidosis, either in presentation or in drug sensitivity pattern and has drawn attention to the potential difficulties in diagnosis and management of the patient. In conclusion, any similar presentation should always be supported by microbiological opinion, since delay in diagnosis and treatment for this type of localised lesion may rarely become acute and fulminate, especially in immunocompromised patients.[2] One should be aware that this emerging organism may occur in cases of recurrent, non-responsive chronic granulomatous osteomyelitis.

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