

Outbreak of Nosocomial Infection from an Unusual Source

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ABSTRACT

Hospital-acquired infections have been a wide-ranging concern in the medical field, as it increases mortality and incurs longer hospital stays and higher medical costs. Infection control practices and antimicrobial stewardship are thought to be emergent measures to curtail hospital-acquired infections, but adherence to such standard practices has been a concern globally, ultimately leading to poor clinical outcomes. Organisms isolated from rare sources have been reported to cause pathogenic infections in humans. Instances such as contamination of intravenous fluids and parenteral medications with gram-negative bacteria and fungus have been reported in the past. We present here, a rare outbreak of *Ralstonia pickettii* bacteremia from an unthought source among four critically ill patients. The epidemiological investigations confirmed the source of contagion to be fentanyl ampoules. The immediate action of disusing the batch of fentanyl ampoules was taken. Timely action and isolation precautions prevented a major outbreak within the intensive care unit (ICU).

Keywords: Bacteremia, Fentanyl, *Ralstonia pickettii*.

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HIGHLIGHTS

Medical science has advanced in the last century saving lives with the usage of intravenous fluids, antibiotics, blood products, etc. However, infections arising from contaminated parenteral medications had costed lives. Treating physician should be vigilant of such outbreaks as timely identification of source and appropriate action can prevent death.

INTRODUCTION

Ralstonia pickettii is a gram-negative, aerobic, oxidase-positive, non-fermentative bacillus found in moist environments such as soil, rivers, and lakes.¹ Infections due to *R. pickettii* are very rare in healthy individuals. Although this is a low-virulence microorganism, it may be associated with bloodstream infections, mainly in immunocompromised patients.² Bacteremia mainly occurs due to contamination of medications, blood products, intravenous fluids, dialysis fluids, skin disinfectants, and water supplies.²⁻⁴

CASE PRESENTATION

Case 1

A 67-year-old male patient with no comorbidities had complaints of high-grade fever, expectorant cough, and breathlessness for 10 days. On admission to the ICU, the patient was febrile, hemodynamically stable with a Glasgow Coma Scale (GCS) of 7/15. Arterial blood gas (ABG) analysis was suggestive of type-II respiratory failure and chest X-ray showed left lower lobe consolidation. In view of worsening respiratory failure, the patient was initiated on invasive mechanical ventilation. The patient was sedated and paralyzed with injection fentanyl 100 µg/hour and injection atracurium 30 mg/hour, respectively. Sepsis screening was sent. Routine blood investigations were normal. With a provisional diagnosis of community-acquired pneumonia (CURB-65 score-3), he was started on piperacillin/tazobactam and azithromycin.

The following day, he developed fever spikes (101°F) which subsided with antipyretics. On follow-up of blood cultures,

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R. pickettii sensitive to piperacillin/tazobactam was detected. Meanwhile, his respiratory mechanics got better; hence, he was weaned and extubated and was shifted to the ward on day 4 of hospitalization.

Case 2

A 25-year-old primigravida with no comorbidities presented at 32 weeks of gestation with complaints of breathlessness and anasarca for 3 days. On examination, she was conscious, tachycardic, and tachypneic with chest X-ray suggestive of pulmonary edema. Her high blood pressure (150/90 mm Hg) and proteinuria were suggestive of preeclampsia. She was supported with non-invasive ventilation and was started on labetalol and magnesium sulfate infusion. After an hour of admission, she developed generalized tonic-clonic seizures, hence was initiated on invasive mechanical ventilation and emergency cesarean section was done. The patient was sedated and paralyzed with injection fentanyl 100 µg/hour and injection atracurium 25 mg/hour perioperatively and magnesium sulfate was continued as per protocol. Blood cultures were sent and the patient was initiated on cefoperazone/sulbactam.

On day 2 of hospitalization, she had persistent fever spikes. Following the blood cultures, *R. pickettii* was detected and was sensitive to cefoperazone/sulbactam. However, the patient died on day 3 of hospitalization because of intracranial bleed.

Case 3

A 32-year-old male patient, with no comorbidities, presented with complaints of loose stools, vomiting, productive cough, and yellowish discoloration of sclera for 3 days. His sensorium was normal. He had severe hypoxic respiratory failure; hence, he was immediately initiated on invasive mechanical ventilation and was prone. The patient was sedated with injection fentanyl 100 µg/hour and paralyzed with injection atracurium 25 mg/hour. Further evaluation revealed multiorgan dysfunction including acute liver and renal failure. Pan cultures and tropical infections screening were sent. He was empirically started on injection meropenem, capsule oseltamivir and capsule doxycycline. Despite proning, his oxygenation status did not improve; hence, he was initiated on veno-venous extracorporeal membrane oxygenation on day 6. Blood cultures sent then revealed the growth of *R. pickettii* which was sensitive to meropenem. However, the patient developed secondary bacterial infections with worsening of shock and organ failure and he succumbed to his illness on day 25 of hospitalization.

Case 4

A 43-year-old male patient, a chronic alcoholic with no comorbidities, presented with complaints of abdominal pain for 5 days. He had elevated serum amylase (569 U/L) and lipase (989 U/L) levels pointing towards the diagnosis of acute severe pancreatitis. He had altered renal function with anuria warranting intermittent hemodialysis. The patient was empirically started on piperacillin/tazobactam.

On day 2, he had a cardiac arrest secondary to high anion gap metabolic acidosis and was revived after 4 cycles of cardiopulmonary resuscitation. The patient was initiated on invasive mechanical ventilation and sedated with injection fentanyl 100 µg/hour. The contrast-enhanced computed tomography (CECT) abdomen revealed severe necrotizing pancreatitis. The following day, the patient had persistent fever spikes and became hemodynamically unstable. Blood cultures were sent and antibiotic was escalated to meropenem. Since his sensorium remained poor after cessation of sedation, magnetic resonance imaging (MRI) brain was done which revealed severe hypoxic-ischemic encephalopathy. Blood cultures grew *R. pickettii* and was sensitive to meropenem. The patient underwent tracheostomy on day 10. Repeat blood cultures on day 13 were sterile and the patient was shifted to the ward with oxygen support for further management.

DISCUSSION

Ralstonia pickettii is a low-virulence, water-borne, and gram-negative bacillus that has been identified as an emerging opportunistic pathogen. It was first isolated in 1973 and was included in the genus *Pseudomonas*. Subsequently, it was reclassified into the genus *Burkholderia*, and the genus *Ralstonia* was named in 1995.²

Conditions associated with *R. pickettii* range from minor infections to severe invasive infections in critically ill patients such as pneumonia, endocarditis, peritonitis, and catheter-associated infections.^{1,3,5} Infections with *R. pickettii* were reported due to the use of contaminated magnesium, heparin, ranitidine, blood products, chlorhexidine, and saline solution as well as the colonization of medical devices.^{6,7} Contamination may occur during the manufacturing phase as *R. pickettii* can pass through 0.2 and

0.45-micron (µm) filters used for the sterilization of medicinal products.^{1,3}

Four patients in our ICU had *R. pickettii* bacteremia and were treated with sensitive antibiotics. An immediate meeting was conducted with representatives from the ICU, microbiology and pharmacy departments. The unusual pathogen in blood culture leads to an investigation for identifying the source of the microbe. As all four patients had received fentanyl (10- and 2-mL ampoules), Atracurium (2.5-mL ampoules) and intravenous fluids (Kabilyte, 0.9% normal saline), we examined the samples of respective batches. Water supplies and skin disinfectants were also analyzed. Significant growth of *R. pickettii* was detected in 10-mL fentanyl ampoules. Hospital authorities and the manufacturing company were notified about this outbreak and 10-mL fentanyl ampoules of the respective batch were recalled as per the procedure. No further infections with *R. pickettii* were found in patients.

The treatment of *R. pickettii* infections is often challenging as there are no standard recommendations regarding the choice of drug or duration.^{8,9} The presence of two inducible β-lactamases (blaOXA-60, blaOXA-22) has been reported to be responsible for the high level of resistance to β-lactams, also presence of aminoglycoside acetyltransferase explains the widespread resistance to aminoglycosides. The study conducted by Ryan et al. concluded that sulfamethoxazole/trimethoprim and ciprofloxacin are the best antimicrobials to treat infections with *R. pickettii*.^{1,3,10} However, the majority of the reported infections are treated with piperacillin-tazobactam, meropenem, or a combination of cephalosporins and aminoglycosides with good results.

CONCLUSION

In conclusion, four cases of mechanically ventilated patients developed bacteremia from fentanyl contaminated with *R. pickettii* and were treated with sensitive antibiotics. When bacteremia with *R. pickettii* or other unusual isolates are detected, medical product contamination should be suspected, and an epidemiological investigation should be initiated, which includes the microbiological examination of the administered intravenous fluids, medications, dialysis fluids, skin disinfectants, and water supplies. Although *R. pickettii* is thought to be a rare infectious organism, it is important to quickly recognize and treat as it has been identified as causing many potentially harmful infections resulting in increased morbidity and mortality.

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