

Purple Urine Bag Syndrome in a Patient with an Ileal Conduit and Clostridium Difficile Infection

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Abstract

Purple urine bag syndrome is a potentially alarming phenomenon caused by bacterial metabolism of urinary tryptophan into indigo (blue) and indirubin (red) pigments. We report the case of a 46-year-old female with an ileal conduit who presented with a 2 week history of abdominal pain and purple discolouration of her urine. In addition, we review the literature on purple urine bag syndrome, and identify potential new risk factors and management considerations.

Background

Purple urine bag syndrome (PUBS) is a relatively rare disease entity attributed to pigment metabolism from urinary bacteria. It has an estimated prevalence of 8.3% to 42.1% in patients with long-term catheters,¹ with other risk factors including female gender and constipation.¹ Management includes reassurance, antibiotics and judicious catheter changes.¹

Case presentation

A 46-year-old female with multiple comorbidities presented to the emergency department with a 2-week history of generalised abdominal pain and purple discolouration of her urine. In addition she reported several months of intermittent diarrhoea, attributed to recurrence of Clostridium Difficile (C.Difficile) (confirmed by stool culture) which had been unsuccessfully treated with two courses of vancomycin in the community.

Her background included medically unexplained chronic dysphagia, requiring permanent percutaneous endoscopic gastrostomy (PEG) feeding, as well as cystectomy and ileal conduit formation for idiopathic detrusor activity. She had also previously undergone bilateral mastectomies following breast cancer, as well as prophylactic salpingo-oophorectomy and hysterectomy. Other comorbidities included insulin dependent diabetes mellitus (type 1), asthma, previous pulmonary emboli and deep vein thrombosis, endometriosis and hidradenitis suppurativa. She lived alone, although was heavily reliant on carers for assistance with activities of daily living as well as medication administration.

Her medication included analgesia: paracetamol, ibuprofen, amitriptyline, oramorph and buprenorphine patches, anti-emetics: cyclizine, domperidone and ondansetron, and diabetic medication: pioglitazone, liraglutide, insulin

glargine and novorapid. Other medications included laxatives, antidepressants, antihistamines, anastrozole and dalteparin.

On admission she was afebrile, however appeared pale and agitated. Clinical examination revealed a soft and generally tender abdomen with well-healed surgical scars from her previous cystectomy and bilateral salpingo-oophorectomy. A PEG and ileal conduit were in situ, and a purple discolouration of urine was noted in the ileostomy bag (Figure 1).

Investigations

Blood tests on admission demonstrated a mildly raised C-reactive protein and a mild acute kidney injury (Table I).

Urine dipstick was negative for leucocytes and nitrites and demonstrated alkaline pH. Urine culture revealed mixed growth of uncertain significance.

Abdominal and chest radiographs as well as abdominal ultrasound detected no abnormalities beyond those expected given her past medical and surgical history.



Figure 1. Ileostomy bag from patient on admission demonstrating purple discolouration of urine

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Table 1. Blood results on admission

Haemoglobin	116 g/L	Range 120-155 g/L
White cell count	4.7×10^{12} /litre	Range 4.0-10.5 $\times 10^{12}$ /litre
Platelet count	429×10^9 /litre	Range 150-400 $\times 10^9$ /litre
Urea	2.3 mmol/L	Range 1.7-8.3 mmol/L
Creatinine	73 μ mol/L	Range 49-92 μ mol/L
Sodium	141 mmol/L	Range 135-145 mmol/L
Potassium	4.8 mmol/L	Range 3.5-5.5 mmol/L
Bilirubin	4 μ mol/L	Range <17 μ mol/L
Alanine transaminase	62 U/L	Range 7-55 U/L
Alkaline phosphatase	92 U/L	Range 20-140 U/L
Albumin	38 g/L	Range 35-55 g/L
C-reactive protein	13.1 mg/L	Range 0-5 mg/L

Working diagnosis

Based on the history and investigations, two working diagnoses were hypothesised:

1. PUBS: precipitating abdominal pain and purple discolouration of the urine
2. Untreated *C. Difficile* infection: causing diarrhoea and contributing to abdominal pain

Treatment

On presentation to the emergency department the patient was initially treated with intravenous gentamicin due to suspected urinary sepsis (despite not meeting the criteria for sepsis), however this was subsequently de-escalated to oral nitrofurantoin as the diagnosis was revised to urinary tract infection with PUBS. As mentioned, *C. Difficile* infection was also detected in stool culture, and vancomycin was continued (having recently been restarted in the community) with follow-up arranged with a gastroenterologist.

Discussion

PUBS is a rare phenomenon associated with bacteriuria in patients with long term catheters. It typically occurs in elderly women with chronic constipation,² and can be alarming for both the patient and medical team. The aetiology is thought to be due to bacterial metabolism of indoxyl

sulphate excreted by the kidney, a product of dietary tryptophan metabolism (an amino acid found in large quantities in mozzarella cheese, soy products, pumpkin seeds, and egg whites).^{1,3} In the presence of certain sulphatase or phosphatase producing bacteria; notably *Pseudomonas Aeruginosa*, *Proteus Mirabilis*, *Morganella Morganii* and *Escherichia coli*, indoxyl sulphate is converted to indoxyl.⁴ In alkaline urine this forms indigo and indirubin pigments, which react with contents of the plastic catheter bag and tubing to form a purple discolouration.^{5,6} The indirubin dissolves in the plastic of the bag whilst indigo coats the surface giving it the distinct purple appearance, although this may vary (pink / dark red / blue / deep purple) depending on the constituent parts.⁷

In the above case, whilst the urine cultures did not grow a specific organism, urine dipstick demonstrated an alkaline pH (which may be a consequence of her diarrhoea and dehydration). This highlights an issue around diagnosing PUBS. Whilst other reported cases have relied on the confirmation of bacteriuria following culture,⁵ this case presented initial diagnostic uncertainty, and a therapeutic trial of antibiotics was ultimately required to establish the diagnosis.

Constipation has often been reported as a risk factor for PUBS, increasing colonic bacterial growth and subsequent metabolism of dietary tryptophan.¹ However in the case reported here, the patient was suffering from chronic diarrhoea due to current infection with *C. Difficile*, possibly exacerbated by the use of multiple laxatives. Tryptophan is an essential amino acid for *C. Difficile* growth, and is converted into a number of products including indole (precursor to indoxyl sulphate) within the colon.⁸ Absorption of these metabolites by the gut with subsequent renal excretion may precipitate the development of PUBS. Alternatively, the colonisation with *C. Difficile* or antibiotic regimen used to treat it may alter the colonic microbiome in a way that bias towards tryptophan metabolising organisms. Moreover, the resultant diarrhoea can cause dehydration and oliguria, which may in turn alkalinize the urine facilitating development of PUBS.

The majority of case reports describe PUBS in the context of urethral catheterisation. However in the above case, PUBS was identified in the output of an ileal conduit. Urinary tract infections have shown to be a common complication of ileal conduits, with sulphatase and phosphatase producing organisms such as *Escherichia coli*, *Proteus Mirabilis* and *Pseudomonas Aeruginosa* often identified as part of the mixed microbial flora.⁹ We therefore hypothesise that ileal conduits may be an additional risk factor for PUBS.

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Table 2. Differential diagnosis for discolouration of urine^{11,12,13}

	Rifampicin, Sulfasalazine
	Indomethacin, Propofol, Pseudomonas Aeruginosa UTI, Amitriptyline
	Metronidazole, Chloroquine, Primaquine, rhabdomyolysis, bilirubin
	Porphyria, haematuria, beetroot
	Purple urine bag syndrome

Of particular note in this case was the initial treatment with gentamicin, which may seem surprising given that the patient had normal observations and only mildly raised inflammatory markers on admission. This may have simply been due to alarm caused by the discoloured urine. PUBS is thought to be a relatively benign condition, which can be appropriately treated by changing the catheter or, in some cases, oral antibiotics in the absence of features of sepsis.¹⁰ It could be argued that this case resulted in the unnecessary administration of medication with high side effect profile due to lack of awareness of PUBS. It is therefore important to recognise this apparently frequent, benign condition. Nevertheless, it is also important to ensure due care and attention is paid to ruling out other possible causes of urine discoloration. Urinary tract malignancy, stones, rhabdomyolysis, porphyria, food substances such as beetroot or blackberries or medications such as rifampicin (orange), propofol (green), amitriptyline (blue/green), indomethacin (blue) should all be considered⁵ (Table II).

This case highlights the importance of early consideration and diagnosis of PUBS in order to avoid unnecessary antibiotic burden. Whilst PUBS suggests bacteriuria, there may not be an infection. Asymptomatic bacteriuria does not always require antibiotics. If PUBS is spotted earlier, the catheter can be changed promptly, which may negate the need for antibiotics. Furthermore, we have identified C. Difficile infection, diarrhoea and ileal conduits as further potential risk factors for the development of PUBS. It is postulated their effects on microbial flora and bacterial load may increase susceptibility to developing PUBS, although further research is needed in this area.

Alkaline urine may increase the risk of complications for a urostomy including hyperkeratosis,

bleeding, ulceration, stenosis and infections or calculi. Purple urine may highlight this to the patient, carers and staff looking after the patient.

Conclusion

This case highlights three important differences from previous case reports. Firstly, previous cases have relied on positive urine culture to confirm a diagnosis of PUBS. In this case urine dipstick was negative and urine cultures revealed a mixed growth, presenting diagnostic uncertainty. Secondly, whilst PUBS has previously been reported in the context of chronic constipation, this patient suffered from chronic diarrhoea due to C. Difficile infection resulting in dehydration and alkaline urine, both of which are risk factors for PUBS. Thirdly this case of PUBS was diagnosed in the context of an ileal conduit, in contrast to previously reported catheter associated infections.

Learning points take home messages

- PUBS is a relatively benign condition which may indicate alkaline urine, which in the presence of a urostomy can precipitate complications such as skin damage and further infections
- PUBS is a spot diagnosis which could indicate a bacteriuria
- Ileal conduits may facilitate growth of certain bacterial species, increasing risk of PUBS
- C. Difficile and associated diarrhoea may also potentiate risk of PUBS
- It is not always necessary to treat PUBS with broad-spectrum antibiotics
- PUBS aetiology is multi factorial

Conflict of interest

The authors have no conflicts of interest to declare

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