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# Polymicrobial community-acquired *Acinetobacter baumannii* and *Burkholderia pseudomallei* bacteremia: opportunistic infections with similar risk factors in northern Australia

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ABSTRACT

We report the case of a 61-year-old man from northern Australia with concurrent community-onset *Acinetobacter baumannii* complex and *Burkholderia pseudomallei* bacteremia presenting as severe tropical pneumonia requiring intensive care unit support. The pneumonia was complicated by L3/4 discitis and vertebral osteomyelitis presumed to be due to melioidosis. His risk factors included chronic lung disease and immunosuppression with etanercept. This case of concurrent infection highlights the similar risk factors, presentation and epidemiology of both infections, emphasises the importance of accurate microbiologic identification and reinforces the current Australian empiric antimicrobial treatment recommendations for severe tropical pneumonia.


## Case

A 61-year-old Indigenous man presented to our hospital in northern Australia with a four-day history of fever, malaise, cough and breathlessness. He had a history of seropositive rheumatoid arthritis (RA), cutaneous lupus erythematosus, emphysema, ischaemic heart disease and functional hyposplenism presumed secondary to his autoimmune disease. His RA was well controlled on weekly subcutaneous etanercept introduced 18 months earlier with methotrexate and hydroxychloroquine ceased due to anemia two months prior to presentation. He reported an allergy to sulfanilamide in the form of a blistering skin rash ten years prior. He was a cigarette smoker, had not consumed alcohol for over three years and had never injected intravenous drugs. He gave no history of recent gardening or soil exposure.

On presentation, his observations revealed the following: heart rate 104 beats per minute; respiratory rate 24 breaths per minute; blood pressure 101/56 mmHg; oxygen saturation 97% on room air; temperature 39.7 °C. Physical examination identified a hypopigmented rash across both upper limbs, right upper chest bronchial breath sounds with crepitations and mild left flank tenderness. Initial laboratory testing revealed normocytic anemia, leucocytosis with neutrophilia and an acute kidney injury (Table 1). A plain chest radiograph showed right upper lobe and left heart border opacification (Fig. 1A).

A diagnosis of community-acquired pneumonia was made, and intravenous ceftriaxone, intravenous gentamicin and oral doxycycline were commenced but he deteriorated rapidly with hypoxia, hypotension and hyperlactatemia. He was administered oxygen via high-flow nasal-prongs, intravenous noradrenaline, intravenous meropenem, intravenous vancomycin and oral azithromycin in the Emergency Department and was transferred to the intensive care unit (ICU). Chest computerized tomography (CT) (Fig. 1B) revealed pulmonary infiltrates in the right upper lobe and lingula consistent with pneumonia, without definite features of abscess formation, empyema or cavitation.

On day two of admission, blood cultures collected at presentation identified Gram-negative bacilli. This isolate was subsequently identified as *Acinetobacter baumannii* complex and was sensitive to meropenem, ceftazidime, co-trimoxazole and gentamicin. On day three of admission, a second set of blood cultures collected four hours after presentation, also isolated Gram-negative bacilli. However, this organism was identified as *Burkholderia pseudomallei*, sensitive to meropenem, co-trimoxazole and doxycycline. Due to the unexpected result, the isolates were subsequently re-assessed for error; both specimens had been labelled appropriately, collected at different times and sites and review of the electronic ordering system identified no errors. Blood group testing of both sets of blood cultures and the patient were the same. Both blood culture bottles were re-plated and re-cultured and again

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**Table 1**
Laboratory data.

| Variables | Admission | Day 3 | Day7 |
|---|---|---|---|
| Haemoglobin (g/dL) | 9.7 | 8.8 | 9.7 |
| White cell count ($10^3/\mu L$) | 25.7 | 11.4 | 8.9 |
| Neutrophil count ($10^3/\mu L$) | 22.50 | 9.09 | 6.36 |
| Platelets ($10^3/\mu L$) | 296 | 333 | 552 |
| Albumin (g/dL) | 2.7 | 1.9 | 2.3 |
| Blood urea nitrogen | 7.2 | 4.0 | 6.2 |
| Creatinine (mg/dL) | 1.38 | 0.96 | 1.03 |
| C Reactive Protein (mg/L) | | 166 | 62 |
| pH | 7.24 | 7.47 | |
| Lactate (mmol/L) | 7.7 | 0.8 | |
| Bicarbonate (mmol/L) | 17 | 20 | |

confirmed separate growth of each organism. Sputum samples were unable to be collected.

The patient continued to receive intravenous meropenem and he improved clinically. He was discharged from ICU after four days with no ongoing oxygen requirement. Subsequent blood cultures from day two and day three of admission showed no growth. After seven days of intravenous meropenem, antimicrobials were changed to intravenous ceftazidime. Given his diagnosis of melioidosis, a CT scan of his abdomen and pelvis was performed and visceral disease was excluded. The imaging was, however, suggestive of L3/L4 discitis and vertebral osteomyelitis (Fig. 1C). Lumbar spine magnetic resonance imaging confirmed this finding (Fig. 1D). A peripherally inserted central catheter was inserted to facilitate a further five weeks of intravenous ceftazidime via elastomeric infusion. Etanercept was withheld for the duration of treatment, and his inflammatory arthritis managed with simple analgesia and low-dose corticosteroids. Despite his distant history of allergy to sulphur drugs, after consultation with an immunologist, he was concurrently commenced on oral trimethoprim/sulfamethoxazole (TMP/SMX). This was initially well tolerated and following six weeks of combined intravenous ceftazidime and oral TMP/SMX, he was prescribed six further months of oral TMP/SMX. He did, however, subsequently develop a fixed drug eruption requiring cessation of TMP/SMX and change to doxycycline for continued eradication therapy.

## Discussion

*Burkholderia pseudomallei* and *Acinetobacter baumannii* complex are environmental bacteria endemic to northern Australia and South-East Asia. Both infections are seasonal, occurring largely during the region's wet season and both are opportunistic, predominantly occurring in people with diabetes, hazardous alcohol use, chronic renal disease, chronic lung disease and those receiving immunosuppressive therapy [6,12].

*B. pseudomallei* is present in water and soil of the tropics and infection is strongly associated with monsoonal rains. Rises in temperature, rainfall, dew point, cloud cover and the water table have been associated with an increased risk of the disease as the bacterial load increases at the soil surface and bacterial survival improves with high soil moisture content [1]. In Australia, transmission usually occurs through percutaneous inoculation or inhalation but can occur through aspiration or ingestion.

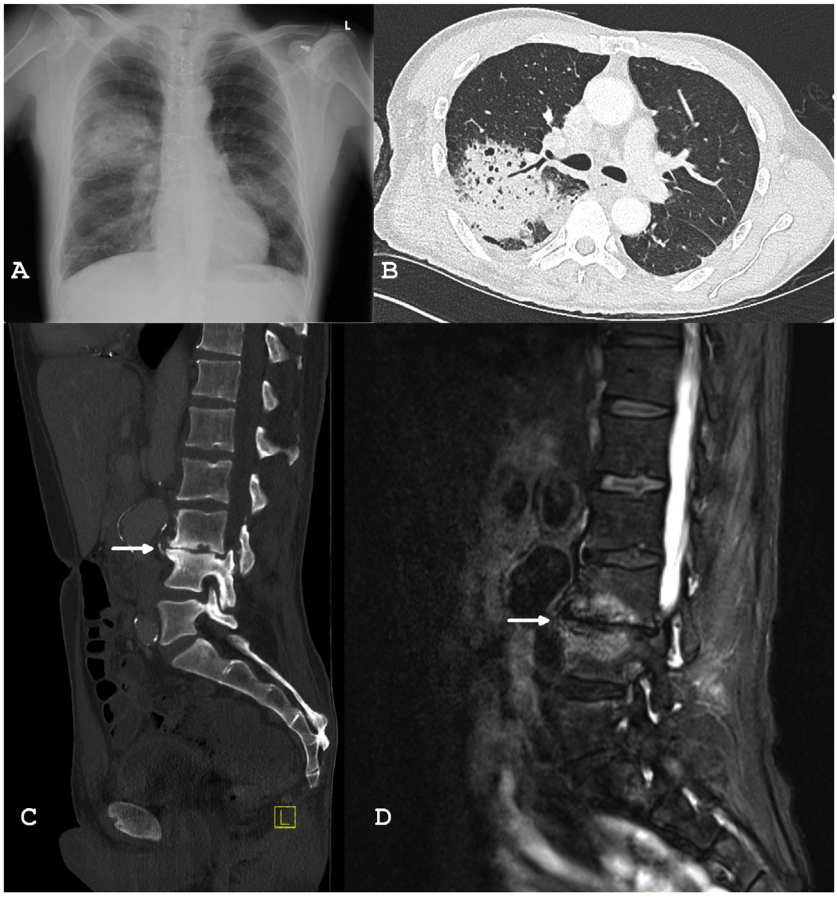


**Fig. 1.** (A) Plain chest radiograph, illustrating right upper lobe and lingula consolidation. (B) Computerized tomography (CT) chest. Axial section, right upper lobe consolidation illustrating air bronchograms. (C) CT lumbar spine, sagittal section, anterior L3/L4 hyperdensity reflecting discitis/osteomyelitis (arrow). (D) MRI lumbar spine, sagittal section, T2-weighted image, L3/L4 discitis and adjacent bone marrow oedema (arrow).

*Acinetobacter* species are abundant in the environment and, although *A. baumannii* is not strictly ubiquitous, it is the most common genospecies responsible for invasive infections. Globally, *A. baumannii* is most commonly associated with nosocomial infections [2] but in the tropics it is an important cause of community-acquired pneumonia (CAP) with associated high mortality [4]. There is a high incidence of nasopharyngeal and skin carriage of *Acinetobacter* species, with up to 1.6 positive body sites per healthy subject in one series [5]. Community skin carriage is highest in the summer, and rates of carriage potentially decrease once subjects begin working in air-conditioned and humidity-controlled environments [2].

Risk factors for melioidosis are well documented and include diabetes mellitus, excessive alcohol use, chronic lung disease and chronic renal disease. *B. pseudomallei* is an intracellular bacterium that can multiply within macrophages and neutrophils. The innate immune response is central to defence against melioidosis and many of these risk factors have been linked to impaired neutrophil function with inhibition of chemotaxis, phagocytosis and killing activity known to occur as a result of these conditions [6]. Iatrogenic immunosuppression is also a risk factor for melioidosis [6]. There is a reported case of infection in a patient whose only risk factor was receiving ustekinumab therapy for psoriatic arthritis [9]. In murine models, tumour necrosis factor alpha (TNF-α) is required for optimal control of *B. pseudomallei* infection and inhibiting TNF-α leads to increased susceptibility to melioidosis [10]. The inhibition of TNF-α in our patient, in addition to his chronic lung disease, likely made him significantly more susceptible to melioidosis.

Risk factors for community-onset *Acinetobacter* pneumonia (COAP) are similar. Hazardous alcohol intake was identified in 82% of cases in an Australian study [4]. Alcohol has been linked to *A. baumannii* pharyngeal carriage in Australia during the wet season [7], suggesting microaspiration as a possible etiology. This theory is supported by the predominance of right hemithorax involvement clinically [8]. Diabetes mellitus and chronic renal disease are also common in patients with COAP [4].

Melioidosis most frequently presents as pneumonia, but other organs can be involved. Osteomyelitis and septic arthritis occur in up to 16% of Australian presentations. Diseases can be severe; approximately one third of patients require admission to an ICU [11]. Access to care in Australia's well-resourced hospitals has resulted in decreased case-fatality rates over time; mortality rates for melioidosis are now approaching 10% in Australia [12].

While community-acquired A. *baumannii* infection classically causes pneumonia and bacteremia, other organ involvement and abscess formation is much less common. COAP is often a severe disease; one Australian series found 82% of patients required ICU admission with an overall mortality of 18% [4], although mortality rates as high as 64% have been documented particularly where appropriate antimicrobial therapy has not been initiated [13]. The severity of these presentations was not associated with specific virulence factors or antimicrobial resistance patterns, suggesting host factors are more relevant in case severity [14].

Although COAP and melioidosis may both present as severe pneumonia, there may be some subtle observable differences. One series identified that in comparison to melioidosis pneumonia, COAP tended to have a more acute onset (<2 days), greater rates of leukopenia, and typically have right-sided lobar changes on plain film X-ray [19].

The mainstay of diagnosis of melioidosis is isolation of *B. pseudomallei* from cultured specimens. As with our case, in Australia, 55-74% of patients are bacteraemic [11,15]; highlighting the need for blood cultures at presentation in patients with CAP. Due to the nature of melioidosis, assessment for visceral abscesses is performed routinely with a CT of the abdomen and pelvis, irrespective of patient symptoms. In our patient, a bone biopsy was not performed as melioidosis osteomyelitis was considered much more likely. The antibiotic regimen required to treat melioidosis osteomyelitis would also be adequate to treat *A. baumannii,* so the procedure was avoided.

Vitek 2 (Biomeriux, France) is routinely used to confirm the presence of *B. pseudomallei* from cultures. Matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) has the potential to be utilised to quickly identify *B. pseudomallei* [16] however further work needs to be done to improve databases in endemic areas to avoid misidentification of other Burkholderia species. E-test and disk diffusion are used in antimicrobial susceptibility testing for *B. pseudomallei* but the microbroth dilution method is considered the gold standard. This has been used in northern Queensland to provide epidemiological cut-off values of clinical isolates to meropenem, ceftazidime, trimethoprim-sulfamethoxazole (TMP-SMX) and doxycycline [17]. Meropenem and ceftazidime are reliable first-line agents against melioidosis, with primary resistance to these and TMP-SMX extremely rare [18].

*A. baumannii* is not easily differentiated by routine microbiological testing. Oxidase negativity on benchtop testing is an important differentiating feature from other Gram-negative bacilli such as *B. pseudomallei*. Diagnosis is predominantly achieved through culture from blood or sputum specimens, although the Vitek 2 instrument is frequently unable to differentiate between Acinetobacter genospecies [2].

Australian guidelines recommend treating all patients with severe CAP in the tropics with empiric antimicrobials that includes cover for *B. pseudomallei* and *A. baumannii* complex [19]. Intravenous gentamicin is also included in the moderate severity CAP regimen to empirically treat *A. baumannii*.

The duration of targeted melioidosis therapy is based on the clinical syndrome [20]. Treatment consists of both an induction and a prolonged eradication phase with intravenous meropenem or ceftazidime being administered in the induction phase and oral TMP-SMX being the preferred agent for the eradication phase. Relapse is well documented and is most commonly due to inadequate initial source control or poor adherence with eradication therapy [12]. Relapse most commonly occurs in the first year and is also associated with alternative antimicrobials (doxycycline or amoxicillin-clavulanate) used in the eradication phase as well as severe disease [6].

Directed therapy for COAP varies worldwide in accordance with local susceptibility patterns with meropenem usually the preferred agent. Multi-drug resistant Acinetobacter isolates are rare in Australian community presentations [14] and treatment failure of empiric therapy with a third-generation cephalosporin and aminoglycoside is uncommon. Ciprofloxacin or TMP-SMX are used as oral therapies in COAP to complete a typically two-week treatment duration [19].

Relapse with *A. baumannii* is not well documented as in melioidosis. In an Australian series of 30 patients who survived a COAP, recurrent infection rather than relapse was identified in 10% of patients, all of whom participated in ongoing heavy alcohol use [3].

## Conclusion

We report a case of concurrent *Burkholderia pseudomallei* and *Acinetobacter baumannii* complex bacteremia with risk factors of chronic lung disease and immunosuppression. While patients regularly present to our institution with either of these infections, having both simultaneously is exceptionally rare and highlights the similar environmental and host factors that puts people at risk of these infections. The case demonstrates the importance of

appropriate empiric antimicrobial therapy and accurate microbiologic diagnosis in severe tropical pneumonia.

## Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

## Declaration of competing interest

None.

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