

(CASE REPORT)



Case report: Rare case *Pandoraea* ssp causing bacteremia associated with CRBSI in patients with hydrocephalus post intraventricular hemorrhage drain revision at Prof. Ngoerah Hospital, Denpasar, Bali

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Abstract

Introduction: *Pandoraea species* is a multidrug-resistant, gram-negative bacillus usually isolated from patients with cystic fibrosis (CF) and also commonly found in water and soil. Bloodstream infection with *Pandoraea ssp* in non-CF patients is uncommon. We report the first case of post-revision VP shunt hydrocephalus with bacteremia and associated CRBSI caused by *Pandoraea ssp*.

Case description: A 50-year-old Balinese man with underlying disease of sepsis by *Pandoraea ssp*. after several histories of surgery, a patient with non-communicating hydrocephalus and intraventricular hemorrhage after endoscopic Intra Ventricular Hemorrhage evacuation and revision of the proximal shunt. The patient complained of being unconscious for 2 days, slurred speech, weakness in half of the body, vomiting once, seizures, and a fever. The CVC device was installed for 20 days, and he had a fluctuating fever during the hospitalization. Ceftriaxone and levofloxacin were given intravenously for empiric treatment. *Pandoraea ssp*. were isolated from both his blood samples and exit site; once the pathogen and drug sensitivity were confirmed, levofloxacin was planned for definitive treatment. One month after the patient was admitted, his condition worsened and he was pronounced dead.

Discussion: *Pandoraea ssp*. had been reported in this patient with multiple organ dysfunction as a complicating factor. In our case, the potential source of this bacteria was considered to be contamination from the environment. This infection is considered CRBSI during hospitalization. This bacteria is multi-drug-resistant, which makes treatment of *Pandoraea* infections complicated.

Conclusion: The finding case will be beneficial to clinicians because it provides additional information about the lesser-known *Pandoraea species*.

Keywords: *Pandoraea spp*; Catheter-related bloodstream infection; Case report; Multidrug-resistant

1. Introduction

Pandoraea species were first described by Coenye et al. in 2000. [1] These organisms were obtained from human clinical samples and environmental samples, primarily from individuals with cystic fibrosis (CF). [4] The aerobic, non-sporeforming, non-nitrate-reducing, non-lactose-fermenting, gram-negative rod-shaped bacteria with polar flagella

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make up the genus *Pandoraea*. They assimilate D-gluconate, L-malate, and phenylacetate and have been cultivated at 30-37 °C in 0.5 and 1.5% NaCl or on Drigalski agar. [2] They also exhibit leucine arylamidase, catalase, and acid and alkaline phosphatase activity. [2] The genus *Pandoraea* contains five species: *Pandoraea apista* sp. nov. (the type species), *Pandoraea pulmonicola* sp. nov., *Pandoraea pnomenus* sp. nov., *Pandoraea sputorum* sp. nov. and *Pandoraea norimbergensis*. [1,4] Both CF patients and non-CF individuals may develop bacteremia from some of these pathogens. [1,4] In addition, a range of clinical samples from non-CF patients, includes blood, sputum, urine, the upper airways, and lung tissue Even so, the pathogenicity of *Pandoraea* is still not well recognized due to the paucity of available data. [2,3] In addition, the resistance of these bacteria to numerous medications complicates the management of infections associated with *Pandoraea*. Because of misidentification and varied lung settings, *Pandoraea* is rarely detected in non-CF patients³. We report the first case of post-revision VP shunt hydrocephalus with bacteremia and associated CRBSI caused by *Pandoraea* ssp. The patient's medical history, the methods used for microbiological diagnosis, the results of drug sensitivity testing, and the course of treatment were all carefully examined. Furthermore, this topic's pertinent literature was examined and debated for a better understanding.

2. Case description

A 51-year-old man presented with a complaint of unconsciousness for 2 days, difficulty in waking up, unclear speech, and weakness in the left half of his body. He denied a history of headaches, seizures, and fever. Upon initial examination, he was found to have delirium, blood pressure of 150/90 mmHg, heart rate of 68 beats per minute, and temperature of 36.5°C. He was on a ventilator, with a urinary catheter and nasogastric tube in place for nutrition. Physical examination revealed equal-sized pupils, rhonchi in the right and left lung bases, and right-sided lateralization. Laboratory results showed a white blood cell count of $14,05 \times 10^3/\mu\text{L}$, neutrophils at 84.80 %, Blood Urea Nitrogen 44,20 mg/dl, Serum creatinine 0.91 mg/dl, and procalcitonin 0,84 ng/mL. A CT scan of the head revealed intraventricular hemorrhage in the left lateral ventricle, ventricles III and IV, intracerebral hemorrhage in the occipital lobe, and communicating hydrocephalus. The patient was diagnosed with septic shock, hospital-acquired pneumonia, non-communicating hydrocephalus, IVH pan ventricular post-VP shunt, Kocher S, post-aff VP shunt keen D post-endoscopi, and IVH evacuation, irrigation, and revision of proximal shunt. The patient underwent surgery for evacuation of the intraventricular hemorrhage, irrigation, and placement of a VP shunt on the right side on June 23, 2022, and was subsequently admitted to the ICU, and ceftriaxone was administered as an empirical antibiotic for 3 days. He had a history of multiple previous head surgeries, including a craniotomy for tumor removal in 2012 and two revisions of the VP shunt in 2016 and 2022. During the hospitalization, On June 27, 2022, the patient developed a fever of 38°C, occasional cough, and inadequate contact, leading to a change in antibiotics from ceftriaxone to cefoperazone/sulbactam combined with levofloxacin supported by chest X-ray results showing pneumonia. On June 29, 2022, the patient deteriorated, experiencing persistent fever and oxygen saturation of 95% with a non-rebreathing mask at 15 lpm, necessitating intubation, ventilation, and CVC placement. A chest X-ray on June 30, 2022, showed consolidation in the lower left lung zone, suggestive of worsening pneumonia compared to previous X-rays. The patient's condition worsened on July 12, 2022, with symptoms including hypotension, decreased consciousness, and fluctuating fever. Laboratory results revealed a white blood cell count of $10,08 \times 10^3/\mu\text{L}$, neutrophils 89,60%, and procalcitonin 7,36 ng/mL. The patient received ceftriaxone therapy, and blood culture samples and sputum cultures were taken for examination. The patient was diagnosed with hospital-acquired pneumonia and underwent a tracheostomy on day 13 of treatment.



Figure 1 Chest_x-ray on July 1, 2022. consolidation in the lower left lung zone, suggestive of worsening pneumonia

Two-sided blood culture results revealed *Serratia marcescens* bacteria with antibiotic sensitivity patterns: sensitive to ceftazidime, ceftriaxone, cefepime, gentamicin, ciprofloxacin, levofloxacin, and trimethoprim/sulfamethoxazole; and resistant to ampicillin, ampicillin/sulbactam, ceftazidime, and ceftazidime sulbactam. The sputum culture results from the same date showed that *Pseudomonas aeruginosa* bacteria were sensitive to gentamicin antibiotics, ciprofloxacin, and levofloxacin. However, they were found to be intermediate resistant to antibiotics Piperacillin/Tazobactam and ceftazidime, and resistant to the cephalosporin group. (cefazolin, ceforuxime, cefixime) and ceftazidime sulbactam.

Subsequently, he developed a fever, shortness of breath, dark NGT output, and dark stool on July 21 Cultures exit site and blood on July 22, 2022, revealed gram-negative bacilli. Blood was drawn from both arms for blood cultures. Gram stain of the blood showed gram-negative bacilli.

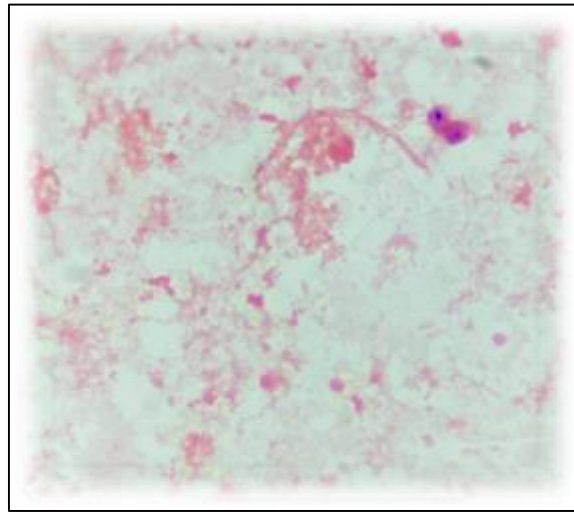


Figure 2 A number of gram-negative bacilli were found in the blood smear (Gram stain, × 100)

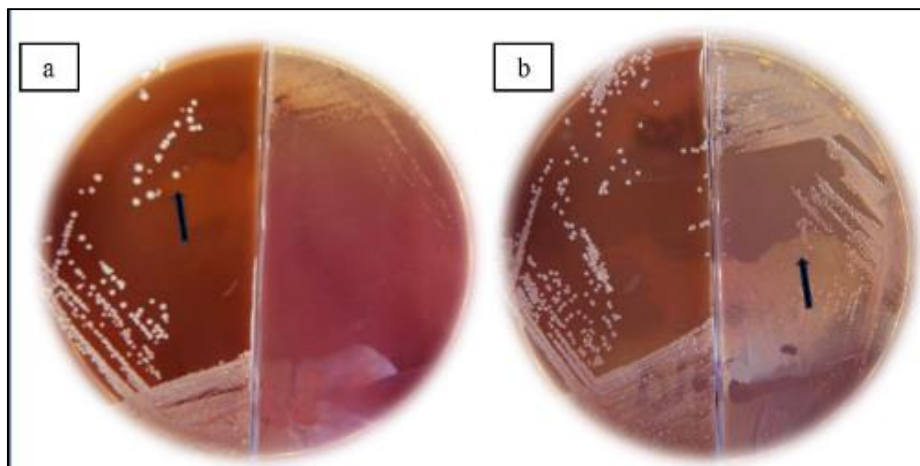


Figure 3 a *Pandora* ssp showed non-hemolysis small-sized, off-white, smooth, moist colonies on sheep blood agar. b. Small round, well-defined, non-lactose fermenter colonies on MacConkey

After 22 hours of incubation, the two blood BACTEC bottle cultures were inoculated on blood agar and MacConkey agar, the results showing the growth of one type of colony on blood agar and one colony on MacConkey. Identification tests and antibiotic sensitivity tests using VITEK-2 Antimicrobial Susceptibility Testing (VITEK 2 AST-GN67). The results of the identification of blood culture and also the exit site isolated the same bacteria, *Pandora* ssp, with The Analysis result of was 99% probability, considered significant as the causative agent of infection. Diagnosis of definite CRBSI is established based on isolating the same organism from peripheral blood and quantitative or semi-quantitative culture of catheter segments or tips⁶. Antibiotic sensitivity testing as per the recent Clinical and Laboratory Standards Institute

(CLSI) guidelines revealed the organism to be sensitive to cefoperazone/sulbactam, levofloxacin, and trimethoprim/sulfamethoxazole antibiotics. It was resistant to cefazolin, ceftazidime, cefepime, meropenem, gentamicin, tigecycline and amikacin⁵. Levofloxacin was recommended but the patient's condition worsened and he was declared dead on July 23, 2022.

3. Discussion

Pandoraea ssp are aerobic, gram-negative rod-shaped bacteria. They are non-spore forming, have polar flagella, do not reduce nitrate, and do not ferment lactose. These bacteria thrive at temperatures between 30–37 °C. ^[2] *Pandoraea* species is a newly emerging multidrug-resistant pathogen that is typically found in cystic fibrosis (CF) patients. It has been isolated from various clinical samples including blood, sputum, urine, the upper airways, and lung tissue and it has been linked to cases of bacteremia in both CF and non-CF patients. ^[2,4,7] However, there is limited data on the isolation of this pathogen from the bloodstream, largely due to either a lack of identification or misidentification. ^[5]

The patient initially presented with decreased consciousness and weakness on the left side of the body for two days, without fever, seizures, or headache. The head CT scans revealed an intraventricular hemorrhage in the occipital lobe. The patient underwent IVH evacuation, irrigation, and revision of proximal shunts. The patient had multiple head surgeries from 2012 to 2016 due to a brain tumor. In 2012, the patient underwent craniotomy for tumor removal, and the VP shunt was revised twice in 2016 and 2022. Despite this, the patient's infection appeared to be improving. After the surgery, the patient had used a ventilator and was admitted to the ICU room, then the patient complained of worsening conditions and fever, so a chest X-ray examination was performed with the results of pneumonia.

Patients with a history of multiple head surgeries and the use of shunt devices are at risk of bacterial colonization. ^[3,10] 2019 case report, Hangzhou, China reported a case of a 44-year-old man with multiple injuries, brain injury, and coma due to a fall from a height of 7 m, and performed a decompressive craniotomy and removal of traumatic intracranial hematoma, The patient, who is currently intubated and receiving ventilator-assisted ventilation, had a large number of Gram-negative rod bacteria identified as *Pandoraea apista* in a sputum specimen taken on day 5. The identification was made using MALDI-TOF MS. The report was received on day 8, but no antimicrobial susceptibility test results were available. The antibiotic regimen remained unchanged due to a lack of knowledge about this genus. ^[3]

Pandoraea species can trigger inflammatory responses and elevate interleukin 6 and 8 levels in cultures of lung epithelial cells. ^[4] Some isolates of this bacteria are capable of crossing lung epithelial cell monolayers and forming biofilms. ^[7] The recovery of *Pandoraea ssp* isolates from the blood of patients indicates that this organism is capable of invading tissue. Several virulence factors have been associated with the clinical virulence of *Pseudomonas aeruginosa* and *Bcc*, including stimulation of pro-inflammatory cytokine secretion, biofilm formation, and in the case of *Bcc*, the ability to invade lung epithelial cells, which may contribute to the persistence of the strains in the CF lung. ^[8]

Based on the lack of significant improvement in the patient's condition, it was decided to perform blood cultures and exit site cultures. Supported by the patient's lab results, it was found that the leukocyte count increased from $15.53 \times 10^3/\mu\text{L}$ on July 17 to $17.95 \times 10^3/\mu\text{L}$. The results suggest *catheter-related bloodstream infection* (CRBSI) based on blood culture and *central venous catheter* (CVC) tip culture, both showing bacterial growth of the same species and the same antibiotic sensitization pattern. According to the 2009 IDSA guidelines, it is emphasized that a definitive diagnosis of CRBSI requires the same organism growth from peripheral blood culture (not catheter) and catheter tip culture. ^[12,13] or the in vitro susceptibility testing results indicate the same resistance pattern and a DTTP of ≥ 2 hours. For quantitative blood cultures, there is a ≥ 3 -fold greater colony count of microbes grown from a blood culture obtained from a *central venous catheter* (CVC) compared to the colony count from a peripheral vein-¹³

As per the *Centers for Disease Control and Prevention* (CDC), *catheter-related bloodstream infection* (CRBSI) is a subset of a *catheter-related infection* (CRI), which includes catheter colonization, various types of local CRI, *infusion-related bloodstream infections* (IBI), and CRBSI. ^[13] Diagnostic procedures for detecting CRBSI are initiated when clinical signs of infection are present. The clinical presentation may include signs of local infection, fever, sepsis, or a combination of these. Diagnostic procedures should be consistent regardless of whether short-term or long-term catheters are used. ^[13]

Limited clinical evidence is available for *Pandoraea ssp*, and the true pathogenic nature of this genus is unknown. ^[9] The potential for invasive infection by *Pandoraea* species was suggested by blood isolates in patients without CF and further demonstrated by a report of sepsis and subsequent death in a lung transplant patient caused by *P. pnomenusa*. ^[9] There is no previous clinical description of *Pandoraea* bacteremia in patients with non-CF. This seems to be the first case report of CRBSI, but a similar case was reported in 2004 involving a 16-year-old boy with *Pandoraea bacteremia* and cystic fibrosis., the organism was previously isolated from the sputum with similar antibiotic susceptibilities, except for

trimethoprim-sulfamethoxazole. This suggests that the lung is the potential source of bacteremia. Additionally, the patient had a central venous catheter removed secondary to candidemia during the hospitalization, and the catheter could have been the route of infection. [9]

Identification of *Pandora* in blood correlated with fever and continued requirement for supplemental oxygen. [9] In the case we reported, we observed a link between the patient's fever and respiratory symptoms and clinical evidence of systemic illness indicated a requirement for aggressive treatment of this potentially fatal infection.

Pandora is resistant to most antibiotic agents in most cases, such as aminoglycosides, most β -lactam agents, and quinolones.[9,11] Most *Pandora* strains are sensitive to imipenem, tetracycline, and trimethoprim-sulfamethoxazole.[3] This isolate had susceptibility to only 3 drugs among those that were tested: cefoperazone/sulbactam, levofloxacin, and trimethoprim/sulfamethoxazole. In this case report, empirical treatment with Ceftriaxone was administered before confirming the identification of the pathogen. Based on the results of the blood culture, *Serratia marcescens* bacteria were isolated and are still sensitive to ceftriaxone. However, the results of the sputum culture also showed isolated *Pseudomonas aeruginosa* bacteria, which are intrinsically resistant to ceftriaxone. Since both of these bacteria are considered to be the causative agents of the infection in this patient, it is recommended to use levofloxacin antibiotics. However, the patient continued with ceftriaxone therapy until day 7. Research suggests that co-colonization with *Pseudomonas aeruginosa* may be another reason for the milder behavior of *Pandora* species in CF patients.[3,11,12]

The pathogenic potential of *Pandora* species is demonstrated by our patient's severe sepsis with bacteremia, *hospital-acquired pneumonia* (HAP), and multiple organ failure. The isolation of *Pandora* *ssp* from blood cultures and exit site culture during the period of hemodynamic instability and fever postoperatively, 8 days later, and at the time of death supports causality and also therapeutic options to date have been limited due to *Pandora*'s multidrug-resistant profile, and the possibility of increased resistance to antibiotics is a concern, especially in patients with CF receiving chronic antimicrobial therapy.[9]

Abbreviations

AST- GN : Antimicrobial Susceptibility Testing Gram Negative; BCC : Burkholderia Cepacia Complex; CF: Cystic fibrosis; CLSI : Clinical and Laboratory Standards Institute; CRBSI : catheter-related bloodstream infection; CRI: catheter-related infection ; CT: Computed tomography; CVC : central venous catheter ; DTTP: differential time to positivity of CVC blood culture and peripheral blood culture ; ICU: intensive care unit; IL: Interleukin; IVH : Intra Ventricular Hemorrhage ; MALDI-TOF MS : Matrix-assisted laser desorption ionization–time-of-flight mass spectrometry; NGT : Nasogastric Tube; PCT: Procalcitonin;

4. Conclusion

We have discovered that *Pandora* *ssp*. is a multidrug-resistant opportunistic pathogen. It can cause pneumonia and bacteremia through several mechanisms. While this bacterium is more commonly found in CF patients, there have been reports of infection in non-CF patients. There is evidence supporting that *Pandora* species could be more virulent in non-CF patients. The genus is usually sensitive to imipenem, tetracycline, and SMT, but susceptibility varies greatly. It is important to conduct species-level identification and antibiotic susceptibility tests. This information will be particularly useful for doctors as it provides additional insights into the less recognized *Pandora* species.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors state that this study was conducted without any commercial or financial ties that could be seen as a possible conflict of interest.

Statement of ethical approval

If studies involve the use of animal/human subjects, authors must give an appropriate statement of ethical approval. If not applicable then mention 'The present research work does not contain any studies performed on animals/human subjects by any of the authors'.

Statement of informed consent

Informed consent was obtained from individual participants included in the study.

Author Contribution

Kade Cintya contributed to the study conception and design and drafted the manuscript. and Ida Sri Iswari and I Nengah Tony revised the manuscript critically for important intellectual content. Kade Cintya and I Wayan Nirvana performed the main part of the data collection, and I Wayan Nirvana provided help with the analysis and interpretation of the patient's data.

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