International Journal of Science and Research (IJSR)
ISSN: 2319-7064
Impact Factor 2024: 7.101

A Case Series on Melioidosis: Unveiling the Clinical Spectrum and Challenges

Dr. Ipsita Paul[1], Dr. Shiva Priya Eswaran[2]

[1]M. B. B. S, DNB, Department of Microbiology, KIMS, Secunderabad, 500003 Hyderabad, India
Corresponding Author Email: *drpaul.ipsita[at]yahoo.com*

[2]M. B. B. S., MD, DNB, Sr. Consultant and HOD, Department of Microbiology, KIMS, Secunderabad, 500003 Hyderabad, India
Email: *shivapriya69[at]rediffmail.com*

Abstract: ***Melioidosis presents with a wide range of clinical manifestations, from acute localized infections to pulmonary infections (often resembling tuberculosis), acute septicaemia, and chronic suppurative infections. Below, four cases of melioidosis with varying clinical features are discussed. Case 1 involved swelling of the right shoulder, Case 2 presented with a pyogenic abscess at D10 and L4 - L5, Case 3 experienced intermittent right knee pain accompanied by fever and chills, and Case 4 had fever and a dry cough. Effective management and outcomes rely on the prompt initiation of appropriate intravenous antibiotic therapy, followed by an extended maintenance course of antibiotics.***

Keywords: Melioidosis; Burkholderia pseudomallei; Meropenem; Cotrimoxazole

1. Introduction

Melioidosis, also called Whitmore's disease, Vietnamese time bomb, is a non - notifiable infectious disease caused by *Burkholderia pseudomallei.* It is referred to as the "great mimicker" due to the wide diversity of clinical symptoms. However, it is highly under - reported, primarily due to lack of disease awareness, misdiagnosis, and lack of seeking healthcare. It is a select agent by the U. S. Centres for Disease Control and Prevention (CDC) and should be handled within a biosafety level 3 facility or equivalent. [1].

It is endemic in Malaysia, Northern Australia, Singapore, Thailand. [2] The first indigenous case from India was detected in Mumbai in 1991. From 1991 to 2018, 583 cases were reported, with the southern coastal region of Karnataka, Kerala and Tamil Nadu. Most cases have been reported from Udupi district in Karnataka. [3]. Predisposing factors include Diabetes mellitus, Chronic renal failure, Retroviral infections, travel to endemic areas (past 30 days), heavy rainfall, aerosolized soil dust, flood water exposure, injury/ accident with soil exposure, outdoor fall, road traffic accident (RTA), etc. Routes of transmission are direct contact with *B. pseudomallei* - contaminated soil or water, or via Percutaneous inoculation/ inhalation/ ingestion of the bacterium. [2]

Investigations include

1) Gram stain: Small Gram - negative bacilli with bipolar staining giving them a safety pin appearance. [4] This is shown in Figure 1 below.

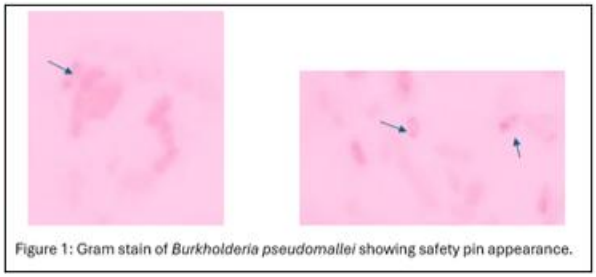

Figure 1: Gram stain of *Burkholderia pseudomallei* showing safety pin appearance.

Figure 2: White non haemolytic wrinkled colonies of *B. pseudomallei* on 5% Sheep Blood Agar

2) Culture: Gold standard for diagnosis of melioidosis, as shown in Figure 2. Serial cultures is considered in patients with a suspicion for *B. pseudomallei* infection.
3) Serological tests (paired specimens) include Indirect hemagglutination tests (Titre of >=1: 320), Immunofluorescent antibody test (IFAT), IgM and IgG ELISA, Rapid immunochromatographic test (ICT) targeting the exopolysaccharide, Lateral flow assay e. g., Active Melioidosis Detect (AMD) [2]
4) Molecular tests like T3SS - 1 real - time assay Polymerase chain reaction (PCR).

However, laboratory automated identification algorithm (e. g. MALDI - TOF, VITEK - 2) may misidentify *B. pseudomallei* as *Burkholderia cepacia, Burkholderia thailandensis. Chromobacterium violaceum, Pseudomonas* spp., *Acinetobacter* spp., *Aeromonas* spp. because the panels made for the system are small and not diverse enough and lack the addition of a select agent panel software. [2]

B. Pseudomallei is intrinsically resistant to many antibiotics including Colistin and Polymyxin B. But it is susceptible to Doxycycline, Chloramphenicol, Co - trimoxazole, Ceftazidime, Amoxycillin - clavulanic acid, Imipenem, Meropenem. It needs long - term antibiotic therapy consisting of an intensive phase of at least 2 weeks (IV Ceftazidime preferred, Meropenem or Imipenem for critically ill patients), and a maintenance phase of at least 3 months of oral antibiotics (Co - trimoxazole preferred). [5]

VACCINE DEVELOPMENT Due to lack of standardization of organism strains and dose tested, animal models, route of inoculation, and duration of follow - up, no vaccine has been trialed in a human model yet. [2]

Here, we present 4 cases of Melioidosis affecting different systems and having varied clinical features.

Case 1:
A 44 - year - old male k/c/o Type II Diabetes Mellitus was admitted with complaints of intermittent fever with chills since 18 days and swelling of right shoulder. On examination of the right shoulder there was local rise in temperature, painful range of motion (ROM), palpable distal pulses. Cultures taken at the time of admission from both the pus from right shoulder abscess and blood grew *Burkholderia pseudomallei* after 3 days of incubation, confirming the diagnosis of Melioidosis. CRP, ESR, D - dimer, and Procalcitonin were raised. Antimicrobial susceptibility Testing (AST) by automated microbroth dilution in Vitek 2.0 Compact BioMérieux yielded susceptibility to Ceftazidime, Imipenem, Meropenem and Cotrimoxazole, interpreted as per 3rd ed. CLSI guideline M45.

He was put on Inj. Meropenem 1 g. However, his clinical condition worsened, and he needed multiple inotropic support, ventilatory and dialysis support over the past 4 days. On day 4, Inj. Doxycycline 100 mg was added. As he stabilized after 2 days, right shoulder wound debridement was done and tissue was sent for cultures, which showed no growth. Symptomatically he improved and his lab investigations were also normal. He was then discharged in a hemodynamically stable condition with discharge advice: Inj. Meropenem 250 mg for 2 weeks followed by Tab. Cotrimoxazole for the next six months.

Case 2:
A 52 - year - old male previously admitted and diagnosed with pyogenic abscess D10, L4 - L5 presented with back pain and difficulty in walking since 1 month. The patient underwent L3 - S1 decompression, fixation, debridement under GA and tissue sent for culture and sensitivity. Procedure was uneventful. He was treated with IV antibiotics Cefoperazone Sulbactam 1.5 g and Inj. Teicoplanin 400 mg and other supportive medications.

Spinal tissue was sent for Culture and sensitivity. It grew non - lactose fermenting Gram negative bacilli on MacConkey agar, further identified as *Burkholderia pseudomallei* by Vitek 2.0 Compact BioMérieux. The isolate was susceptible to Ceftazidime, Imipenem, Meropenem and Cotrimoxazole. Antibiotics of the patient were changed to Inj. Meropenem 1gm IV - Twice daily. He was then discharged in a haemodynamically stable condition after a total hospital stay of 10 days with the following antibiotics:
INJ. Meropenem 1 g thrice daily X 3 WEEKS in 100 mL NS
Tablet Cotrimoxazole for 3 months.

Case 3:
A 46 - year - old male k/c/o Hypertension, Type II Diabetes mellitus presented with complaints of intermittent right knee pain associated with fever and chills since 10 days. He was managed elsewhere with knee intra - articular injections and antibiotics. On examination of Right knee, swelling, tenderness, localized warmth was present with painful range of motion (ROM). Knee aspiration fluid was sent for microbiological examination and cytology examination. He was started on Inj. Meropenem 1g and Inj. Teicoplanin 400 mg. However, the patient had sudden onset breathlessness, tachypnoea and tachycardia within 24 hours of admission for which immediate CT Pulmonary angiogram was done. CT Pulmonary angiogram showed Bilateral Lung nodules, bilateral consolidations with septal thickening – suggestive of ARDS, done in response to sudden onset breathlessness, tachypnoea and tachycardia. CRP, ESR and procalcitonin were raised.

Synovial fluid on Gram's stain had moderate pus cells and moderate short bipolar stained Gram - negative bacilli showing safety - pin appearance seen. *Burkholderia pseudomallei* was isolated from Synovial fluid after 3 days of incubation, which was sensitive to Ceftazidime, Imipenem, Meropenem and Cotrimoxazole. Inj. Cotrimoxazole and Inj. Doxycycline 100 mg were added after 4 days of admission in view of Melioidosis.

Patient was intubated after 3 days of positive culture report due to worsening respiratory distress. Inotropes were started in view of refractory hypotension. He had sudden bradycardia and cardiac arrest after 24 hours. However, he could not be revived despite all the aggressive resuscitative measures and was declared dead the next day. Cause of Death: sepsis with shock, mods - multi organ dysfunction syndrome, severe ARDS, AKI - metabolic acidosis.

Case 4:
A 64 - year - old male k/c/o Hypertension, Type II Diabetes mellitus presented with complaints of fever and dry cough since 6 months. He was evaluated elsewhere and diagnosed with pulmonary TB and started on ATT since the last 20 days. He was referred to pulmonologist for pulmonary Koch's on ATT who advised PET CT whole body with contrast. PET CT showed hypermetabolic soft tissue lesion in Right Upper Lobe and Right Lower Lobe, Pulmonary nodules, Hypermetabolic mediastinal and abdominal lymph nodes seen.

Due to continuous fever, Bronchial wash and mediastinal lymph node tissue was sent to microbiology laboratory for culture and sensitivity. GeneXpert Ultra was negative for Tuberculosis. On Gram's stain: Short bipolar stained Gram - negative bacilli showing safety - pin appearance. On culture: Non - lactose fermenting Gram negative bacilli on MacConkey agar, further identified as *Burkholderia*

pseudomallei which was sensitive to Ceftazidime, Imipenem, Meropenem and Cotrimoxazole.

Patient was started on Inj. Meropenem 1g IV - Twice daily and Inj. Doxycycline 100 mg - Twice daily IV. He was the discharged in a haemodynamically stable condition after a total hospital stay of 10 days with the following advice:
Inj. Meropenem 1gm IV - Twice daily for 2 weeks.
Tab. Cotrimoxazole 2 tab - Thrice daily at 8am, 2pm, 8pm for 3 months.

2. Discussion

Melioidosis has a wide array of clinical features ranging from acute localized infections (nodule with acute lymphangitis), Pulmonary infections (High grade fever, Chest pain, Non - productive/ productive cough), Acute septicemia (Fever, Respiratory distress, Diarrhoea, Multiple boils, Muscle tenderness, Confusion) and Chronic suppurative infection involving joints, viscera, Lymph nodes, skin, brain, liver, lungs, bones, and spleen. [2]

All the 4 cases presented with different clinical features. While Case 1 presented with swelling of right shoulder, Case 2 with pyogenic abscess D10, L4 - L5, Case 3 with intermittent right knee pain associated with fever and chills and Case 4 with fever and dry cough. This wide array of signs and symptoms make the diagnosis of Melioidosis more challenging. Recovery rate was found to be 75% where three patients were discharged in a haemodynamically stable condition while one case could not be revived.

As seen in Case 4, Melioidosis mimics tuberculosis, which is highly prevalent in India. This conclusion was like that of R. Mohanty et. al. [6], where a 73 - year - old diabetic male had a low - grade fever for 3 months and lymphadenopathy, mimicking tuberculosis and in the study done by Vidyalakshmi et. al. [7], where out of the twenty - two culture - proven melioidosis cases, eight cases mimicked pulmonary TB, five tubercular arthritis, three tubercular spondylitis, two tubercular lymphadenitis, two splenic abscess, and one each mimicked tubercular pericarditis and parotid abscess.

Of the 4 cases, 3 were known diabetic patients, thus making diabetes mellitus the most common risk factor for melioidosis (75%). This inference could be backed up by that of Vidyalakshmi et. al. [7], where 20 (90.9%) out of 22 culture proven melioidosis patients had diabetes mellitus.

In all the 4 cases, inflammatory markers like ESR, CRP and Procalcitonin was raised, with a mean of 59 mm/hr, 27.98 mg/dL and 76.3 ng/dL respectively. This is shown in Table 1. Peripheral smear showed neutrophilic leucocytosis in 100% of the cases. Thus, it can be inferred that high ESR, CRP, Procalcitonin with neutrophilia not improving with routine antibiotics should raise a suspicion of Melioidosis, which is like the findings of Vidyalakshmi et. al. [7], where all had high erythrocyte sedimentation rate (ESR) values (mean 111 mm +/ - 23.7 SD), and 68.2% had neutrophilic leuco - cytosis.

Table 1: Inflammatory markers on admission

	ESR	CRP	Procalcitonin	CBC
Case 1	71 mm/hr	19.78 mg/dL	>100ng/mL	Neutrophilic leukocytosis and toxic granules
Case 2	68 mm/hr	29.65mg/dL	72.7 ng/mL	Neutrophilic leucocytosis
Case 3	35 mm/hr	26.05 mg/dL	32.4 ng/ml	Neutrophilic leukocytosis and toxic granules and cytoplasmic vacuolations
Case 4	62 mm/hr	36.46 mg/dL	>100ng/ dL	Neutrophilic leucocytosis

3. Conclusion

Melioidosis presents with a wide spectrum of clinical manifestations, making its diagnosis challenging, as demonstrated by the varying symptoms in the four cases. These ranged from localized infections to chronic suppurative conditions involving multiple organs. The disease often mimics other infections like tuberculosis, particularly in regions like India, where TB is highly prevalent. Diabetes mellitus emerged as the most common risk factor, with 75% of the patients being diabetic. Additionally, elevated inflammatory markers such as ESR, CRP, and procalcitonin, along with neutrophilic leucocytosis, should raise suspicion for melioidosis, especially when routine antibiotics fail to improve symptoms. Despite the diagnostic challenges, the recovery rate was 75%, underscoring the importance of early detection and appropriate treatment for improved outcomes.

Acknowledgments
We declare that there are no conflict of interest.

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