

Purple urine bag syndrome in end-stage chronic kidney disease

Síndrome da urina roxa na doença renal crônica terminal

Autores

Guillermo Delgado¹
Michel Martínez-Reséndez¹
Adrián Camacho-Ortiz¹

¹ University Hospital,
Autonomous University of
Nuevo León.

ABSTRACT

Introduction: When faced with violet, purple or purplish-blue urine, clinicians should consider urinary tract infection in their differential diagnosis. **Case report:** A 60-year-old woman with end-stage kidney disease and non-adherence to renal replacement therapy was admitted to our hospital for placement of hemodialysis catheter. During her hospitalization she had purple urine, and purple urine bag syndrome (PUBS) was diagnosed. She was effectively treated with antibiotics and her urine returned to a dark yellow color. **Discussion:** Although this condition is often easily treated, diagnosing PUBS in chronic renal patients probably means an increased serum concentration of indoxyl sulfate, metabolite that is involved in the progression of both CKD and cardiovascular disease. **Conclusion:** Hence, in the context of our renal patients, perhaps PUBS is not as benign as supposed.

Keywords: color; klebsiella infections; *klebsiella pneumoniae*; patient compliance; renal dialysis; urinary tract infections.

RESUMO

Introdução: Quando observar uma urina violeta ou roxa, os clínicos devem considerar a infecção do trato urinário no diagnóstico diferencial. **Relato de caso:** Mulher de 60 anos de idade, com doença renal crônica terminal e baixa adesão à sua terapia de substituição renal, foi internada em nosso hospital para colocação do cateter de hemodiálise. Durante sua hospitalização, ela tinha urina roxa e foi diagnosticada com síndrome da urina roxa (SUR). Ela foi efetivamente tratada com antibióticos e sua urina voltou à cor amarela escura. **Discussão:** Embora esta condição seja muitas vezes facilmente tratada, o diagnóstico da SUR no contexto da DRC provavelmente reflete um aumento da concentração sérica de sulfato indoxil, metabólito que está envolvido na progressão da DRC e doença cardiovascular. **Conclusão:** Assim, no contexto dos nossos pacientes renais, talvez SUR não seja tão benigna como se supõe.

Palavras-chave: cooperação do paciente; cor; diálise renal; infecções do trato urinário; infecções por *klebsiella pneumoniae*.

INTRODUCTION

Visual inspection of the urine has been an integral part of clinical medicine since, at least, the Middle Age. Discoloration of this fluid usually draws the attention of any health care professional and frightens patients and relatives. Urinary tract infection (UTI) is a cause of discoloration. Therefore, clinicians should consider it in the differential diagnosis especially when faced with violet, purple or purplish-blue urine, because these colors, although not commonly observed, suggest infection.^{1,2}

We present one case of purple urine in a department of internal medicine at a Mexican university hospital, and briefly discuss its pathophysiology and relevance for clinical practice.

CLINICAL REPORT

A 60-year-old woman with end-stage kidney disease and non-adherence to renal replacement therapy was admitted to our hospital for placement of tunneled hemodialysis catheter. She was diagnosed with chronic kidney disease (CKD) in

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Correspondência para:
Guillermo Delgado.
Department of Internal Medicine,
University Hospital, Autonomous
University of Nuevo León.
Av. Madero y Gonzalitos s/n, Col.
Mitras Centro, Monterrey, Nuevo
León, México.
E-mail: grdelgadog@gmail.com/
guillermo.delgadogr@uanl.edu.mx

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the previous year, and underwent hemodialysis for nearly six months using a temporary jugular catheter, which was removed due to malfunction. Her past medical history was significant for type 2 diabetes and hypertension, both diseases diagnosed about ten years ago, and treated irregularly with subcutaneous intermediate-acting insulin, prazosin, and a dihydropyridine-calcium channel blocker. She recently came to the emergency room for a hypertensive crisis, and her antihypertensive regime was optimized at the discharge. The patient's medical history also included primary hypothyroidism, treated irregularly with levothyroxine.

A urinary catheter was placed to quantify urine output. Twenty four hours after admission the urine acquired a purple color (Figure 1). The patient was afebrile, denied chills and lower-urinary tract symptoms, and had a normal white blood-cell count. The urinalysis revealed a pH of 8.5, positive leukocyte esterase (2+), 1-2 WBC, 10 RBC, marked bacteriuria, and absence of nitrites. The diagnosis of purple urine bag syndrome (PUBS) was made and she was started empirically on ciprofloxacin. The urine culture was reported positive for *K. pneumoniae* (> 100,000 CFU/ml) with resistance to fluoroquinolones and nitrofurantoin, but susceptible to aminoglycosides, second and third generation cephalosporins and co-trimoxazole. She was changed to co-trimoxazole. After forty-eight hours the urine returned to a dark yellow color.

DISCUSSION

PUBS consists of violet, purple or purplish-blue discoloration of the urinary drainage bag and catheter,³ and was first described by Barlow &

Dickson, from the London Hospital for Sick Children, in 1978. In this first communication, they proposed insoluble indigo as the direct cause of this discoloration, and intestinal obstruction and constipation as risk factors. They also stated that these risk factors were quite common in pediatric patients with spina bifida and urinary diversion.⁴ By contrast, this syndrome is currently reported more frequently in the elderly population.^{2,5} Other factors associated with its development are female sex, alkaline urine, constipation, institutionalization, feeding route, higher bacterial counts, and previous urinary catheterization.^{5,6}

In terms of frequency, its prevalence has been reported as high as 27% in a Korean geriatric hospital.⁶ However, only 7.5% of internal medicine inpatients in an Italian general hospital manifested this syndrome. Of these, 73% were females, and all were over 65 years of age. In this Italian study, over eighty percent of patients with PUBS diagnosed had a urinary pH > 8, and *E. coli* and *P. mirabilis* were the most frequently isolated bacteria.⁵ *Enterococcus* species, *P. aeruginosa*, *K. pneumoniae*, *M. morgani*, and *Providencia* species, have been also repeatedly isolated from patients with PUBS. By 2007, the association between PUBS and *K. pneumoniae* had been reported 8 times.²

The purple color observed in PUBS cases is due to a violet discoloration (indirubin) of the plastic and blue crystals of indigo in the urine.^{7,8} *K. pneumoniae* produce blue colonies on agar enriched with the urine of patients diagnosed with PUBS.⁷ This pathogen is able to produce indigo and indirubin (indigo red) from indoxyl sulfate (indican), whose origin can be traced back to dietary tryptophan, in the following manner:

Figure 1. Purple urine bag syndrome.



this essential amino acid is deamidated by enteric bacteria to yield indole, which is hydroxylated to indoxyl, and thereafter sulfonated in the liver to form indoxyl sulfate.⁸⁻¹⁰ Besides having indoxyl sulfatase activity, *K. pneumoniae* also has indoxyl phosphatase activity.⁸ The degree of urine discoloration appears to be proportional to the urinary bacterial load.⁶ Alkaline urine may be a contributory factor for PUBS, but not a necessary cause, since it also occurs in the context of acidic urine.⁶ There is also an increased urinary concentration and daily excretion of indoxyl sulfatase in patients with PUBS; high tryptophan diet and constipation (via bacterial overgrowth) partially explained this finding.^{2,8}

Moreover, in patients with CKD, serum concentration of indoxyl sulfate had a linear correlation with the severity of azotemia.² Indoxyl sulfate removal during dialysis is limited, since it is bound to plasma albumin.¹¹ CKD was shown to be a potential risk factor for PUBS in a Taiwanese hospital-based cohort study.¹² Although this condition is often easily treated with antibiotics, we must bear in mind that diagnosing PUBS in chronic renal patients probably reflects an increased serum and urinary concentration of indoxyl sulfate, and that this uremic toxin is involved not only in the progression of CKD, but also of cardiovascular disease in chronic renal patients.¹³

CONCLUSION

PUBS is an infrequent condition and CKD has been recently recognized as a potential risk factor for its development. Considering the deleterious effects of indoxyl sulfate, perhaps PUBS is not as benign as supposed. Thus, we believe it is important that health care providers should be especially aware of this uncommon manifestation of UTIs in chronic renal patients. To the best of our knowledge, this is the first case of PUBS reported in our country and one of the first reported in Latin America.^{14,15}

The above is probably due to underdiagnosis or underreporting of this striking condition.

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