

Case Report

Melioidosis: a case series from coastal Karnataka, India

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Received: 24 June 2019

Revised: 02 September 2019

Accepted: 07 September 2019

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ABSTRACT

Melioidosis is an infectious disease caused by gram negative bacteria *B. pseudomallei*. The disease is largely under diagnosed globally. Sporadic cases have been reported from India, distributed mostly in the coastal areas. Authors present a series of seven culture proven cases of Melioidosis treated at a tertiary care Hospital in the coastal city of Mangalore in South India.

Keywords: *B. pseudomallei*, Gram negative bacteria, Infectious disease, Melioidosis, Pneumonia, Vietnamese time bomb, Whitmore's disease

INTRODUCTION

Melioidosis, also known as Whitmore's disease, is an infectious disease caused by soil inhabiting gram negative bacteria *B.pseudomallei*. It is a disease of public health importance in Southeast Asia and Northern Australia.¹ Melioidosis is also largely under diagnosed globally.² In India, the disease has been on the rise and is distributed mostly in the coastal areas of southwestern India.² Here we present a series of seven cases of culture proven Melioidosis treated at a tertiary care hospital in a coastal city of Mangalore in South India.

CASE REPORT

Case 1

A 38 year old male, farmer by occupation with past medical history of type 2 diabetes mellitus presented with complaints of high grade fever and right knee joint pain and swelling since 15 days and altered sensorium since 1 day. Tubercular meningitis was suspected and a lumbar puncture and a Magnetic resonance imaging (MRI) of the brain were done and were found to be inconclusive.



Figure 1: Computerized tomography images showing enlarged liver with multiple heterogeneously enhancing thick walled hypodense lesions and a small heterogeneously enhancing ill-defined hypodense lesion in the spleen.

Concurrently right knee tubercular suppurative arthritis was suspected and a Fine needle aspiration and cytology (FNAC) of pus from the knee was done which showed features suggestive of suppurative synovial effusion. As a part of the evaluation for Pyrexia of unknown origin

(PUO), successive blood cultures were sent. Meanwhile an ultrasonogram of the abdomen and pelvis was done which showed multiple ill-defined hypoechoic lesions in the liver suggestive of abscess. Contrast enhanced computerized tomography (CECT) scan (Figure 1) done subsequently showed thick walled hypodense lesions in both lobes suggestive of hepatic abscess and multiple small splenic abscesses. Blood culture sent on the second day of admission showed growth of *B.pseudomallei*. He was administered meropenem, doxycycline and trimethoprim / sulfamethoxazole and discharged. Patient was subsequently lost for follow up.

Case 2

A 62-year-old male with past medical history of type 2 diabetes mellitus presented with lower back pain for a duration of one month. It was associated with fever, productive cough and weight loss. A diagnosis of tuberculosis was considered, and sputum Acid fast bacilli (AFB) and cultures were sent which were negative. Ultrasonogram of the abdomen showed hepato-splenomegaly with a focal lesion in the caudate lobe of liver. Chest X ray was normal, Computerized tomography scan (Figure 2) done showed loculated pleural effusion with gross splenomegaly. Pleural fluid aspiration was done and culture was positive for *B. pseudomallei*. Patient was then treated with Intravenous (IV) meropenem for 14 days with continuation regimen of doxycycline and trimethoprim / sulfamethoxazole for 12 weeks.

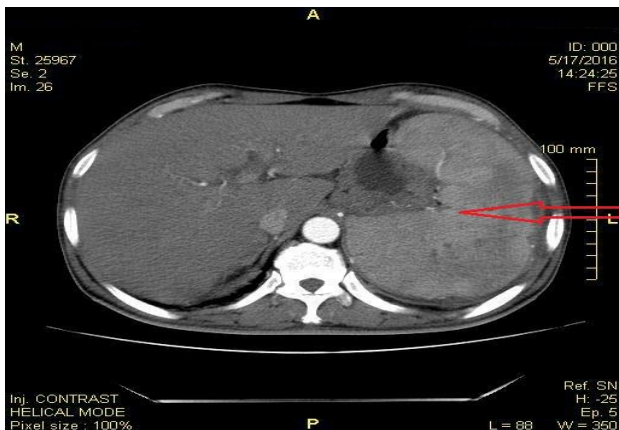


Figure 2: Computerized tomography scan showing Splenomegaly.

Case 3

A 55-year-old female came with complaints of fever, headache and loose stools since 20 days. Based on clinical suspicion, patient was diagnosed as Leptospirosis and appropriate treatment was started. Sputum acid fast bacilli, culture and blood culture were sent, blood culture subsequently showed the growth of *B.pseudomallei*. Antibiotics were changed accordingly, and patient was started on IV meropenem for 14 days followed by oral

trimethoprim / sulfamethoxazole for 4 weeks to which the patient showed significant improvement during follow up.

Case 4

An 18-year-old female with type 1 Diabetes mellitus and on active therapy for pulmonary tuberculosis, with anti-tubercular medications presented with fever since 8 days, cough with expectoration and breathlessness since 2 days. On examination, patient was tachypneic with a saturation of 96% on room air. She was started on non- invasive ventilation (NIV) and later required invasive mechanical ventilation. Chest X-ray showed right-sided pneumothorax, timely intercostal drainage tube was placed. She was started on IV piperacillin/tazobactam, clindamycin and colistin. Results of the sputum culture showed growth of staphylococcus aureus. Culture results of intercostal drainage (ICD) fluid showed the growth of *B.pseudomallei*. Hence antibiotics were changed to IV ceftazidime to which patient showed marked improvement. She was gradually weaned off the ventilator and shifted to the ward. Unfortunately she suffered a cardiorespiratory arrest due to a suspected pulmonary embolism. She was resuscitated and put back on ventilator support. At this point the patient's family requested discontinuation of treatment and the patient was discharged against medical advice.

Case 5

A 50-year-old female with recent diagnosis of type 2 diabetes mellitus presented with the complaints of fever and right hypochondrial pain since 6 days. Clinical examination of the abdomen revealed tender hepatomegaly. Ultrasonogram of the abdomen and pelvis showed features suggestive of multiple liver abscesses largest measuring 11x6cms. Computerised tomography scan (Figure 3) done subsequently showed thick walled lesions in the liver.

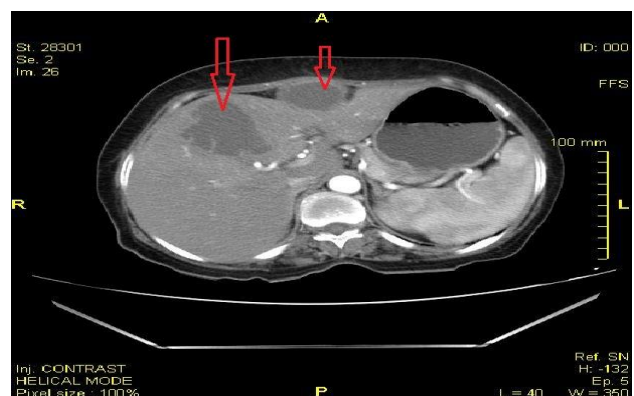


Figure 3: Computerized tomography images showing thick walled lesions in the liver.

An Amoebic abscess of the liver was suspected and hence an ultrasound guided aspiration of the contents was done and sent for culture and sensitivity. Meanwhile the

patient was started on IV piperacillin/ tazobactam and ornidazole response to which was unsatisfactory. Follow up on the culture results of the aspirated contents showed the growth of *B.pseudomallei*. The patient was then treated for Melioidosis with IV ceftazidime for two weeks constituting the intensive phase followed by oral trimethoprim/sulfamethoxazole for a period of 12 weeks as a part of continuation phase and discharged. Patient showed significant clinical improvement and resolution of the abscesses on ultrasonogram on follow up.

Case 6

A 49-year-old female, known case of type 2 diabetes mellitus, with prior hospital admission for pyrexia of unknown origin presented with complaints of generalised weakness since one week and vomiting since 4 days. Abdominal examination revealed hepatomegaly.

Ultrasonogram of the abdomen showed multiple cystic lesions in the liver, spleen. This was followed up with a contrast enhanced computerized tomography scan of the abdomen which showed resolving hepatic and splenic granulomas. Serial blood cultures were sent, one of which showed *B.pseudomallei*.

Patient was started on intensive therapy with IV meropenem for three weeks and planned for eradication therapy with trimethoprim- sulfamethoxazole for twelve weeks. However during the first week of eradication therapy she developed an allergic reaction to trimethoprim- sulfamethoxazole due to which she was switched to second line therapy with doxycycline. Patient was followed up during the course of eradication therapy with repeat blood cultures showing no growth and repeat ultra-sonogram showing complete resolution of granulomatous cysts.

Table 1: Details of the case in concise.

Age/sex	Comorbidities	Clinical presentation	Investigation	Treatment	Outcome
38/M	Type 2 DM	Fever, joint pain and altered sensorium	Ultrasound and CECT-abscesses in the liver and spleen Blood culture- <i>B pseudomallei</i>	Meropenem, Doxycycline and Trimethoprim/Sulfamet hoxazole	Recovered
62/M	Type 2 DM	Lower back pain, fever, productive cough, weight loss	Ultrasound –focal lesion in the caudate lobe of liver. CECT-gross splenomegaly and loculated pleural effusion. Pleural fluid aspirate culture sensitivity- <i>B pseudomallei</i> .	Meropenem, Doxycycline and Trimethoprim/ Sulfamethoxazole	Recovered
55/F	Type 2 DM	Fever, headache and loose stools	Chest X ray-left upper lobe consolidation Blood culture- <i>B pseudomallei</i>	Meropenem and Trimethoprim/Sulfamet hoxazole	Recovered
18/F	Type 1 DM	Fever, breathlessness, productive cough	Chest X ray-Right sided pneumothorax Sputum culture- <i>S. aureus</i> Intercostal drainage tube fluid culture- <i>B. pseudomallei</i> .	Ceftazidime	Lost for follow up
50/F	Type 2 DM	Fever, right hypochondrial pain	Ultrasound Abdomen-multiple liver abscesses Culture of aspirate- <i>B. pseudomallei</i>	Ceftazidime, Trimethoprim/Sulfamet hoxazole	Recovered
49/F	Type 2 DM	Generalised weakness and vomiting	Ultrasound Abdomen-cystic lesions in the liver and spleen. CECT abdomen-Hepatic and splenic granuloma Blood culture- <i>B.pseudomallei</i>	Meropenem, Trimethoprim/Sulfamet hoxazole Doxycycline	Recovered
57/M	Type 2 DM	Fever	Chest X ray-Right upper zone opacity. FNAC of mediastinal mass-granulomatous lymphadenitis Bone marrow biopsy- Hypocellular marrow Bronchoalveolar fluid culture- <i>B pseudomallei</i>	Ceftazidime, Trimethoprim/Sulfamet hoxazole	Recovered

Table 2: Laboratory evaluation on the day of admission.

Case no	Haemoglobin in gram/deciliter	Erythrocyte sedimentation rate in millimeter/hour	Glycated haemoglobin in percentage	Total leucocyte count in cells/millimeter cube
Case 1	10	120	10	5100
Case2	10.4	50	7	11200
Case 3	10.3	25	12	6300
Case 4	10.3	75	>13	15700
Case 5	10.5	12	11	7400
Case 6	7.6	30	>13	5000
Case 7	9.9	85	10	11100

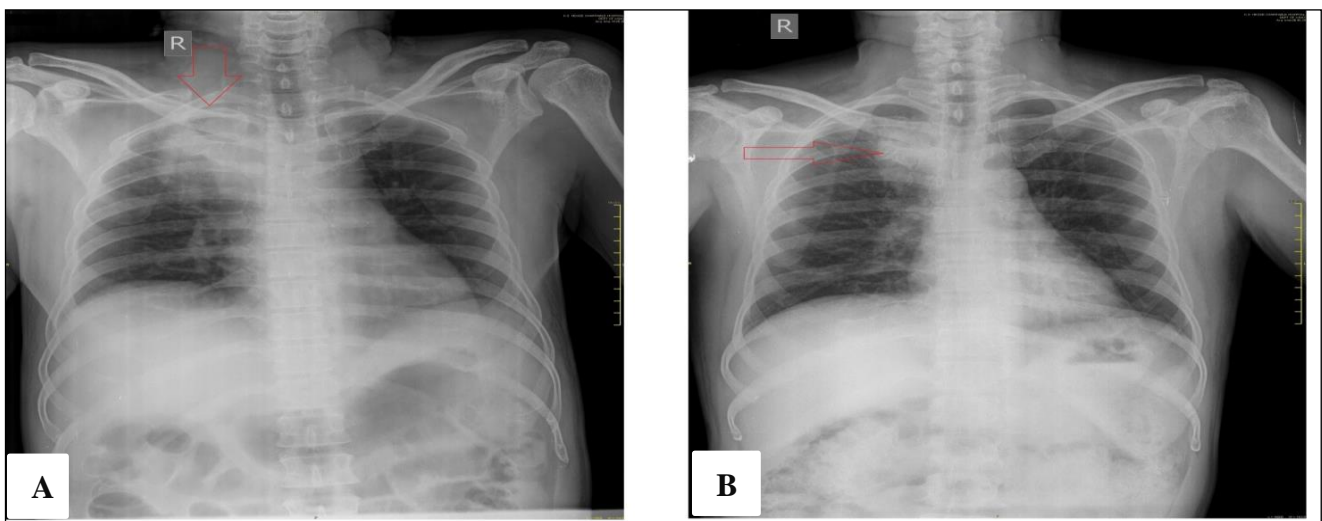


Figure 4: (A) and (B): Right upper zone opacity on admission and resolution after intensive therapy.

Case 7

A 57-year-old male, known case of type-2 diabetes mellitus presented with complaints of intermittent fever with chills since 2 months and dry cough since 5 days. clinical examination did not yield any significant findings. laboratory evaluation showed low haemoglobin (9.9g/dl). routine chest x-ray (Figure 4A) showed right upper zone opacity. The suspected mediastinal mass was evaluated with an FNAC of the mass which showed features suggestive of granulomatous lymphadenitis with necrosis suggestive of tuberculosis. Bone marrow aspiration and biopsy during that time showed hypocellular marrow and presence of inflamed fibrous tissue. Bronchoscopy was done to obtain broncho alveolar lavage fluid (BAL). BAL analysis was negative for malignant cells, AFB and gene expert. Culture and sensitivity of BAL fluid resulted in the growth of *B.pseudomallei*. The patient was treated with 14-day course of iv ceftazidime followed by oral trimethoprim/sulfamethoxazole double strength for 10 weeks. Patient

was followed up in outpatient department and was found to have improved significantly (Figure 4B).

DISCUSSION

Melioidosis was first described in 1911 by pathologist Alfred Whitmore and C S Krishnaswami. Multiple cases have been described and the disease is considered endemic in Northern Australia, Thailand, Singapore, Malaysia, Burma and Vietnam. Sporadic case reports have been reported from countries like India, Sri Lanka, Philippines. Out of the cases reported from India, most of them were from tertiary care centers owing to the resources available for diagnosis. Inoculation, inhalation and ingestion are the most common routes of transmission in the order of frequency.¹

Diabetes Mellitus, male gender, soil and water exposure have been implicated as the risk factors.¹ In our study, all of the 7 identified cases had Diabetes Mellitus. Distribution in terms of gender was equal with 4 males and 3 females.

Pneumonia is the most common presentation.³ The other modes of presentation include skin ulcers and abscesses, bacteremia and sepsis, septic arthritis or osteomyelitis and abscesses within organs. Most of our patients presented with fever and respiratory distress. While pneumonia and abscesses in the liver are rather common presentations, presentation with mediastinal lymphadenopathy is one of the rarer presentations in our study.⁴

Ash down agar containing gentamicin and ash down liquid broth containing colistin are the medias used in isolation of *B.pseudomallei*.⁵ All of the above cases were culture proven from blood, ICD fluid, aspirate from abscess and BAL fluid.

The gram-negative bacteria on bipolar staining with gram stain show what is classically described as safety pin appearance. Serologic testing by indirect hemagglutination test is another modality of diagnosis however populations in endemic areas show high false positivity. Polymerase chain reaction and rapid immunofluorescence are newer modalities not used routinely in diagnosis.⁶ Imaging modalities such as Chest radiography, ultrasonography, computerized tomography (CT) and magnetic resonance imaging (MRI) aid in establishing the diagnosis.

Treatment comprises of two phases namely intensive and continuous phase. The intensive phase is followed by a continuous phase lasting for two to three months duration. The antibiotics of choice for the intensive therapy is ceftazidime 50mg/kg upto 2g sixth hourly. carbapenems are used in patients requiring intensive care. Meropenem 25mg/kg up to 1g eighth hourly, imipenem 25mg/kg up to 1g sixth hourly is preferred due to lesser neurological adverse effects.

Also trimethoprim sulfamethoxazole is used as an add-on therapy during intensive phase. Use of chloramphenicol is obsolete due to development of resistance to the drug. High rates of treatment failures were observed with the use of intravenous co-amoxiclav.

Subsequent eradication therapy comprises of oral therapy with trimethoprim sulfamethoxazole with 160mg of trimethoprim component twice daily. Folic acid should be used as an add-on therapy both during initial intensive and subsequent eradication therapy.⁷ All our patients were treated in accordance with the standard therapy. Some of the above patients were able to be followed up to look for clinical improvement. Unfortunately few were lost to follow up. Mortality rates were higher among those with defined risk factors. However, with appropriate treatment with

antibiotics and supportive care, prognosis is good.⁸ The unique presentations of the cases described in the series emphasize the need to understand the wide spectrum of clinical presentation of the disease. Early diagnosis and treatment are paramount in the treatment of Melioidosis. Though under reported globally, it is important to bear in mind the possibility of Melioidosis in patients with pyrexia of unknown origin.

ACKNOWLEDGEMENTS

Authors express our heartfelt gratitude to the department of Medicine, K S. Hegde Medical Academy, Karnataka, India.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: Not required

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Cite this article as: Shabari MS, Ankith V, Chetan V. Melioidosis: a case series from coastal Karnataka, India. Int J Res Med Sci 2019;7:3920-4.