

## The Bug Story: Melioidosis with Candidaemia

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### Abstract

*Candida* infections, particularly Non-*Albicans Candida* (NAC) infections, are increasing in nosocomial settings. Catheter-related bloodstream infections (CRBSI) are fast becoming a significant risk to hospitalised patients. Of these, *Candida parapsilosis* is frequently isolated from blood cultures. In the context of increasing antimicrobial resistance, these infections have gained additional importance.

A 22-year-old woman with young-onset, uncontrolled diabetes presented with cough, fever, and dyspnoea for 1.5 months. Initial blood tests revealed anaemia, leukocytosis and significantly elevated HbA1C and CRP levels. Chest X-ray findings confirmed left lobar pneumonia, leading to the initiation of third-generation cephalosporins. She developed rapidly progressive hypoxia requiring intubation. Given her uncontrolled diabetes and pneumonia, a provisional diagnosis of Melioidosis, *Staphylococcus* and Tuberculosis was considered, and she was initiated on Meropenem. Following confirmation of Melioidosis, additional Trimethoprim/Sulfamethoxazole was prescribed. Despite improvements in X-ray and ventilation, the patient continued to experience persistent fever spikes. Repeat blood cultures from both central and peripheral lines grew *Candida* species. Fluconazole was started while awaiting culture sensitivity reports. However, the patient did not respond to line removal and Fluconazole treatment. Her condition worsened, leading to severe hypotension and cardiac arrest within hours. Despite resuscitation efforts, she could not be revived and died. The blood culture sensitivity report revealed *Candida parapsilosis* with fluconazole resistance.

This case highlights the importance of monitoring critically ill patients for Candidaemia (CRBSI), especially in those with central and peripheral lines. Prompt identification, removal of infected lines, along with appropriate antifungal therapy, may prevent further morbidity and mortality in these patients.

**Key words:** Catheter-related bloodstream infections, Melioidosis, Candidaemia, Non-*Albicans Candida*, *Candida parapsilosis*.

### Introduction

Melioidosis is an infectious disease caused by the bacteria *Burkholderia pseudomallei*, which is present in contaminated soil and water, and can be transmitted through direct contact. It is most commonly found in regions of South-eastern Asia and Northern parts of Australia. As the symptoms are similar to that of other tropical diseases, it is very often misdiagnosed or undiagnosed. According to a recently published article, the global annual infection rate could reach 1,65,000 individuals<sup>1</sup>. Along with this prediction, the study also suggests the disease is more prevalent in South Asia, predicting 44% of the total cases to be from there. A serosurveillance study conducted by Vandana *et al*, estimates a seroprevalence of 29%<sup>2</sup>. However, due to the limited awareness of this disease and the constraints of specific microbiology facilities and experienced microbiologists, the specific burden of this disease in India is unknown<sup>3</sup>. Melioidosis is associated with a global mortality of approximately 89,000 deaths per year. This mortality rate is comparable to other significant diseases such as Leptospirosis (50,000 deaths per year) and Dengue infection (9,100 - 12,500 deaths per year)<sup>1</sup>.

On the contrary, another infection shows a recent in emergence, which could be attributed to improved identification methods microbiologically. Infections caused by *Candida* species, particularly *Candida albicans*, are responsible for a majority of nosocomial infections. Nevertheless, there has been a rise in infections caused by non-*albicans Candida* (NAC), including *Candida parapsilosis*, which is frequently isolated from blood cultures. The significant rise in *Candida* infections can be primarily attributed to various factors, such as the AIDS epidemic, a growing elderly population, increased numbers of immunocompromised patients, and the expanded utilisation of indwelling medical devices in hospitals<sup>4</sup>. Among the list of NAC infections, the most commonly seen species are *Candida glabrata*, *Candida parapsilosis*, and *Candida tropicalis*. Of which, *Candida tropicalis* is the most prevalent in India<sup>5</sup>. According to a recent article, the prevalence of *Candida parapsilosis* in India is thought to be approximately 8.36%<sup>6</sup>. Candidaemia can cause up to 46% mortality in immunocompromised patients as well<sup>7</sup>. Hospitalised patients also have increased morbidity and mortality due to Catheter-related bloodstream infections (CRBSI). Prompt identification and removal of infected lines,

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along with appropriate antifungal therapy, may prevent further morbidity and mortality in critically ill patients.

## Case report

A 22-year-old woman with young-onset, uncontrolled diabetes presented to our department with chief complaints of fever, dyspnoea on exertion, cough with expectoration, and left-sided chest pain for six weeks.

The patient was apparently asymptomatic six weeks ago when she developed a cough with a moderate amount of white, mucoid sputum. The cough was associated with left-sided chest pain during coughing bouts. There was no history of postural or diurnal variation in the cough. She also complained of fever during the same time. The fever was intermittent and high-grade and was also associated with chills. It was relieved on taking antipyretics. She also complained of shortness of breath since 6 weeks. This was insidious in onset and progressive in nature (progressing from MMRC Grade II to Grade III over this time).

Our patient did not have complaints of orthopnoea or paroxysmal nocturnal dyspnoea. There were no complaints of night sweats or recent weight loss in the patient.

While the patient was a home-maker hailing from coastal Karnataka, she was a known case of young onset Diabetes Mellitus since 2 years. Though she was taking oral hypoglycaemic agents, she was not compliant with the medications.

On clinical examination, the patient was found to be tachypnoeic and was noted to have hypoxia. She was started on oxygen supplementation. On general



**Fig. 1:** Chest X-ray on day 1 showing left upper lobe consolidation suggestive of left upper lobe pneumonia.

examination, she did not have pallor, icterus, cyanosis, clubbing, oedema, or lymphadenopathy. Respiratory examination showed bilaterally normal vesicular breath sounds heard with crepitations in the bilateral axillary areas. The cardiovascular, abdominal, and central nervous system examination were within normal limits. She showed no cerebellar or meningeal signs.

The chest X-ray of the patient was suggestive of left upper lobe pneumonia (Fig. 1). Haematological tests revealed anaemia, increased total leucocyte count as well as increased glycated haemoglobin levels (Table I).

**Table I: Haematological tests of the patient.**

Haemoglobin	8.9 g/dL
Total leucocyte count	15.700/mm <sup>3</sup>
Platelet count	3.27 x 10 <sup>3</sup> /mm <sup>3</sup>
Liver function tests	Normal
Renal function tests	Urea - 18 mg/dL, Creatinine - 0.71 mg/dL, Sodium - 130 meq/L, Potassium - 4.4 meq/L
Glycated haemoglobin (HbA1C)	13.1%
CRP	250.69 mg/L
Procalcitonin	1.375 ng/mL

At this time, both sputum and blood cultures were ordered. She developed rapidly progressive hypoxia requiring intubation, within 24 hours of admission. Given her uncontrolled diabetes and pneumonia, a provisional diagnosis of Melioidosis/Staphylococcus/Tuberculosis was considered, and she was initiated on Meropenem. Blood culture reports showed growth of *Burkholderia pseudomallei* suggestive of Melioidosis. In view of this, the patient was given Co-trimoxazole along with Meropenem.

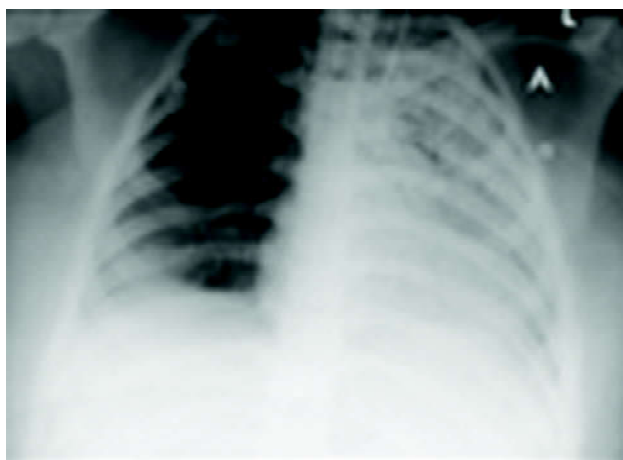
Despite being treated with Meropenem and Co-trimoxazole, she had persistent fever spikes and required continuous ventilatory support. Although chest X-rays and ventilation showed improvement (Fig. 2a and b).

Since the patient continued to have persistent fever spikes, blood cultures were repeated from both central and peripheral lines. Both of the cultures grew *Candida species* on Day 10, hence Fluconazole was started while awaiting culture sensitivity reports. On day 11, since the patient continued to need mechanical ventilation, tracheostomy was done. Patient continued to have fever spikes and blood cultures were sent again on Day 14 where they grew Gram-negative bacilli. In view of the worsening condition, Gram-negative bacterial sepsis was suspected and hence Tigecycline was added for the patient. After the addition of Tigecycline, the patient had further worsening of sepsis-Acute Kidney Injury with oliguria, hepatitis, and disseminated intravascular coagulation.

Despite removal of the lines along with Fluconazole treatment, the patient showed no improvement. Tragically, the patient's condition deteriorated rapidly within 12 hours, leading to a cardiac arrest that proved fatal, despite resuscitation efforts. The post-mortem blood culture sensitivity results indicated that the *Candida parapsilosis* isolated from her blood was sensitive to Amphotericin B and Caspofungin, while showing resistance to Fluconazole. Nonetheless, due to the timing of the report, it was not possible to implement the treatment change in time to impact the patient's clinical outcome.

## Discussion

In this case report, we present the case of a young diabetic patient with disseminated melioidosis who developed



**Fig. 2a:** Chest X-ray on day 4. **b:** Chest X-ray on day 13. The progression of these X-rays shows significant improvement of the patient's initial respiratory condition.

candidaemia and subsequently succumbed due to the overwhelming infection. This case highlights the importance of CRBSI, which refers to catheter-related bloodstream infections in critically ill patients, particularly those with diabetes and other co-morbidities. CRBSI is a type of infection that develops when bacteria or fungi enter the bloodstream through an intravenous catheter.

In present-day medical care, the usage of intravascular catheters is crucial for delivering fluids, blood products, medications, nutritional solutions, as well as monitoring haemodynamic status. However, compared to other medical devices, central venous catheters (CVCs) carry an increased susceptibility to infections associated with medical devices, which can result in notable adverse effects on morbidity and mortality rates. Hospitalised patients are particularly susceptible to bacteraemia and septicaemia, with CVCs being a primary source of these infections. Research has indicated that the majority of catheter-related bloodstream infections (CRBSIs) are linked to CVCs, with CVCs carrying a relative risk for CRBSI that is up to 64 times higher compared to peripheral venous catheters<sup>8</sup>.

The incidence rates of CRBSI varies between countries and even from hospital to hospital. In a study conducted by Singh *et al*, the infection rate for intravenous catheter-related bloodstream infections (IV-CRBSI) was determined to be 0.48 per 1,000 device days<sup>9</sup>. Furthermore, a study done at the Johns Hopkins University attributed the mortality rate for CRBSI to be between 12 - 25%<sup>10</sup>. According to a study conducted in our tertiary care centre, by Parameswaran *et al*, the incidence of CRBSI was 8.75 per 1,000 days of catheter use<sup>11</sup>. In a similar study conducted in a teaching hospital in Mumbai, providing specialised care at a tertiary level, the mortality rate in CRBSI was found to be 33.3% cases in patients having central venous catheters compared to the 20% mortality among cases of BSI in catheterised patients not associated with central venous catheters<sup>12</sup>.

Candidaemia is a common cause of CRBSI in hospital patients with the most common species being *Candida albicans*. However, Non-Albicans Candida (NAC) have seen a significant increase in incidence rates over the years. *Candida tropicalis* is the most commonly seen species of NAC along with *Candida glabrata* and *Candida parapsilosis*<sup>5</sup>. In India, the overall incidence of candidaemia was observed to be 6.51 cases/1,000 ICU admissions<sup>13</sup>. When diagnosing Candidaemia, it is important to note that *C. parapsilosis* has mixed-morphology culture plates. However, diagnostically, the organism's ability to form pseudohyphae and adhesions is also very important. *Candida parapsilosis* forms adhesions and biofilms on the surface of intravascular devices, such as catheters, and this allows them to cause bloodstream infections via indwelling

catheters and TPN.

The sensitivity of *Candida parapsilosis* to commonly used antifungal agents such as Fluconazole and echinocandins (Example: Caspofungin) is high, making these agents the first-line treatment for candidaemia caused by *Candida parapsilosis*<sup>14</sup>. Fluconazole is commonly used as a first-line drug in the treatment of candidaemia for treating patients without any prior exposure to azoles and in situations where there is no indication of colonisation with a strain that exhibits decreased susceptibility to azoles<sup>15</sup>. Both of these situations were reasons for starting our patient on Fluconazole therapy while still awaiting the blood culture reports. However, when reports became available, the patient was noted to be resistant to Fluconazole. In this case, Caspofungin was planned to treat candidaemia in the patient.

Young onset diabetes and disseminated melioidosis are in itself, responsible for significant mortality<sup>1</sup> in patients. In this case, the patient developed candidaemia, which further complicated her condition and led to overwhelming infection. Candidaemia is a serious and potentially life-threatening complication, particularly in critically ill patients. The addition of candidaemia to the patient's existing condition likely contributed to her poor outcome and eventual death.

It is concerning to note that CRBSI cases are increasing annually<sup>8</sup>. Additionally, the use of central venous catheters, prolonged ICU stay, and underlying diseases such as diabetes mellitus have been associated with CRBSI. Prompt identification and removal of infected lines, along with appropriate antifungal therapy, may prevent further morbidity and mortality in critically ill patients.

## Conclusion

CRBSI poses a substantial risk of morbidity and mortality in critically ill patients, with *Candida species* being a common cause. NAC is becoming a more widespread source of infections, especially in patients with central and peripheral lines.

Being aware of the potential risk factors and associations of CRBSI is crucial in the prevention of CRBSI. Regular monitoring of critically ill patients for CRBSI can help to identify and treat infections early, which can prevent further

morbidity and mortality.

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