

CASE REPORTS

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Case report
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PURPLE URINE BAG SYNDROME – A SIGN OF URINARY TRACT INFECTION, OR JUST OF URINARY CATHETER BACTERIAL COLONIZATION – A CASE REPORT

SINDROM LJUBIČASTE KESE ZA URIN – ZNAK URINARNE INFEKCIJE ILI SAMO BAKTERIJSKE KOLONIZACIJE URINARNOG KATETERA – PRIKAZ SLUČAJA

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Summary

Introduction. Purple urine bag syndrome is a condition where the urinary catheter bag turns purple as a result of the interaction between bacteria, urine and components of the urine bag. It appears in a certain group of patients with the following risk factors: urinary tract infection, older age, long-term indwelling urinary catheter, constipation, chronic kidney disease. **Case Report.** Two patients with purple urine bag syndrome are presented. The first patient, a 66-year-old man, was hospitalized due to decompensation of alcoholic liver cirrhosis. A urinary catheter was placed on admission, and on the fourteenth day of hospitalization, a purple discoloration of the urine in the urinary bag was noticed. Multidrug-resistant *Proteus mirabilis* and *Enterococcus faecalis* were isolated by microbiological analysis of urine. The second patient was a 92-year-old man, hospitalized for acute gastrointestinal bleeding in the form of hematochezia, with an indwelling urinary catheter and a history of a prostate cancer surgery. On the third hospital day, a purple content in the urinary catheter bag was detected and *Klebsiella pneumoniae* and *Morganella morganii* were confirmed by bacteriological analysis. Both patients were without clinical and laboratory signs of acute infection. In both cases, the urinary catheter was replaced and ceftriaxone was administered empirically. **Conclusion.** Current guidelines for purple urine bag syndrome recommend catheter replacement and empiric antibiotic therapy. In clinical practice, it is necessary to emphasize that urine sampling for bacteriological analysis is performed only after replacing the catheter, in order to establish the exact etiology of the syndrome and radical use of antibiotics.

Key words: Urinary Tract Infections; Urine; Urinary Catheters; Bacteria; Biofilms; Risk Factors

Introduction

Purple urine bag syndrome (PUBS) is a condition where the urinary catheter bag and tubing turn

Sažetak

Uvod. Sindrom ljubičaste kese za urin predstavlja pojavu urina ljubičaste boje u vreći urinarnog katetera kao posledica interakcije bakterija, urina i gradivnih elemenata kese za urin i vezuje se za određenu grupaciju pacijenata sa faktorima rizika za ovo stanje – urinarna infekcija, starije životno doba, dugo plasiran kateter u mokraćnom sistemu, opstipacija, hronična bubrežna insuficijencija.

Prikaz slučaja. Prikazana su dva bolesnika sa sindromom ljubičaste kese za urin. Prvi bolesnik, muškarac star 66 godina, hospitalizovan je zbog dekompenzacije alkoholne ciroze jetre. Na prijemu je plasiran urinarni kateter, a četrnaestog dana hospitalizacije primećena je ljubičasta prebojenost urina u kesi za urin. Mikrobiološkom analizom urina izolovani su multirezistentan *Proteus mirabilis* i *Enterococcus faecalis*. Drugi bolesnik je muškarac starosti 92 godine, hospitalizovan zbog akutnog gastrointestinalnog krvarenja u vidu hematohezeje, sa prisutnim stalnim urinarnim kateterom i istorijom operacije karcinoma prostate. Trećeg hospitalnog dana zbog ljubičastog sadržaja u kesi urinarnog katetera urađena je bakteriološka obrada i verifikovane su *Klebsiella pneumoniae* i *Morganella morganii*. Oba bolesnika su bila bez kliničkih i laboratorijskih znakova akutne infekcije. U oba slučaja zamenjen je urinarni kateter i sprovedena je empirijska terapija ceftriaksonom. **Zaključak.** Aktuelne smernice kao terapiju za ovo stanje navode zamenu katetera i empirijsku antibiotsku terapiju. U kliničkoj praksi neophodno je naglasiti da se tek nakon zamene katetera vrši uzorkovanje urina za bakteriološku analizu, sa ciljem postavljanja tačne etiologije sindroma ljubičaste kese za urin i radikalne upotrebe antibiotika.

Glavne reči: infekcije urinarnog trakta; urin; urinarni kateteri; bakterije; biofilm; faktori rizika

purple as a result of the interaction between bacterial enzymes, elements of the urine, and polyvinyl chloride from the urinary catheter [1]. It is a rare clinical presentation, although among patients in

Abbreviations

PUBS	– purple urine bag syndrome
CRP	– C-reactive protein
UTI	– urinary tract infection

long-term care institutions with indwelling urinary catheters, it accounts for 9.8% of cases [2, 3].

The pathophysiological basis of PUBS is explained by an entire array of processes in the body, starting with metabolism of amino acid tryptophan. The degradation of tryptophan begins in the intestines, where it is transformed into indole by means of the intestinal flora. Afterwards, indole reaches the liver through the portal circulation, where the final metabolite is obtained through the action of 2 enzymes. First, by the action of the enzyme cytochrome P450 2E 13-hydroxyindole is formed, and then with the help of the sulfotransferase isoform 1A1 of the enzyme indoxyl sulfate (indican) is created. In this form, it is eliminated from the body via the kidneys. In case when indoxyl sulfate in urine makes contact with bacterial enzymes (indoxyl sulfatases or phosphatases), two colored compounds are produced - blue indigo and red indirubin. When they are mixed with polyvinyl chloride, which is a component of the urine bag and urinary catheter tube, a purple shade is obtained [2, 4]. It is thought that alkaline environment and the large number of bacteria in the urine may contribute to the formation of this specific urine color [1]. The geriatric population, people who have mobility difficulties, long-term indwelling urinary catheters, and people with constipation are at increased risk for developing PUBS [5, 6].

Case Report

Our case report presents two patients treated at the Clinic of Gastroenterology and Hepatology, Clinical Center of Vojvodina.

The first patient was a 66-year-old man, admitted due to decompensated alcoholic liver cirrhosis with accumulation of a large amount of ascites. The patient was diagnosed with cirrhosis and complications including portal hypertension, fourth-degree esophageal varices, secondary sideropenic anemia and hypersplenism. He was immobile, and had stage 3 chronic kidney disease as comorbidity. On admission, a urinary catheter was placed due to the patient's condition and the need to measure the 24-hour urine output. On the 14th hospital day, a purple discoloration of the urine in the urine bag was noticed (**Figure 1**). On the same day, the urine was sent for microbiological examination, the urinary catheter was replaced and intravenous antibiotic therapy with ceftriaxone 2 g/day was initiated. The urine bacteriological analysis revealed two pathogens, both higher in concentrations than 100,000/ml - multi-drug-resistant *Proteus mirabilis* (sensitive only to piperacillin + tazobactam, meropenem, ceftazidime-avibactam, and moderately sensitive (with increased antibiotic exposure) to imipenem, and resistant to tested antibiotics from the group of semi-synthetic penicillins with and without clavulanic acid, first and third generation cephalosporins, fluoroquinolones, aminogly-

cosides, sulfonamide + trimethoprim) and *Enterococcus faecalis* (sensitive to teicoplanin, vancomycin, tigecycline and linezolid, and resistant to tested penicillin antibiotics and fluoroquinolones). The patient was afebrile during hospitalization. The laboratory findings showed no increase in inflammation markers: C-reactive protein (CRP) upon admission was 9.6 mg/l (reference values 0 - 5 mg/l), and on the day when purple urine was observed, CRP was 3.2 mg/l. A nephrologist was involved in the treatment due to the retention of nitrogenous substances in the blood. Moreover, during hospitalization the patient had gastrointestinal bleeding in the form of enterorrhagia and endoscopic band ligation was done. Due to anemia, the patient received red blood cell transfusions. In the further course of hospitalization, the patient showed signs of encephalopathy and became hemodynamically unstable with a fatal outcome.

The second patient, a 92-year-old man was hospitalized for acute gastrointestinal bleeding in the form of hematochezia. Esophagogastroduodenoscopy was performed and a Forest Ib duodenal bulb ulcer was found. After hemostasis was achieved with hemoclips and adrenaline solution was infused, the patient was hemodynamically stable, without recurrence of bleeding. Anemia was corrected with red blood cell transfusions. The patient had a chronic kidney failure, a heart pacemaker, and a prostate cancer surgery 30 years ago, with an indwelling urinary catheter. On the third hospital day, it was noticed that the urine in the bag was purple



Figure 1. Purple urine in the first presented patient
Slika 1. Ljubičast urin prvog prikazanog bolesnika



Figure 2. Purple urine coloration in the second patient
Slika 2. Ljubičasta prebojenost urina drugog prikazanog bolesnika

(**Figure 2**) and a sample was sent for biochemical and bacteriological analysis. The chemical urine examination revealed alkaline urine (pH 8), specific gravity less than 1.005 (normal values 1.005 - 1.025), cloudy and light purple in color, while the microscopic analysis of urine sediment indicated an increased number of leukocytes (10 - 30 p/HPF, normal up to 5 p/HPF) and erythrocytes (5 - 10 p/HPF, normal up to 5) and a mass of bacteria. *Klebsiella pneumoniae* (resistant only to penicillin antibiotics) and *Morganella morganii* (resistant to penicillin antibiotics, trimethoprim + sulfamethoxazole and fluoroquinolones, sensitive to other tested antibiotics) were isolated from the urine sample. Both bacteria were present in numbers over 100,000/ml. The patient was treated with ceftriaxone (2 g/day) administered intravenously; the antibiotic was given empirically, and there was no need for correction according to the antibiogram results. Although the patient did not have a fever, a monitoring of C-reactive protein was performed, and all the time it was within the reference range (on admission < 0.5 mg/l, then 1.3 mg/l). Since the gastrointestinal bleeding was resolved and there was a clinical and laboratory improvement, the patient was discharged from hospital.

Discussion

A change in urine color may indicate various congenital disorders (porphyria, alkaptonuria), but it may

also be caused by the use of certain drugs (rifampicin, methylene blue, IV hydroxocobalamin). In elderly people without knowledge about the mentioned congenital diseases, it is more likely that urine discoloration is caused by therapeutic changes or due to PUBS. Taking into account that population at high risk of PUBS development has poor outcomes of catheter-related urinary infections, it is important to emphasize the importance of effective diagnostic assessment and early application of adequate therapy [5]. The data from a review article including 116 cases of PUBS in a 36-year period suggest that there was a decrease in mortality from 6.8% to 4.3% among patients with PUBS in the last few years, which was considered to be a consequence of a prompt and targeted antibiotic therapy [7].

The most common pathogens causing urinary tract infection (UTI) accompanied by PUBS listed in the literature are *Escherichia coli*, *Providentia stuartii*, *Providentia rettgeri*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Enterococcus* species and *Morganella morganii* [2, 6], four of which were isolated from the urine of our two patients.

Due to the communication difficulties, we could not obtain any information about the symptoms that would indicate UTI in our patients. Since the patients had neither clinical nor laboratory signs of acute infection, the purple color of urine was the only indication that a microbiological examination of urine was needed. All four bacteria detected in the urine of the presented patients were over 100,000/ml. According to previous research, UTIs associated with PUBS are most often asymptomatic, with a higher number of bacteria per ml of urine, compared to those that are not accompanied by PUBS [8, 9]. Consequently, there is a dilemma on how to interpret PUBS, as a symptom of an UTI or just bacterial colonization of the urinary catheter tube and bag at that moment. A case report from California presented a patient with a drainage catheter in the kidney and urinary bladder (nephrostomy and urostomy) and PUBS. Under the assumption that there was no real infection, only the replacement of the catheters and the bag was performed, without administration of antibiotics, with normalization of urine color afterwards [10]. In order to eliminate the possibility of misinterpretation of laboratory findings, only the first sample after replacing the urinary catheter should be used for biochemical and microbiological analysis.

Our first presented patient had multidrug-resistant strains of bacteria in the urine, which showed sensitivity only to reserve antibiotics according to the antibiogram. Taking into account the moment of urinary catheter placement upon admission and the appearance of purple coloration of the urine in the second week of hospitalization, a hospital-acquired infection is highly suspected. On the other hand, the second patient already had a permanent urinary catheter on admission, purple urine was observed on the third hospital day and a high sensitivity of the isolated bacteria to antibiotics was detected, so it is very likely that the patient already had that infection on admission.

Both presented patients had multiple factors that may have contributed to the development of PUBS, including long-term catheterization, chronic renal insufficiency and mobility difficulties [8]. The appearance of PUBS is more common in people with constipation, which can be explained by the retention of tryptophan in the intestines [3]. In patients with liver cirrhosis, there is a slow movement of contents through the small intestine as well as a change in the gut microbiota in terms of increased bacterial multiplication [11] and there is a possibility that this contributed to the appearance of PUBS in our patient.

In most cases, PUBS is an indolent condition, usually resolved simply by replacing the urinary catheter and antibiotic therapy. However, cases of complicated urinary infections accompanied by this syndrome have been reported in the literature. Moreover, cases of Fournier's gangrene development have been described in repeated PUBS and it is also associated with increased mortality [1, 5, 12].

Recommendations for the treatment of this condition are limited to urinary catheter replacement and empiric antibiotic therapy per os, while intravenous antibiotic administration is reserved for patients with recurrent PUBS and immunocompromised patients [1]. In our two patients, considering the clinical assessment (immunological status of the patient with cirrhosis and increased risk of the patient with sideropenic anemia for developing UTI) [7, 13, 14], it was decided to empirically introduce

antibiotic therapy as soon as purple urine was observed. The choice was intravenous application of antibiotics due to the general condition of the patient with cirrhosis and to bypass the gastrointestinal tract in the bleeding patient.

Conclusion

To our knowledge, there are still no definitive guidelines for the treatment of purple urine bag syndrome, but current recommendations emphasize the importance of preventive measures in terms of handling and regular catheter replacement. Previous studies dealing with this condition suggest the replacement of the urinary catheter and the bag as the first step in the therapeutic algorithm. However, according to the literature, it is necessary to place a new catheter first and only then take a urine sample for analysis. In case the bacteriological test of urine sampled in this way is positive, it indicates the presence of bacteria in the urinary system. On the other hand, the possibility of misinterpreting bacterial colonization of the urinary catheter as a urinary tract infection would be avoided. This would contribute to a more accurate diagnosis of urinary tract infection and a more rational use of antibiotics. When deciding whether to introduce antibiotic therapy and to what extent an individual approach is necessary, it is necessary to take into account the entire clinical condition of the patient.

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