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Colistin-Induced Acute Kidney Injury in the Treatment of Extensively Drug-Resistant Klebsiella Pneumoniae: A Case Report

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Abstract

This case report describes a 59-year-old male with uncontrolled type 2 diabetes mellitus who presented with recurrent urinary tract infections caused by multi-drug resistant Klebsiella pneumoniae. The patient's condition progressed from initial sensitivity to ceftazidime-avibactam to eventual resistance, leaving colistin as the only effective antibiotic. During the 19-day course of colistin therapy (900 mg daily), the patient developed severe acute kidney injury, with serum creatinine rising from 1.3 to 10.1 mg/dL, and colistin-induced peripheral neuropathy. Following discontinuation of colistin, partial renal recovery was observed, with creatinine decreasing to 2.5 mg/dL. This case highlights the challenges in managing extensively drug-resistant infections, the limited treatment options available, and the significant adverse effects associated with last-resort antibiotics like colistin. It underscores the urgent need for new antimicrobial strategies and emphasizes the importance of careful monitoring during treatment with potentially toxic antibiotics.

Keywords: Colistin-Induced, Klebsiella Pneumoniae, India

Introduction

Klebsiella pneumoniae, a Gram-negative bacterium, belonging to the Enterobacterales family, is a natural inhabitant of the gastrointestinal tract of humans and animals. Nevertheless, it is also encountered as a nosocomial pathogen causing various infections such as pneumonia, urinary tract infection and bloodstream infection. It is a significant pathogen responsible for infections with high mortality and morbidity rates, particularly in hospitalized and immunocompromised patients. This microorganism possesses a diverse arsenal of resistance mechanisms against multiple antimicrobial classes, including beta-lactams, fluoroquinolones, and aminoglycosides. Traditionally, K. pneumoniae (Kp) has been known to cause opportunistic infections in vulnerable populations such as immunocompromised individuals, the elderly, newborns, and patients with indwelling medical devices. However, the situation has become increasingly concerning due to the remarkable ability of Kp strains to acquire antimicrobial resistance genes. The evolution of multi-drug resistant *K. pneumoniae* (MDRKP) strains, defined as those resistant to three or more categories of antimicrobial agents, has created a mounting global challenge in selecting effective antibiotics for treating hospital-acquired infections. This rapid development and spread of multidrug-resistant K. pneumoniae strains pose a substantial threat to public health, challenging current treatment strategies and necessitating urgent action to address this growing crisis [1, 2]. The rise of MDRKP in healthcare settings can be attributed to several factors: The acquisition of novel resistance genes, widespread use of invasive medical devices, suboptimal diagnostic and surveillance systems, compromised immune states in patients, and injudicious antibiotic use. This confluence of factors has led to a critical situation that demands urgent attention and coordinated efforts to combat the spread of these highly resistant pathogens.

Multi-drug resistant Klebsiella pneumoniae (MDRKP) is defined as strains exhibiting resistance to three or more antimicrobial categories that would normally be active against this bacterium. This typically involves key antibiotic classes such as

extended-spectrum cephalosporins, carbapenems, fluoroquinolones, and aminoglycosides. The classification is determined through standardized. Furthermore, the concept of multi-drug resistance exists on a spectrum, with extensively drug-resistant (XDR) and pan-drug resistant (PDR) strains representing even more severe cases with extremely limited treatment options. The emergence and spread of MDRKP pose significant clinical challenges and underscore the urgent need for new therapeutic strategies and enhanced infection control measures [3, 4]. Klebsiella pneumoniae employs several mechanisms to achieve antimicrobial resistance, with enzymatic inactivation of antibiotics being a primary strategy. The production of extended-spectrum β-lactamases (ESBLs) and carbapenemases are particularly concerning. ESBLs, such as CTX-M, SHV, and TEM types, hydrolyze a wide range of β-lactam antibiotics, including third-generation cephalosporins. Carbapenemases, like KPC, NDM, and OXA-48, confer resistance to almost all β-lactams, including carbapenems. Other mechanisms include the modification of antibiotic targets (e.g., alterations in penicillin-binding proteins), the upregulation of efflux pumps that expel antibiotics from bacterial cells, and changes in outer membrane porins to reduce antibiotic entry. Additionally, K. pneumoniae can acquire plasmid-mediated resistance genes, enabling rapid spread of resistance within bacterial populations. These mechanisms often coexist, leading to multi-drug resistance and severely limiting treatment options [5, 6, 7, 8].

Multiple risk factors contribute to the development and spread of multi-drug resistant Klebsiella pneumoniae (MDRKP) infections in healthcare settings. Prolonged hospital stays increase exposure to nosocomial pathogens and create opportunities for colonization and subsequent infection. Immunosuppression, whether due to underlying medical conditions, medications, or interventions like chemotherapy, compromises the body's natural defenses against bacterial invaders. The use of invasive medical devices, such as central venous catheters, urinary catheters, and mechanical ventilators, provides potential entry points for bacteria and surfaces for biofilm formation. Prior antibiotic exposure, particularly broad-spectrum or prolonged courses, can disrupt the normal microbiota and selectively pressure resistant strains. These factors often coexist in critically ill patients, synergistically elevating the risk of MDRKP infections. Recognition of these risk factors is crucial for implementing targeted prevention strategies and early intervention in high-risk populations [9, 10]. We present a case of a 59-year-old male with recurrent urinary tract infections (UTIs) caused by multi-drug resistant Klebsiella pneumoniae (MDRKP). Initial antimicrobial susceptibility testing revealed sensitivity to Ceftazidime-Avibactam and Aztronam. However, subsequent testing in recurrent UTI demonstrated further resistance development, with the isolate eventually exhibiting sensitivity only to colistin. Given the limited treatment options, the patient was initiated on colistin therapy at a dose of 900 mg once daily. The treatment course extended for 19 days. During this period, the patient developed acute kidney injury (AKI) evidenced by a progressive elevation in serum creatinine levels from a baseline of 1.3 mg/dL to a peak of 10.1 mg/dL. This case highlights the challenges in managing MDRKP infections, the potential for rapid development of antibiotic resistance, and the significant adverse effects associated with last-resort antimicrobial agents such as colistin.

Case Report

A 59-year-old male with a history of uncontrolled type 2 diabetes mellitus (diagnosed in 2015) presented to the Department of Nephrology on September 15, 2023, with complaints of abdominal pain and vomiting for two weeks. Initial evaluation revealed borderline renal function and pyuria without bacteriuria on urine culture. Given the prolonged history and culture-negative status, empirical treatment with intravenous Meropenem was initiated, resulting in improvement of serum creatinine from 2.2 to 1.0 mg/dL. During follow-up, the patient exhibited uncontrolled blood glucose levels, worsening renal function, and persistent pyuria. In October 2023, urine culture grew multi-drug resistant (MDR) Klebsiella pneumoniae, sensitive to Ceftazidime-Avibactam and Aztreonam. The patient received a 10-day course of this combination, followed by oral Fosfomycin prophylaxis. The patient remained asymptomatic until the first week of February 2024, when he developed loose stools and bilateral lower and upper limb weakness. Laboratory tests revealed severe hyperkalemia (K+ 9.1 mEq/L) and urine culture again positive for Klebsiella. Treatment with Ceftazidime-Avibactam and Aztreonam was reinitiated for two weeks, followed by oral Chloramphenicol. However, symptoms recurred, leading to discontinuation of Chloramphenicol on February 23, 2024.

On April 4, 2024, the patient developed community-acquired pneumonia, which responded to Cefoperazone-Sulbactam and Levofloxacin. He was readmitted on April 22, 2024, with recurrent fever and chills. Evaluation showed pyuria with elevated white blood cell count. Abdominal ultrasound and plain CT revealed a narrow left ureteric orifice with pus discharge. Left ureteric stenting was performed on April 25, 2024. Urine culture from the ureteric sample showed heavy growth of Klebsiella, now sensitive only to Colistin and resistant to Ceftazidime, Avibactam, and Aztreonam. Further investigations included urine GeneXpert for tuberculosis (negative) and urine next-generation sequencing, which did not reveal Mycobacterium tuberculosis. Ultrasound showed post-void residual urine of 6 cm, prompting plans for catheter-based drainage.

On May 13, 2024, the patient was readmitted with fever, disorientation, and altered sensorium. Vital signs showed tachycardia (110 bpm), hypertension (160/90 mmHg), and tachypnea (22 breaths/min). Initial investigations revealed severe hyponatremia (sodium: 111 mEq/L) and necessitating transfer to the Medical Intensive Care Unit. Given the limited treatment options, colistin therapy was initiated at 900 mg once daily. The treatment course lasted 19 days, during which the patient also received 3% saline infusion and other supportive measures. A PET-CT on May 22, 2024, showed no evidence of metabolically active lesions suggestive of infection. Nerve conduction studies on June 4, 2024, revealed sensory-motor axonopathy affecting lower limb nerves and bilateral distal median sensory-motor neuropathy, possibly Colistin-induced. Neurological consultation was obtained for this complication. During Colistin treatment, the patient's serum creatinine progressively increased from 1.3 to 10.1 mg/dL over 19 days. Colistin was discontinued on June 1, 2024, after 19 doses. The patient's condition improved symptomatically, and he was discharged with close follow-up. In subsequent follow-up, his renal function improved, with serum

creatinine decreasing to 2.5 mg/dL.

This case highlights the challenges in managing recurrent urinary tract infections caused by MDR Klebsiella pneumoniae, the evolution of antibiotic resistance, and the significant adverse effects associated with last-resort antibiotics like colistin, including nephrotoxicity and peripheral neuropathy.

Discussion

Colistin, an antibiotic first discovered in 1949, is derived from a specific subspecies of *Bacillus polymyxa* known as colistinus. It was introduced for clinical use in the 1960s, marking an important addition to the antimicrobial arsenal. However, its prominence was short-lived; within a decade, colistin was largely supplanted by newer antibiotics perceived to have more favorable safety profiles.

In recent years, however, the antibiotic landscape has dramatically changed. The global emergence of multidrug-resistant Gram-negative bacilli (MDR-GNB) has posed a significant threat to public health. Particularly problematic pathogens include *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, and *Klebsiella pneumoniae*. Compounding this issue is the notable lack of new antibiotic development, especially those effective against these resistant organisms. Consequently, there has been resurgence in the use of colistin worldwide. This revival of an older antibiotic underscores the critical need for effective treatments against MDR-GNB infections, even when faced with potential toxicity concerns [11].

Colistin administration is associated with a notable risk of nephrotoxicity, with acute kidney injury (AKI) being a significant concern. Several factors have been identified that increase the likelihood and severity of colistin-induced AKI. Advanced age, the need for vasopressor support, and pre-existing chronic kidney disease (CKD) are key risk factors for developing AKI. Furthermore, older age and vasopressor requirement are specifically linked to a higher incidence of Stage 3 AKI, the most severe form. The temporal aspects of colistin-induced nephrotoxicity are crucial for clinical management. Typically, AKI manifests relatively quickly, with a median onset time of 4 days after initiating colistin therapy. This rapid development underscores the importance of vigilant monitoring of renal function. Healthcare providers should implement early and regular assessments of kidney function immediately upon commencing colistin treatment.

Recovery from colistin-induced AKI, while possible, can be protracted. The median time to recovery is approximately 10 days, highlighting the potentially prolonged impact on renal function. This extended recovery period emphasizes the need for continued monitoring and supportive care even after discontinuation of colistin therapy [12]. These findings underscore the critical importance of judicious use of colistin, careful patient selection, and rigorous monitoring protocols to mitigate the risk of severe and potentially irreversible kidney damage.

Conclusion

This case report illuminates the complex challenges in managing recurrent urinary tract infections caused by multi-drug resistant Klebsiella pneumoniae in a patient with underlying comorbidities. It highlights the rapid evolution of antibiotic resistance, necessitating multiple changes in antimicrobial therapy, and underscores the limited treatment options available for extensively drug-resistant organisms, ultimately leading to the use of colistin as a last resort. The case vividly demonstrates the significant adverse effects associated with colistin therapy, particularly nephrotoxicity and neurotoxicity, emphasizing the crucial need for close monitoring of renal function and neurological status during treatment. The partial recovery of renal function post-treatment offers a glimmer of hope, while also underlining the potential long-term impacts of such aggressive therapies. This case emphasizes the urgent need for new antimicrobial agents, alternative treatment strategies, and the importance of antibiotic stewardship to prevent the emergence of resistant strains. It also highlights the necessity of a multidisciplinary approach in managing such complex cases. Moving forward, research should focus on developing novel antimicrobials with improved safety profiles, exploring combination therapies, and investigating strategies for early detection and prevention of colonization with resistant organisms in high-risk patients. This case serves as a stark reminder of the ongoing challenges posed by multi-drug resistant infections and the critical importance of judicious antibiotic use in clinical practice.

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