

CASE REPORT

PURPLE URINE BAG SYNDROME: A RARE CLINICAL ENTITY IN A FEMALE PATIENT WITH A LONG-TERM INDWELLING URETHRAL CATHETER

Venyo A K-G

Department of Urology, North Manchester General Hospital, Manchester, U.K.

Summary

Background: Discoloration of urine is commonly encountered in clinical practice and this at times may indicate significant pathology. Nevertheless, the majority of instances are benign. Blue and purple dye discoloration of the urinary catheter drainage system is rare and can be alarming to both patients and health care workers who are not aware of the condition which is called Purple-Urine-Bag-Syndrome (PUBS). PUBS, is associated with urinary tract infections occurring in catheterised patients, generally elderly females with significant co-morbidities and constipation. The urine is usually alkaline. Gram-negative bacteria that produce sulfatase and phosphatase are involved in the formation of pigment, indigo which gives a blue coloration and indirubin which gives a purple coloration. Tryptophan metabolism is involved in the pathogenesis.

Case Report: A 60-year-old lady who had a long-term urethral catheter for four years went to see her General Practitioner on few occasions with a report that her urine has been draining blue dye into her urine bag which was followed by drainage of purple dye into the catheter bag. The General practitioner did not know the cause of the problem but gave the patient antibiotic on each occasion and the blue/purple dye urine discoloration cleared each time she was given empirical antibiotic treatment. Her urine culture grew E coli at the time of the discoloration.

Conclusion: PUBS occurs in long-term catheterised patients; is associated with UTI; presents with symptom-less blue/purple discoloration of urine; resolves with appropriate antibiotic treatment.

Key Words: Purple urine bag syndrome

Introduction

Purple discoloration of the urinary catheter and urinary drainage bag in chronically catheterised patients has been described as the "Purple Urine Bag Syndrome" (PUBS); which is a rare clinical entity. PUBS occurs due to a complex chemical reaction which is initiated in the constipated bowel and ending in the production of indigo blue and indirubin dyes in the infected urine resulting in the purple coloration of the urinary catheter and urinary bag. Because of the rarity of the syndrome a number of clinicians may not be aware of its existence. A case of intermittent blue and purple dye discoloration of urinary catheter bag is reported with a review of the literature.

Case Report

A 60-year-old woman was seen in the Urology follow up clinic. She has had long-term urethral catheter for about four years. She developed retention of urine four years earlier and was catheterised. Fifteen years earlier she had elsewhere a Hartman's procedure for a rectal tumour followed by radiotherapy, since then she has had lower urinary tract symptoms. She had ultrasound scan of the renal tract and pelvis as well as flexible cystoscopy and these were normal. She failed trial without catheter and was re-catheterised. She also had urodynamics which showed evidence of bladder outlet obstruction. In view of this she had cystoscopy and urethral dilatation on two occasions but on each occasion she failed trial without catheter. She was offered intermittent self-catheterisation but she refused to catheterize herself and opted for a long-term urethral catheter. She was noted to have a degree of cognitive impairment. Her daughter (her principal carer) has been helping her with regard to her catheter care at home. Her urethral catheter has been changed at regular 10 to 12 weeks intervals by the district nurse.

At the follow-up clinic her daughter stated that: her mother was well but on and off she and her mother had noticed blue dye in the mother's urine, urethral catheter and in the urine bag and then the colour would change

Author for Correspondence:
Mr Anthony K. Venyo
Department of Urology
North Manchester General Hospital
Manchester M8 5RB
United Kingdom
E mail: akodzogrey@yahoo.co.uk
Conflict of interest: None declared

to purple; Despite this her mother was well. On each occasion that she noticed the dye discoloration of the urine and catheter and urinary bag she took the mother to see her General Practitioner (GP) and she was given a course of antibiotics. The General Practitioner noticed the discoloration too but did not know what was responsible for the purple bag discoloration of the urinary bag and advised that she should discuss it with the Urologist. On each occasion the blue and purple discoloration resolved after taking the antibiotics. The last episode of the purple discoloration of the urinary bag was two weeks prior to her clinic attendance.

Her general and systematic examinations were normal. Her colostomy bag was draining well and her urethral catheter tube and urinary bag had clear urine.

A review of her last urine culture results of the specimen of urine obtained two weeks earlier at the time of the purple dye urinary bag discoloration revealed a growth of *Escherichia coli* (*E coli*); >100,000 (10^5) colony forming units per mL; urine white cell count of 262/uL (normal range - 0 to 40 /uL) determined by flow cytometry. The *E coli* were sensitive to trimethoprim and nitrofurantoin but resistant to amoxicillin. Her other investigations including full blood count, serum urea and electrolytes were normal.

The patient and her daughter were told she had Purple Urine Bag Syndrome which is a rare condition and tends to be associated with long-term catheterisation, urinary tract infection as well as constipation. She was reassured she did not have any urinary tract malignancy which they had feared. Her urine specimen obtained on consultation that day grew mixed flora; > 100,000 (10^5) colony forming units per mL. Despite this explanation she was listed for flexible cystoscopy and ultrasound scan of her renal tract and pelvis were requested to prove to her nothing was wrong. She was given a request card for urine culture to take home and anytime the blue/purple dye discoloration is noted she should submit a sample of the urine for culture in order to know the causative organism of her urinary tract infection and the sensitivity pattern to enable the GP prescribe the appropriate antibiotic. The patient and daughter were advised further about catheter care and a letter was written to the GP about 'Purple Urine Bag Syndrome'.

Discussion

Purple Urine Bag Syndrome is a rare phenomenon in which the urine catheter collecting bag and the tubing as well as the urine of the patient is noted to turn blue and then purple hours to days after urinary catheterisation¹ (Figure 1). PUBS, was first reported in 1978 by Barlow and Dickson² and this was reportedly seen in patients with urinary diversion. PUBS, is most often found in bedridden, elderly ladies who require long-term urinary bladder catheterisation³. There is no proven documented explanation for why PUBS is not as common in elderly men as in elderly ladies. Howev-

er, it could be said that considering the fact that females have short urethras in comparison to men, constipated bed-ridden elderly ladies, with overflow incontinence may be more prone to developing urinary tract infections than elderly men.



Figure 1: Example of purple discoloration of a patient's urinary bag

A number of postulations exist regarding the aetiology of PUBS and these include:

Ribeiro and associates⁴ have stated that the chain reaction responsible for PUBS begins with dietary tryptophan being metabolized by gastrointestinal bacteria, which produces indole (the most popular theory); see Figure 2.

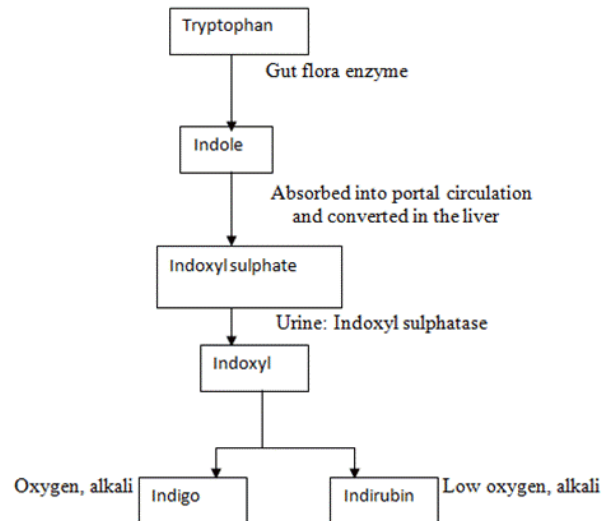


Figure 2: The Formation of indigo and indirubin from tryptophan.

Indole is then converted into indoxyl sulphate (or indican) in the liver, which is excreted in the urine. Some bacterial strains possess an enzyme (a phosphatase with minor sulfatase activity) which acts on the indoxyl sulphate to produce indigo⁵. The purple discoloration of the urine bag is reported to occur as a sequel of indirubin.

bin (which is red) dissolving in the plastic and mixing with the fine blue indigo crystals in the urine⁶.

On the other hand, Barlow and Dickson² have suggested that indoxyl sulphate is oxidized to indigo only after urinary excretion and exposure to air. In addition, Sammons and associates⁷ have postulated that indicanuria in patients, leads to a blue colour only when the urine is treated with an oxidizing agent such as sodium hypochlorite (bleaching powder). In addition Vallejo-Manzur and associates observed that purple discoloration of the urine was associated with a highly alkaline urine in contact with the plastic collecting bag, which caused the dye used to eliminate the yellow tint of the bag to discolour the urine³. In 1993, Umeki suggested that the occurrence of PUBS was associated with strong alkaline urine⁸. Nevertheless, Mantani and associates have observed PUBS in acidic urine⁹. Mantani and associates in a study using mass spectroscopy suggested that the molecular structure of the causative pigment is a steroidal or bile acid conjugate, not indigo⁹.

Constipation has been reported as a frequent symptom of patients exhibiting PUBS^{9:10:11:12:13}. It has been suggested that chronic constipation may alter gastrointestinal motility or the specific intestinal bacteria flora which are responsible for dietary tryptophan being converted to indole, pyruvic acid and ammonia by specific bacterial flora containing tryptophanase^{13:14}. Under such abnormal conditions, indole may be absorbed in the portal circulation and oxidised in the liver to indoxyl, which is then excreted into urine, in which medium indigo (the purple pigment) is formed pursuant to the oxidation of indoxyl in an alkaline environment^{5:12:13:15:16}. It has been suggested that with the presence of little oxygen, there is a tendency for indoxyl to form into isatin and then combine further with an indoxyl residue to yield indirubin (the blue pigment)¹². Umeki in 1993 suggested that the occurrence of PUBS was associated with strong alkaline urine⁸. The patient in this reported case had alkaline urine.

Nevertheless, there have been some reported cases of PUBS which have presented without any evidence of indicanuria^{15:17:18}. The violet pigment in the urine is believed to be due to the activity of a steroidal or bile-acid conjugate^{17:18}. Considering the fact that there are a variety of postulates regarding the causation of PUBS, it would be said that at the moment the causative factors of PUBS have not been very well characterized¹⁹.

With regard to clinical features and course, published case reports have revealed that patients with PUBS have similar features. PUBS, is most commonly observed in chronically catheterised and constipated women who have alkaline urine and urinary tract infections¹⁹. Most patients with PUBS were bedridden and many had cognitive impairment¹³. Most patients with PUBS had a benign course, with resolution of the purple colour after antibiotic therapy and replacement of the urinary catheter. One patient developed sepsis em-

anating from pneumonia and urinary tract infection but improved after a course of antibiotics³. Two patients died of unrelated causes (carcinomatosis²⁰), and sepsis not related to UTI¹⁰. The reported patient is a female, has had a long term urethral catheter, she had urinary tract infection, was not mobile (and is being cared for by her daughter), she was noted to have cognitive impairment, she also had a colostomy, and she was asymptomatic; her clinical features were consistent with other published case reports. Even though the patient had alkaline urine on admission to hospital prior to the development of the purple / blue coloration her urine at the time of her development of PUBS was not available. Her urine sample was sent to the laboratory where flow cytometry was done to determine her cell count and the urine was cultured

The most commonly involved pathogen in PUBS is *Providencia stuartii*. Other reported species of PUBS associated bacteria include: *Klebsiella pneumoniae*, *Escherichia Coli*, *Providencia rettgeri*, *Proteus mirabilis*, *Pseudomonas aeruginosa*, *Enterobacter agglomerans*, methicillin-resistant *Staphylococcus aureus*, *Citrobacter spp*, group B streptococci, and *Morganella morganii*^{5:9:13:19:20:21:22}. In addition, some others including: *Yersinia enterocolitidis*, *Providencia alcalifaciens*, *staphylococcus aureus* have demonstrated the ability to generate sulphates and phosphates which, under some conditions, are able to produce blue-coloured colonies on agar following incubation for about 48 hours⁵. Apart from the aforementioned, other bacterial species have been isolated in PUBS including: *Klebsiella pneumonia*, *Providencia stuartii*, *Enterobacter cloacae*, *Citrobacter fundii*, and *Proteus vulgaris*.²²

It is thought that *Providencia var. Spp.*, as a family is an unusual clinical entity because the long term catheterised urinary tract appears to offer an attractive niche for this particular family of microorganisms²³. Fu-Hsiung Su and associates observed that the duration of catheterisation is not an absolute criterion for the development of PUBS²². They also made the following observations from their study:

- the longer the PVC bag stayed in use for a patient, the deeper the colour purple the bag became, despite the use of two different sterile PVC drainage bags from different companies, a result compatible with the 1989 findings of Dealler and associates¹²
- "PUBS" affected not only the drainage bags but also the indwelling catheters.
- The use of PVC Foley catheter is more likely to harbour the presence of microorganisms associated with the development of PUBS than using a silicon Foley catheter.
- PUBS-associated discoloration appeared to have affected all catheters, irrespective of catheter material¹¹.

The diagnosis of PUBS is not well defined. PUBS, is associated with purple urine, catheter tube, bag and urinary tract infection. Nevertheless, there has never been a description of a method of confirming the diagnosis. Dealler and associates⁵ stated that patients with PUBS have a higher concentration of indoxyl sulphate than control patients. Among the 41 species of bacteria tested, only three were able to produce indigo from indoxyl sulphate: *Providencia stuartii*, *Klebsiella pneumoniae*, and *E agglomerans*. Barlow and Dickson² used spectroscopic analysis of affected patients' urine, which demonstrated that the pigment responsible for the urine discoloration was indigo. Lin and associates¹⁰ suggested that it is unnecessary to perform tests other than microbiology and biochemistry. At the moment there is no definite recommended diagnostic approach to PUBS apart from visual identification of the purple urine, bag, and tubing.

PUBS is treated with antibiotics directed at the specific UTI causative organism⁶. However, some authors argue that it is unnecessary to aggressively treat patients with PUBS and advocate constipation control as well as urologic sanitation as the fundamentals of treatment for PUBS⁶. It has been suggested that PUBS and catheter associated UTIs can be prevented by improvement in catheter care¹⁹. Literature review indicates that most patients who presented with PUBS were, mostly asymptomatic^{11:24}. In view of this it has been suggested that PUBS is apparently not a disease per se, nor does it appear to represent any real danger to the health of the patient and aggressive treatment of PUBS is unnecessary^{9:24}. The reported patient did not have any symptoms associated with her PUBS but when she was treated with antibiotics the purple/blue discoloration disappeared and her urine colour returned to normal. The patient and her daughter were initially alarmed by the PUBS but after the condition of PUBS was explained to them they have become satisfied and happy. What was important in this case is the fact that the patient's General Practitioner had never encountered a case of PUBS and therefore could not reassure the patient. After the diagnosis had been made the patient has not been referred back to the hospital for over a subsequent 18 months because of PUBS. It may be that there is no direct aetiological association between age and PUBS even though PUBS may be common in the older age group. It may be conjectural but the fact that the older age group tend to be more commonly immobile, constipated and tend to have long-term urethral catheter as a result of co-morbidities may explain why PUBS is reported more commonly in the older age group.

An association between purple urine bag syndrome and intussusception has been reported²⁵. Perhaps in order to prevent the occurrence of the discoloration of urine-bag or the development of malodours, drainage bags and indwelling long-term urinary catheters need to be changed on a more regular basis and perhaps sili-

cone Foley catheters should be used instead of PVC Foley catheters.

Conclusion

PUBS at present can be diagnosed by visual identification of blue / purple discoloration of the urinary bag, catheter tubing and urine; urine culture results would identify the associated causative UTI bacteria as well as the sensitivity pattern. PUBS is usually not life threatening and the patients tend to be asymptomatic. Appropriate antibiotic treatment based upon the sensitivity pattern of the organism causing the urinary tract infection leads to resolution of the discoloration. Regular change of urinary catheter and catheter bag may help prevent PUBS. Patients need to be reassured that PUBS is a benign phenomenon. A school of thought believes that antibiotic treatment is unnecessary in the management of PUBS.

References

1. Roggla G, Kapiotis S, Farhner A. A case of purple urine bag syndrome (PUBS). *Wien Klin Wochenschr* 2002; 114: 306.
2. Barlow G B, Dickson J A. Purple urine bags [letter]. *Lancet* 1978; 1:220-221.
3. Vallejo-Manzur F, Mireless-Cabodevila E, Varon J. Purple urine bag syndrome. *Am J Emerg Med* 2005; 23: 521-524.
4. Ribeiro J P, Marcelino P, Marum S, Fernandes A P. Case report: purple urine bag syndrome. *Crit Care* 2004; 8:R137.
5. Dealler S F, Hawkey P M, Millar M R. Enzymatic degradation of urinary indoxyl sulphate by *Providencia stuarti* and *Klebsiella pneumoniae* causes the purple urine bag syndrome. *J Clin Microbiol* 1988; 262:2152-2156.
6. Wang I K, Ho D R, Chang H Y, Lin C L, Chuang F R. Purple urine bag syndrome in a hemodialysis patient. *Intern Med* 2005; 44: 859-861.
7. Sammons H G, Skinner C, Fields J. Purple urine bags [Letter] *Lancet* 1978; 1:502.
8. Umeki S. Purple urine bag syndrome (PUBS) associated with strong alkaline urine. *Kansenshogaku Zasshi* 1993, 67:487-490.
9. Mantani N, Ochiai H, Imanishi N, Kogure T, Terasawa H, Tamura H. A case control study of purple urine bag syndrome in geriatric wards. *J Infect Chemother* 2003; 9:53-57.
10. Lin HH, Li S J, Su K B, Wu L S. Purple urine bag syndrome: a case report and review of the literature. *J Intern Med Taiwan* 2002; 13:209-212.
11. Robinson J. Purple urinary bag syndrome: a harmless but alarming problem. *Brit J Comm Nurs* 2003; 8:263-266.
12. Dealler S F, Belfield P W, Bedford M, Whitley A J, Mulley G P. Purple urine bags. *J Urol* 1989; 142:769-770.

13. De Bruyn G, Eckman C D, Atmar R L. Purple discoloration in a urinary catheter bag. *Clin Infect Dis* 2002; 34: 285-286.
 14. Nakayama T, Kanmatsuse K. Serum levels of amino acids in patients with purple urine bag syndrome. *Nippon Jinzo Gakkai Shi* 1997; 39:470-473
 15. Ollapallil J, Irukulla S, Gunawardena I. Purple urine bag syndrome. *ANZ J Surg* 2002; 72: 309-310.
 16. Pankan E F. Purple urine bags. *J Urol* 1983; 130:372.
 17. Stott A, Khan M, Roberts C, Galpin I J. Purple urine bag syndrome. *Ann Clin Biochem* 1987; 24:185 -188.
 18. Nobukuni K, Kawahara S, Nagare H, Fujita Y. Study on purple pigmentation in five cases with purple urine bag syndrome. *Kansenshogaku Zasshi* 1993; 67:1172-1177.
 19. Chiou Y K, Yiang G T, Wang C H, Liao C S, Hsu B G. Purple urine bag syndrome -a case report. *Tzu Chi Med J* 2005; 17:279-281.
 20. Ihama Y, Hokama A. Purple urine bag syndrome. *Urology* 2002; 60:910.
 21. Al-Jubouri M A, Vardhan M S. A case of purple urine bag syndrome associated with *Providencia rettgeri* [letter]. *J Clin Pathol* 2001; 54:412.
 22. Su F H, Chung S Y, Chen M H, Sheng M L, Chen C H, Chen Y J, Chang W C, Wang L Y, Sung K Y. Case Analysis of Purple Urine-Bag Syndrome at a Long-Term Care Service in a Community Hospital. *Chang Gungm Med J* 2005; 28: 636-642.
 23. Mobley H L, Chippendale G R, Tenney J H, Warren J W. Adherence to uroepithelial cells of *Providencia stuartii* isolated from the catheterised urinary tract. *J Gen Microbiol* 1986; 132: 2863-2872.
 24. Ishida T, Ogura S, Kawakami Y. Five cases of purple urine bag syndrome in a geriatric ward. *Nippon Ronen Igakkai Zasshi* 1999; 36: 826 – 829.
 25. Pillai R N, Clavijo J, Nayaranan M, Zaman K. An association of purple urine bag syndrome with Intussusception - a care report. *Urology* 2007; 70: 812.
-