

***Pandoraea pnomenusa* Bacteremia in an Acute Myeloid Leukemia Patient: A Rare and Emerging Pathogen**

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Abstract

Pandoraea species are opportunistic pathogens primarily associated with respiratory infections in individuals with chronic lung diseases. Reports of bloodstream infections caused by *Pandoraea spp.* are scarce, and there is limited understanding of their clinical implications.

We present a case of a *Pandoraea pnomenusa* bloodstream infection in a 46-year-old female, who presented to emergency department with history of fever, generalized weakness and easy fatigability and diagnosed as a case of acute myeloid leukaemia with sepsis. Blood culture revealed the presence of *P. pnomenusa*, confirmed through automated microbial identification system. To our knowledge, this is the only reported case of *P. pnomenusa* bloodstream infection in Central India in non-cystic fibrosis (CF) patient. The rarity of *Pandoraea* species causing bloodstream infections underscores the need for increased awareness among clinicians, particularly in immunocompromised patients.

Keywords: *Bloodstream infection; Emerging drug-resistant pathogens; Pandoraea spp.*

1. Introduction

Despite advancements in antimicrobial agents and sepsis management, bloodstream infections (BSIs) continue to pose a significant threat to morbidity and mortality [1]. While well-known bacterial pathogens like *Staphylococcus aureus* and *Escherichia coli* remain primary contributors to BSIs, there is a growing recognition of emerging pathogens, with the *Pandoraea* species being particularly noteworthy. Considered opportunistic pathogens, *Pandoraea spp.* have been identified in environmental samples, including soil, food, sea, and drinking water [2]. Coenye et al. first identified *Pandoraea* species in

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the early 21st century as a novel genus of gram-negative bacilli closely related to and often misidentified as *Burkholderia cepacia complex* (BCC) or *Ralstonia species* due to shared genetic similarities [3]. While these pathogens are frequently associated with lung infections in patients with cystic fibrosis or chronic lung diseases [4,5], their potential to cause systemic infections, especially bloodstream infections, remains an area of limited understanding.

In this report, we present the case of a patient with a *Pandoraea pnomenusa* bloodstream infection—a condition rarely documented in the literature. This case underscores the need for greater awareness and a deeper understanding of the clinical significance of *Pandoraea* spp. in bloodstream infections, particularly in immunocompromised patients.

2. Case Report

A 46-year-old female, resident of a village in Maharashtra, farmer by occupation presented to emergency department with history of fever, generalised weakness and easy fatigability for one month. Patient had breathlessness even on rest for the past 1 week. On general examination, pulse rate was 114/min, blood pressure 90/55 mmHg, respiratory rate of 36/min and SpO₂ was 96%. On respiratory system examination right upper zone crepitations were noted. Her complete blood count revealed total leukocytes count (TLC) of $16.52 \times 10^3/\mu\text{L}$ with 70% blasts and Haemoglobin of 6.7 gm/dl.

Based on immunophenotyping she was diagnosed as a case of Acute myeloid leukaemia, with suspected fungal pneumonia and was admitted in intensive care unit under haematology for further management. Given the patient's critical clinical condition, empirical antimicrobial therapy was initiated before obtaining baseline cultures. Patient was empirically started on Injection Colistin 9 mIU stat followed by 4.5 mIU IV 12 hourly along with Injection Meropenem 1 gm IV 8 hourly and Tab voriconazole 200 mg twice daily. The patient responded initially, becoming afebrile by day 3, with a baseline procalcitonin of 0.81 ng/mL. Noradrenaline was discontinued by day 4, and colistin was stopped on day 5. As her condition stabilized, she was initiated on Azacytidine (75 mg/m²/day for 7 days) due to coexistent sepsis and possible fungal pneumonia. Venetoclax (100 mg once daily) was later added for persistent disease. Importantly, no respiratory specimen (sputum/BAL) was obtained at this stage either. On hospital day 20, the patient developed breakthrough fever along with hypotension requiring noradrenaline support. Investigations at this stage revealed: TLC count of 1800/ μL , Neutrophil count of 270/ μL and 45% blasts. Her procalcitonin increased from 6.96 ng/ml to 11.99 ng/ml.

To investigate the fever episode, blood culture, urine culture, and sputum culture were sent. In Sputum sample, no fungal or bacterial pathogens were identified. Similarly, urine sample showed no bacterial growth. Blood culture bottle flagged positive within 24 hours of incubation in automated blood culture system. Gram staining from the positive flagged blood culture broth revealed gram-negative bacilli. Based on this finding, empirical colistin was restarted pending sensitivity results. The blood culture broth was subcultured on Blood agar and MacConkey agar. After overnight aerobic incubation at 37°C, Blood agar showed growth of nonhemolytic, grey, opaque, circular colonies while MacConkey's agar showed growth of non-lactose fermenting colonies (FIG. 1) which were catalase positive and oxidase negative.

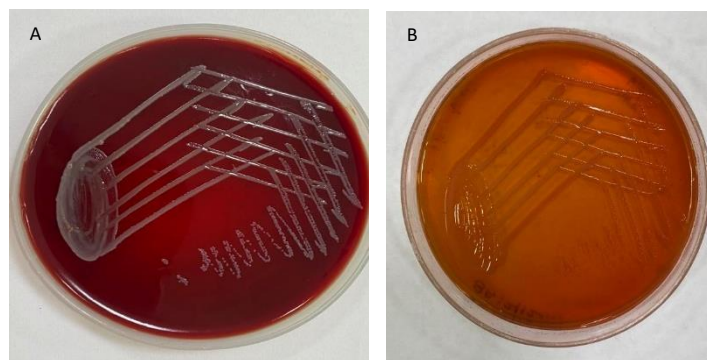


FIG. 1. A. Blood agar & B. MacConkey agar plates showing growth of *Pandoraea spp.*

After subjecting the blood culture isolate to analysis through the VITEK 2 Compact system (Biomeriux Pvt. Ltd., France), it was initially identified as *Pandoraea spp.* with a 99% confidence. Further MALDI-TOF analysis confirmed the species as *P. pnomenusa*. Antibiotic sensitivity testing as per the recent Clinical and Laboratory Standards Institute (CLSI) guidelines revealed the organism to be resistant to ceftazidime, aztreonam, meropenem, ticarcillin-clavulanate, colistin and susceptible to cotrimoxazole, imipenem, cefepime, ciprofloxacin, levofloxacin. However, no repeat blood cultures were obtained, which limited the ability to confirm persistent or transient bacteremia. Given the unusual resistance profile, targeted therapy was initiated based on susceptibility results. However, the patient's condition continued to deteriorate. Due to the absence of repeat blood cultures, it remained unclear whether *P. pnomenusa* was the primary pathogen responsible for the patient's deterioration or an incidental finding. Despite appropriate antimicrobial adjustments, the patient succumbed to gram-negative bacteremia and refractory septic shock in the setting of prolonged neutropenia and persistent AML.

3. Discussion

The *Pandoraea* genus comprises aerobic, non-spore forming, non-nitrate-reducing, non-lactose-fermenting, gram-negative rods with polar flagella. At present, human clinical samples have yielded five identified *Pandoraea* species (*P. apista*, *P. pulmonicola*, *P. pnomenusa*, *P. sputorum*, and *P. norimbergensis*), along with an additional five non-clinical species (*P. thiooxydans*, *P. oxalativorans*, *P. faecigallinarum*, *P. vervacti*, and *P. terrae*), and a minimum of four unnamed genomospecies [6]. Notably, certain organisms previously categorized as members of the Centers for Disease Control and Prevention (CDC) weak oxidizer group 2 (WO-2) have been reclassified as *Pandoraea species*. Among these, four have been isolated from blood samples, indicating their potential to cause invasive diseases [7]. *Pandoraea* strains are known for their catalase activity and the ability to thrive at temperatures of 30°C and 37°C, as well as in solutions containing 0.5% and 1.5% NaCl. These bacteria can assimilate D-gluconate, L-malate, and phenylacetate, and exhibit both acid and alkaline phosphatase activity, along with leucine arylamidase activity [3]. However, identification of *Pandoraea spp.* is difficult by conventional biochemical methods. In this particular instance, the automated bacterial identification system (Vitek 2 compact, Biomeriux) successfully identified the blood isolate as to genus level as *Pandoraea spp.* For more accurate identification, matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) was utilized, which confirmed the species as *Pandoraea pnomenusa*. This highlights the importance of incorporating advanced microbial identification techniques for the accurate detection of rare pathogens. Additionally, it is vital to update databases across diverse characterization instruments, such as automated microbial identification systems and MALDI-TOF MS to enhance the accuracy of identifying bacterial

species that may not have been extensively studied. The antibiotic susceptibility analysis in this case, revealed that the *P. pnomenusa* isolate exhibited resistance to certain antibiotics, specifically aztreonam, ceftazidime, meropenem and colistin. Notably, the isolate showed susceptibility to imipenem and other antibiotics such as ciprofloxacin, amikacin, and cotrimoxazole. Several case reports have noted instances of imipenem resistance across various *Pandoraea spp* [2,4,5].

In a practical context, the first hint regarding the potential identity of *Pandoraea spp.* could be the distinct antimicrobial susceptibility pattern to carbapenems, which seems unique among most *Pandoraea spp.* [6]. *Pandoraea spp.* has intrinsic carbapenem-hydrolyzing oxacillinases, which are responsible for carbapenem resistance [8]. In addition to oxacillinase, they were also reported to have an efflux pump mechanism that contributes to their complicated multidrug resistance ability [6].

Pandoraea spp. can be recovered from a variety of specimens, such as sputum, blood, urine, lung tissue and wounds. Most *Pandoraea spp.* were commonly isolated from respiratory samples of individuals with cystic fibrosis or other chronic lung conditions [5,6]. Instances of bacteraemia caused by these pathogens are infrequent. Historically, such cases have predominantly and exclusively been documented in developed countries due to the challenges in isolating and identifying this uncommon species. Earlier investigations have revealed cases of bacteraemia in a recipient of a lung transplant, a patient with liver cancer who underwent allogeneic liver transplantation, and an infant diagnosed with acute lymphoblastic leukemia respectively [9-11]. A study conducted in North India documented the occurrence of *P. apista* bacteraemia in an elderly diabetic man with pneumonia who tested positive for coronavirus disease (COVID) [12]. Considering these results, it is justifiable to contemplate that *Pandoraea spp.* may act as an opportunistic pathogen in individuals without cystic fibrosis.

This case highlights *P. pnomenusa*, an emerging opportunistic pathogen with intrinsic antimicrobial resistance, as a potential cause of bacteremia in an immunocompromised host. However, the organism's clinical significance in this case is uncertain due to several limitations in microbiological evaluation:

1. No baseline culture specimens were obtained before initiation of antimicrobials, limiting the ability to assess initial microbial etiology.
2. No respiratory specimen (sputum/BAL) was obtained during the first episode, preventing assessment of a possible primary pulmonary source.
3. Only a single blood culture was positive, with no follow-up cultures to confirm persistent bacteremia.
4. The causal association of *P. pnomenusa* with the patient's deterioration remains inconclusive, given multiple confounding factors, including AML progression and neutropenia.
5. Despite these uncertainties, the organism's resistance to multiple antibiotics, including carbapenems and colistin, suggests that it may act as an opportunistic pathogen capable of causing severe, life-threatening infections in immunocompromised hosts.

4. Conclusion

This case underscores the importance of timely comprehensive microbiological investigations, particularly in immunocompromised patients, to ensure accurate diagnosis and antimicrobial stewardship for improving patient outcomes. The emergence of multidrug-resistant *Pandoraea spp.* as a bloodstream pathogen raises concerns regarding its clinical

relevance, resistance mechanisms, and therapeutic challenges. Further research is needed to define its pathogenic potential, establish standardized AST breakpoints, and develop effective treatment protocols to improve outcomes in immunosuppressed patients.

5. Conflict of Interest

All authors declare no conflicts of interest in this report.

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Nil.

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