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CASE REPORT

Purplish Discoloration of Urine in a Patient Receiving Cefiderocol: A Rare Adverse Effect

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Abstract

Drug-induced urine discoloration, although usually benign, can still raise concern in healthcare facilities. This case report presents the second case of purple urine discoloration associated with cefiderocol in a 64-year-old male admitted to the intensive care unit for ventilator-associated pneumonia. The patient required broad-spectrum antibiotic treatment with vancomycin, cefiderocol, amikacin, and micafungin. On the fourth day after initiating antibiotics, the presence of purplish urine in the foley bag was noted. Urinalysis showed 11−25 red blood cells/hpf, but cultures ruled out urinary tract infection. Further laboratory workup did not reveal any evidence of hemolysis or rhabdomyolysis. Cultures from the endotracheal aspirate grew multidrug-resistant Pseudomonas. Cefiderocol and amikacin were continued to complete a seven-day course. Two days after completion of the cefiderocol course, the urine discoloration cleared up, providing strong evidence that cefiderocol was the cause of the discoloration.

Keywords: Cefiderocol, Purple urine discoloration, Urinary tract infection, Purple urine bag syndrome

1. Introduction

While drug-induced urine discoloration is largely benign, it is important to maintain a broad differential and consider potential severe or life-threatening conditions.[1] Accurate interpretation of clinical data, with close attention to associated symptoms such as pain, fever, or dysuria, is helpful in narrowing the list of potential causes. Obtaining basic urine tests, including urinalysis and urine culture, is recommended to eliminate the possibility of any related urinary tract infections (UTIs), which can have higher mortality in the older population.[1,2]

Cefiderocol is the first siderophore cephalosporin approved for treating multidrug-resistant Gram-negative bacterial infections. It is stable against all four classes of β-lactamases and exhibits excellent in vitro activity against various clinically significant Gram-negative bacteria.[3] The kidneys are responsible for the vast majority of its elimination, and typical doses have not been shown to induce urine discoloration.[4] Only one case of dose toxicity involving this drug has been documented.[5] This case describes a rare instance of purplish urine discoloration induced by cefiderocol.

2. Case presentation

A 64-year-old man with multiple medical conditions, including trisomy 21, hypothyroidism, adrenal insufficiency, seizure disorder, and chronic respiratory failure, was admitted to the medical intensive care unit (ICU) for ventilator-associated pneumonia (VAP). He had been in an acute rehabilitation facility for ventilator weaning, with baseline ventilator requirements as follows: Pressure support ventilation (PSV) with positive end-expiratory pressure (PEEP) of 10 mm Hg, pressure support (PS) of 15 mm Hg, and FiO2 of 50%. Over the prior two days, he developed increasing secretions that led to a desaturation event. He was put on a bag and mask ventilation with 100% FiO2, and a rapid response was called.

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The patient had a history of multiple episodes of VAP from Pseudomonas with difficult-to-treat resistance (DTR-P). Earlier that month, he had two episodes of DTR-P-related VAP requiring 7-day courses of cefiderocol and amikacin. His chronic medications included acetaminophen, enoxaparin, hydrocortisone, levetiracetam, levothyroxine, oxycodone, and pantoprazole.

On admission, his vital signs were notable for a heart rate of 70 bpm. The patient was afebrile and hypotensive, with a blood pressure of 94/54 mm Hg. He required an assist-control mode of ventilation with volume control (VC) and his initial settings were as follows: tidal volume (Tv) of 400 mL, respiratory rate (RR) of 24 breaths/min, PEEP set to 14 mm Hg, and fraction of inspired oxygen (FiO2) of 100%. Physical examination revealed an obese man with thick secretions around the tracheostomy site and decreased breath sounds bilaterally.

Laboratory workup, including a complete blood count, showed a hemoglobin level of 8.5 g/dL (baseline 8–9 g/dL), a white cell count of 8.5 K/mcL (compared to baseline values of 4 K/mcL), and a platelet count of 218 K/mcL. The lactate level was 1.4 mmol/L. Arterial blood gas (ABG) analysis revealed a pH of 7.33 with a pCO2 of 66 mm Hg, pO2 of 90 mm Hg, bicarbonate of 34 mmol/L, and SaO2 of 96.5%. A CT angiography (CTA) of the chest showed multifocal pneumonia but no evidence of pulmonary embolism.

The patient required vasopressor support and was empirically treated with broad-spectrum intravenous antibiotics, including vancomycin, cefiderocol (1 g q8h), and amikacin (7.5 mg/kg q8h). With little clinical improvement over the next day, micafungin was added to the treatment regimen. MRSA nasal cultures were negative and the patient began to exhibit signs of clinical improvement. Hence, vancomycin and micafungin were discontinued. On day five of treatment, the urine became dark purple (Fig. 1). Urine output was low despite positive fluid balance. Kidney function was stable, with creatinine ranging from 0.4 to 0.5 mg/dL (baseline: 0.4 mg/dL). Serum bilirubin was within normal limits (0.8 mg/dL). Urinalysis showed 6–10 white blood cells/hpf (normal: 0–5/hpf) and 11–25 red blood cells/hpf (normal: 0–2/hpf) with trace amounts of blood. The urinalysis was negative for bilirubin, urobilinogen, ketones, nitrites, or leukocyte esterase. Urine cultures showed no bacterial growth. Renal ultrasound results were normal, with no evidence of hydronephrosis or bladder pathology.

Cultures of the endotracheal aspirate indicated the presence of DTR-P. Cefiderocol and amikacin treatment was continued for the full seven-day course, and the urine discoloration cleared up two days after completion of the cefiderocol course. A follow-up urinalysis showed resolution of hematuria. The patient was discharged back to the acute rehabilitation facility. Despite appropriate management, the patient's respiratory status further deteriorated, leading to another episode of VAP. Unfortunately, he passed away due to the severity of his condition.

3. Discussion

Purplish discoloration of urine can have various underlying causes, including trauma, malignancy, renal stones, acute intermittent porphyria, and certain foods and medications like beets, hydroxycobalamin, sennosides, phenazopyridine, and rifampin.[6,7] In some cases, the discoloration is associated with UTI, particularly in long-term bedridden patients with an indwelling urinary catheter, a condition known as purple urine bag syndrome. Factors that increase the risk of this syndrome include female sex, chronic catheterization, immobility, dementia, chronic constipation, chronic renal disease, alkaline urine, increased bacterial load in the urine, and the use of certain urine bags made of polyvinyl chloride.[8,9] Similarly, increasing cases of drug-induced urine discoloration are being reported. Cefiderocol has been associated with chromaturia in animal studies, albeit rarely observed in human cases.[5] The discoloration is attributed to the renal clearance of cefiderocol-ferric ion complexes in basic pH conditions.[5] Another potential mechanism could be hematuria related to the medication.

Our patient had significant risk factors for purple urine bag syndrome such as being bedridden and having an indwelling catheter. However, laboratory data ruled out UTI, effectively excluding the syndrome. Additionally, blood counts and bilirubin levels were within normal range, and urinalysis showed no evidence of pigments, making blood loss, hemolysis, or rhabdomyolysis unlikely as the cause. The discoloration of urine was attributed to cefiderocol, as it began a few days after starting the treatment (approximately 12 doses), subsequently improved after the last dose and eventually fully resolved with the discontinuation of the drug. To the best of our knowledge, this is only the second reported case of purplish urine discoloration following cefiderocol treatment. Further cases are required to ascertain if this discoloration is considered a rare adverse event or an incidental finding, and whether this condition is dose-dependent.

Drug-induced urine discoloration is usually benign. However, it can be concerning for patients,

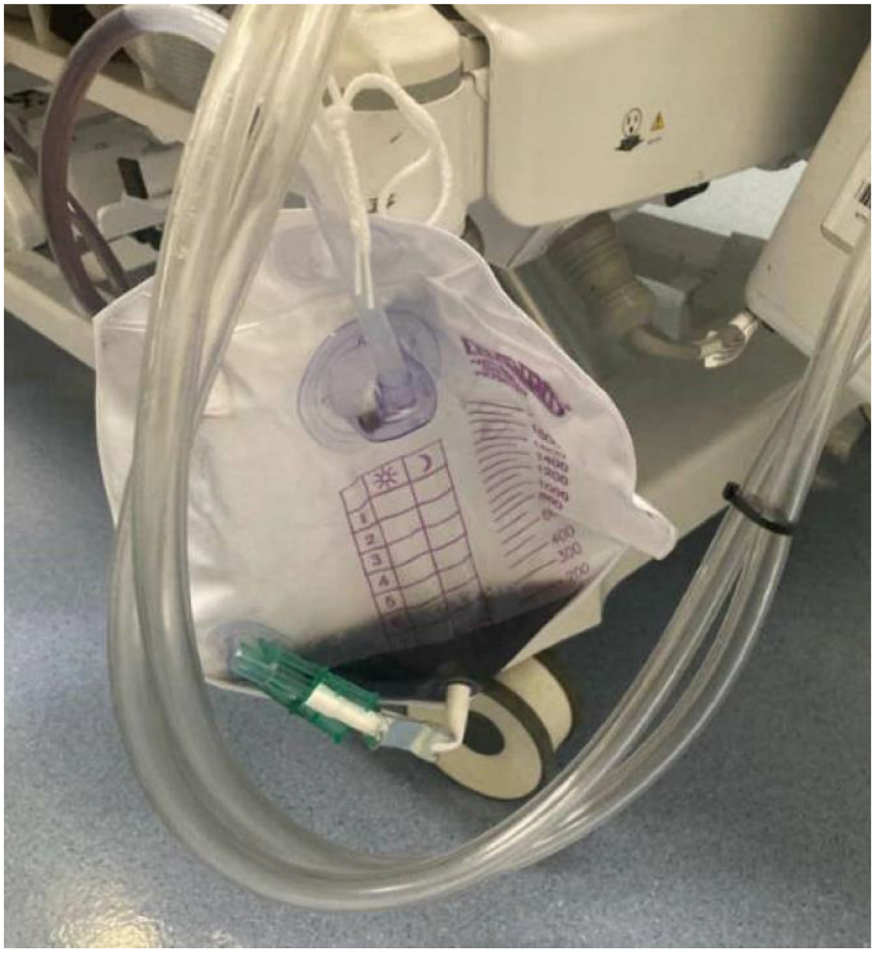

Fig. 1. Foley bag demonstrating Purplish Discoloration of Urine.

family members, and healthcare staff. Therefore, understanding this condition is paramount as it does not always indicate an underlying condition and could lead to unnecessary clinical investigations, such as cystoscopy. While there is no established consensus on managing asymptomatic drug-induced urine discoloration, one approach is to wait for the discoloration to resolve after discontinuing the medication.[10]

4. Conclusion

Thus, we presented a rare instance of cefiderocol-induced urine discoloration, which is only the second reported case in the literature. We underscore the importance of considering medication adverse effects in the differential diagnosis for urine discoloration. While drug-induced urine discoloration is generally benign, it is crucial to comprehensively investigate and rule out other potential causes, such as UTI, blood loss, or hemolysis, to avoid overlooking a critical diagnosis.

Conflict of interest

The above authors have no potential conflicts of interest or sources of financial support.

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