Melioidosis: Series of Eight Cases

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Abstract

Objectives: Melioidosis caused by the Gram-negative bacterium *Burkholderia pseudomallei* is a very serious infection and has been sporadically reported from the Indian subcontinent. This disease entity can have acute and chronic presentations involving different organ systems. The purpose of this study is to analyze the risk factors, clinical presentations, therapy and outcome of culture proven cases of melioidosis.

Methods: We carried out a retrospective study of eight culture proven cases of melioidosis at a tertiary care hospital in West Bengal.

Results: In this series we have found that melioidosis presents with a variety of symptoms ranging from acute presentations in the form of fulminant septicaemia, multiple abscesses in internal organs, osteomyelitis to more chronic form of the infection masquerading as tuberculosis. Bone and joint involvement are particularly common. Diabetes mellitus and chronic alcoholism are significant risk factors.

Conclusions: India or parts of India are possibly endemic areas for melioidosis. Lack of awareness and the diversity of its presentation are probably responsible for underdiagnosis and under reporting.

Introduction

Melioidosis caused by the bacterium *Burkholderia pseudomallei*, is an important cause of sepsis in several tropical areas including South-East Asia and Northern Australia. In India it had been reported sporadically, mostly from large centers in the south.¹² But with better diagnostic facilities coming up and improved awareness there are more and more reports of melioidosis from the rest of India.³ Melioidosis is not generally considered in the differential diagnosis of community acquired sepsis syndrome because of a low degree of suspicion and the similarity of its presentation with a host of other infective conditions. Here we present eight culture proven cases of melioidosis.

All of the patients were residents of the eastern part of India and had presented with a variety of clinical features of varying degrees of severity.

Cases Series

Eight culture proven cases of melioidosis admitted and treated in the Apollo Gleneagles Hospitals, Kolkata were studied from the medical files for clinical features, investigational findings, treatment and outcome.

Case 1

A 71 year old diabetic patient presented with history of high grade intermittent fever (Tmax 102°F) for 3 weeks and a gangrenous ulcer on the right foot for 1 month. He had been treated with various antibiotics (ciprofloxacin, chloramphenicol, and ceftriaxone) by local physicians but there was no remission of fever. He became extremely weak and bedridden. Detailed work up was done. Blood culture revealed growth of *B. pseudomallei*. X ray of the foot lesion did not reveal any osteomyelitic changes. Administration of meropenem resulted in rapid clinical response and the patient was discharged after 2 weeks of antibiotic therapy with the advice to take cotrimoxazole for a further 6 months.

Case 2

A 32 year old male, a resident of Jharkhand, was admitted to our hospital with history of intermittent fever (Tmax 105°F) for 3 weeks and a gangrenous ulcer on the right foot for 1 month. He had been treated with various antibiotics (ciprofloxacin, chloramphenicol, and ceftriaxone) by local physicians but there was no remission of fever. He became extremely weak and bedridden. Detailed work up was done. Blood culture revealed growth of *B. pseudomallei*. X ray of the foot lesion did not reveal any osteomyelitic changes. Administration of meropenem resulted in rapid clinical response and the patient was discharged after 2 weeks of antibiotic therapy with the advice to take cotrimoxazole for a further 6 months.

Editorial Viewpoint

- Melioidosis is probably endemic in India or parts of India.
- Presentations are diverse, bone and joint involvement are particularly common.
- Diabetes in the single most common risk factor.
- Melioidosis associated with high mortality and relapse.
Case 1

A 29 years old diabetic male was admitted with complaints of high grade fever (Tmax 104°F) and altered sensorium for 5 days and pain and swelling of the right knee joint. Further examination and relevant investigations revealed osteomyelitic lesions of the right knee and proximal tibia with overlying skin and soft tissue infection. The patient was advised antibiotic meropenem and teicoplanin. Arthrotomy of right knee with decompression of proximal tibia was done and thick pus was evacuated. The pus sample and the blood culture collected at the time of admission showed growth of B. pseudomallei. Following isolation of B. pseudomallei the teicoplanin was replaced with cotrimoxazole. The patient continued to have low grade fever (Tmax 100°F) till day 6 of antibiotic therapy, following which he became afebrile. The meropenem was continued for 2 weeks and thereafter he was discharged with the advice to take cotrimoxazole and doxycycline. At follow up after 3 months, he was doing well and his inflammatory parameters had subsided.

Case 2

A 57 years old male with poorly controlled diabetes (HBA1C 11%) presented to us with high grade fever (Tmax 102°F) and chills for the past 10 days along with painful swelling of the shoulder and foot. He was unable to stand and move the right upper limb. Further history revealed that the patient was suffering from fever on and off for the last three months. Significant findings of the imaging studies revealed cavitary lesion in the left lung and multiple abscesses in the liver and spleen along with periportal and peripancreatic lymphadenopathy.

Other significant findings included thromocytopenia. The patient was admitted in the ward and was administered meropenem and teicoplanin. His condition deteriorated and he required ionotropes and ventilatory support and was transferred to the ICU the next day. Blood culture collected at that time showed growth of B. pseudomallei. The patient continued to be febrile although his vitals improved and he was off ventilator and ionotropes after 4 days. Meropenem was continued for two weeks and he was discharged with the advice to take doxycycline for 6 months.

Case 3

A 29 years old diabetic male was admitted with complaints of high grade fever (Tmax 104°F) and altered sensorium for 5 days and pain and swelling of the right knee joint. But his condition deteriorated and he became hypotensive and had to be transferred to the ICU. Blood culture collected at the time of admission, showed growth of B. pseudomallei. Fasciotomy, pus drainage and bone decompression of the affected knee joint was done and thick pus was evacuated. The initial antibiotics were changed to imipenem. The pus from the knee lesion also showed growth to imipenem. The pus from the admission, showed growth of B. pseudomallei. The patient was managed in the intensive care unit with all supportive therapy but he succumbed to the infection after about 5 days of imipenem therapy.
Table 1: Demographic details, risk factors, blood picture and outcome of the eight culture proven cases of melioidosis

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>Residence</th>
<th>Occupation</th>
<th>Risk factors</th>
<th>Hb (gm%)</th>
<th>TC (/cumm)</th>
<th>ESR (mm)</th>
<th>Outcome</th>
<th>Presentation</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>57</td>
<td>M</td>
<td>West Bengal</td>
<td>Retired serviceman</td>
<td>DM</td>
<td>7</td>
<td>17100</td>
<td>102</td>
<td>Discharged</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>32</td>
<td>M</td>
<td>Jharkhand</td>
<td>Business</td>
<td>DM</td>
<td>7</td>
<td>1500</td>
<td>130</td>
<td>Death</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>29</td>
<td>M</td>
<td>West Bengal</td>
<td>Doctor</td>
<td>DM</td>
<td>10.8</td>
<td>12500</td>
<td>126</td>
<td>Discharged</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>51</td>
<td>M</td>
<td>Assam</td>
<td>Policeman</td>
<td>DM, Alcoholism</td>
<td>9.5</td>
<td>34000</td>
<td>124</td>
<td>Death</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>57</td>
<td>M</td>
<td>West Bengal</td>
<td>Business</td>
<td>DM</td>
<td>9.2</td>
<td>5740</td>
<td>103</td>
<td>Discharged</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>33</td>
<td>M</td>
<td>Jharkhand</td>
<td>Site engineer</td>
<td>DM, Alcoholism</td>
<td>7.3</td>
<td>29870</td>
<td>135</td>
<td>Relapsed after 1 year</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>55</td>
<td>M</td>
<td>West Bengal</td>
<td>Service</td>
<td>DM, Alcoholism, COPD</td>
<td>11.3</td>
<td>9800</td>
<td>102</td>
<td>Discharged</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>57</td>
<td>M</td>
<td>Tripura</td>
<td>Business</td>
<td>DM, Chronic renal disease</td>
<td>7.8</td>
<td>12000</td>
<td>140</td>
<td>Discharged</td>
<td></td>
</tr>
</tbody>
</table>

Case 7

A 56 year old post operative case of left parietal osteomyelitis, presented to us with swelling and discharge from the surgical site. The patient had undergone left parietal craniotomy one year ago, with evacuation of pus and scraping of infective granulation tissue. Histopathological examination of the excised tissue had revealed granulomatous infection suggestive of tuberculosis for which he was advised antitubercular drugs (ATD). The wound discharge persisted despite regular dressing and even after completion of the ATD regimen. He was admitted again and wound debridement was done and the debrided material was sent for culture and sensitivity. This time the culture showed growth of \( B. \) \( \text{pseudomallei} \). Following isolation of the organism, the patient was treated with Cefazidime for two weeks and was advised to take co-trimoxazole subsequently for 6 months. During his follow up visit after 3 months, his wound had healed and there was no discharge.

Case 8

A 57 year old patient of diabetes mellitus and chronic kidney disease was admitted with history of high grade fever (Tmax 105 °F) and chills for 15 days, associated with jaundice, nausea, vomiting and loss of appetite. USG of abdomen revealed focal splenic lesion and peri-splenic collection along with distal ileal stricture with left para-aortic and retroperitoneal lymphadenopathy. The perisplenic fluid was aspirated and sent for pyogenic and mycobacterial culture. A provisional diagnosis of abdominal tuberculosis was made and the patient was advised ATD initially. The aspirated perisplenic fluid showed growth of \( B. \) \( \text{pseudomallei} \). The ATD was then discontinued and meropenem was administered for 2 weeks. He became afebrile and his symptoms improved and he was discharged with the advice to take doxycycline.

Summary of the eight culture proven cases are shown in Table 1. All the patients were male patients. The age ranged from 29-71 years, the median age being 53 years. Six patients (75%) presented acutely with disseminated disease while 2 patients had localized disease in the form of septic arthritis and chronic osteomyelitis. Four patients (50%) had bone and joint involvement. Diabetes mellitus was the single most common risk factor in that 7 out of the 8 patients (87.5%) had diabetes mellitus. Three patients (37.5%) had history of chronic alcoholism. All the patients had high ESR (>100 mm at 1st hour) at presentation. Two of the patients (25%) died due to fulminant sepsis. One patient had a relapse after one year. The rest 5 patients did well at follow up.

Discussion

Melioidosis, also known as Whitmore’s Disease, is an infectious disease caused by gram negative, oxidase positive bacilli \( B. \) \( \text{pseudomallei} \). \( B. \) \( \text{pseudomallei} \) is a non-fastidious bacteria which can grow on a variety of ordinary culture media (such as blood agar, McConkey agar) producing wrinkled colonies with metallic appearance (Figure 1). In the laboratory it can be confused with Pseudomonas species. The pattern of antibiotic susceptibility provides clue to its identification. The majority of \( B. \) \( \text{pseudomallei} \) isolates are intrinsically resistant to all Aminoglycosides (via an efflux pump mechanism), but sensitive to Co-amoxiclav. This pattern of resistance almost never occurs in \( P. \) \( \text{aeruginosa} \) and is helpful in identification (Figure 2). It is intrinsically resistant to Polymyxin B (PB). Carbapenems like Imipenem (IPM) and Cefazidime (CAZ) have good sensitivity. All the \( B. \) \( \text{pseudomallei} \) strains isolated by us exhibited this typical antibiogram. Unfortunately, it has been shown in Sarawak, Borneo, that the majority of strains there are susceptible to Aminoglycosides and Macrolides, which means that conventional recommendations for isolation and identification do not apply in certain cases. \( B. \) \( \text{pseudomallei} \) is also intrinsically resistant to Polymyxin group of drugs. Thus unusual
In this series we have found bone and joint involvement more common than other presentations and so we feel that inoculation may be the most common mode of acquiring this infection.

The available antimicrobial agents for treating B. pseudomallei are limited. B. pseudomallei exhibits resistance to different groups of antibiotics, including several third-generation cephalosporins, penicillins, rifamycins, and aminoglycosides. In addition, its relative resistance to quinolones and macrolides limits therapeutic options.

Ceftazidime, carbapenem antibiotics (imipenem and meropenem), and to a lesser degree amoxicillin-clavulanate remain the backbone of current initial treatment. Resistance to these antimicrobial agents was not observed in 170 isolates from the Darwin prospective study, and ceftazidime resistance emerged on
therapy in only one patient. In our series 5 patients were treated with carbapenem antibiotics in the intensive phase and the rest three with ceftazidime. It has been suggested that carbapenem antibiotics may have an advantage over ceftazidime since there is less endotoxin released by dying bacteria during Imipenem treatment, and the minimum inhibitory concentration for Imipenem is lower than that of ceftazidime. Also important is the fact that carbapenems are effective against ESBL producing strains. But properly planned clinical trials are required to support or refute this contention.

Without access to appropriate antibiotics (principally ceftazidime or carbapenems), the septicemic form of melioidosis has a mortality rate that exceeds 90%. With appropriate antibiotics, the mortality rate is about 10% for uncomplicated cases but up to 80% for cases with bacteraemia or severe sepsis. Mortality is also high for patients who receive inappropriate antibiotics or delayed appropriate antibiotics. In our series, two of the patients with septicaemic melioidosis succumbed despite adequate aetiological diagnosis, appropriate antibiotics and good intensive care. In both these patients with acute melioidosis, the diagnosis was delayed by more than a month.

**Conclusion**

Melioidosis is a serious and sometimes life threatening infection which seems to be prevalent in our country and is often not diagnosed due to lack of awareness on the part of clinicians and microbiologists. The presentation of this infection is diverse as we have seen in this case series. Diabetes mellitus is an important risk factor.

**References**