CASE REPORT

Renal Replacement Therapy

Open Access

Blue-green urine in traditional medicine consumption: a case report and review of the literature



Stevan Kristian Lionardi^{1*}, Antoninus Hengky² and Sean Peter Haruman³

Abstract

Background Abnormal urine discoloration tends to be concerning for the patient and piques the interest of medical professionals. Different factors can arise in cases of urine turning blue or green. We highlight the necessity of obtaining a thorough history of the patient, particularly regarding previous diets and medications leading up to the condition.

Case presentation We present the case of a 63-year-old man who presented to the emergency room due to an inability to urinate 6 h prior with suprapubic discomfort. He had been having trouble urinating for the past 2 months. The urine bag had a blue-green urine color after urethral catheterization. Further questioning revealed traditional medicine consumption prior to admission.

Conclusions Consideration of the patient's diet, current medications, and any medical conditions or diseases may aid in deducing the causality of urine discoloration. The clinician's awareness of the effects of certain medications and conditions could have merit in avoiding unnecessary and costly investigations.

Keywords Blue urine, Green urine, Traditional medicine

Background

Urine, a complex biological fluid, serves as a valuable source of diagnostic information due to its diverse composition and association with the body's physiological processes. The color of urine has long been recognized as a critical clinical parameter, reflecting the presence of various endogenous and exogenous compounds within the urinary tract. The color of urine can be influenced by various factors. Among them, the presence of erythrocytes, bilirubin, or ingested medications has a more

Stevan Kristian Lionardi

stevanlionardi15@gmail.com

³ Komodo General Regional Hospital, Labuan Bajo, Indonesia

significant impact on altering urine color than diseases related to metabolic conditions, certain foods, or dyes [1, 2].

The convergence of traditional medicine and modern scientific inquiry offers a rich tapestry of intriguing phenomena and therapeutic practices that continue to captivate researchers and practitioners alike. Most people throughout the world prefer using plant or herbal treatments for basic health care due to assumptions of their dependability, lesser toxicity, and environmental friendliness, especially in developing countries. Indonesia is one of the wealthiest countries in biological resources, and its medicinal plants have a vital role in society with local knowledge empirically passed down from generations of various ethnicities [3].

Understanding the processes causing this color shift, on the other hand, is crucial for determining its usage and its repercussions; similarly, the prolonged buildup



© The Author(s) 2024. **Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.gr/licenses/by/4.0/. The Creative Commons Public Domain Dedication waiver (http://creativecommons.gr/licenses/by/4.0/.

^{*}Correspondence:

¹ Sultan Syarif Mohamad Alkadrie General Regional Hospital, Pontianak, Indonesia

² Fatima Hospital, Ketapang Regency, Indonesia



Fig. 1 Blue-green urine color observed in the urine bag



Fig. 2 Urine color on a nonsterile urine container

of unknown chemicals as part of traditional treatments might lead to potential toxicity in patients with impaired renal function [4, 5]. In this case, the patient's history plays an important role in causing a blue-green urine color.

Case presentation

A 63-year-old man arrived at the emergency room experiencing suprapubic discomfort with urinary retention 6 hours earlier. A tender, palpable bladder was discovered on an abdominal exam in the region between the pubic symphysis and the umbilicus. Apart from a blood pressure measurement of 170/90 mmHg, the results of other physical examinations were remarkable for an elderly male who had a history of hypertension for the past few years. The patient had no ongoing medication and refused to take regular medication prescribed by primary healthcare. He had been having trouble urinating for the past 2 months, with an increase in prostate size on a digital rectal examination.

Subsequently, the patient underwent urethral catheterization, leading to the observation of a blue-green hue in the urine collection bag, as depicted in Fig. 1, and this observation was subsequently corroborated in a nonsterile urine container, as illustrated in Fig. 2. Further bloodwork showed no sign of significant abnormalities, while urinalysis showed a slight increase in proteinuria (0.3 g/L) and erythrocyte sediment of 8–10 red blood cells per high power field.

Upon further questioning, the patient and family disclosed a history of consuming a traditional medicine that claimed to aid in urination. The patient had been taking four tablets daily for 5 weeks before being admitted. This was his first time consuming traditional medicine. Through the label, the medicine contains a variety of herbal extracts, including *Panax ginseng* herbal extract 20 mg, *Piperis retrofracti* fructus 100 mg, *Plantago major* folium 100 mg, *Strobilanthes crispus* folium 300 mg, *Orthosiphon stamineus* folium 300 mg, and methyl paraben as a preservative. To the extent of our knowledge following extensive research, no interactions were identified involving either methyl paraben, methylene blue, or bluegreen urine discoloration.

Methylene blue, a nonpathogenic water-soluble dye, is suspected to be the cause of urine discoloration due to its distinctive blue green color and widespread use in traditional medicine. Following the cessation of traditional medicine consumption, the urine color turned clear. The patient was referred to a urologist and revealed that he had benign prostate hyperplasia.

Discussion

Traditional medicine overview

The presence of a variety of bioactive components in medicinal plants is considered to be linked to pharmacological activities that have significant therapeutic benefits. Nisa et al., studied the safety and efficacy of medicinal herbs such as Orthosiphone aristatus and Phyllanthus niruri used for treating urinary tract problems in eastern Indonesia [3]. The European Association of Urology recommends specific herbal medicine of Serenoa repens or saw palmetto extract, which was first used medicinally by Native American Indians to treat lower urinary tract symptoms associated with benign prostatic hyperplasia [6]. Chinese herbal formulations traditionally used for centuries have recently gained increasing attention as a potential alternative or complementary therapy for overactive bladder, named Ba-Wei-Di-Huang-Wan, which has been proven to have more than simply placebo effects [7].

Panax ginseng from the Araliaceae family, the primary extract component of traditional medicine employed in this case, was a perennial plant native to Korea and China that was historically used for thousands of years as an herbal remedy in eastern Asia [8]. According to recent therapeutic claims, sexual function, cancer, cardiovascular illnesses, and immunological function can all be improved, earning the title of "antiaging plant". A study among postmenopausal women with genitourinary syndrome showed improvement in patient-assessed symptoms but no significant effect on clinician-assessed outcomes [9], while among benign prostatic hyperplasia patients, an association of nerve growth factor activation could delay the development of prostate weight and hyperplasia [10].

Another component, *Strobilanthes crispus*, commonly known as "kejibeling" locally, has been studied for anticarcinogenic medicinal chemicals such as cytotoxicity, antitumor immunogenicity, and antioxidant activity created from leaf extracts found to be grown in Malaysia and Indonesia [11].

Despite the fact that the majority of its consumers are even aware of its limitations, the combination of selfmedication and lack of studies raises the possibility of herbal medicine being potentially harmful in certain circumstances. These medications could be more favored due to their affordability, religious affiliation, beliefs, and ease of obtaining, particularly in developing nations [12]. Considering the challenge of funding studies when there is no obvious patent or financial benefit to drive the study. As a result, it is critical to foster competition in herbal medicine research.

Blue-green urine

Urinary discoloration is commonly caused by variations in urochrome concentrations caused by other endogenous or exogenous pigments. A wide range of urine hues can be detected in hospitalized patients' urine bags, which may indicate the presence of illnesses, drugs, toxins, or hemolysis [13].

Blue urine typically appears to be caused by methylene blue ingestion, a substance that is widely used for diagnostic tests and the treatment of methemoglobinemia in the USA. Outside the country, however, oral methylene blue may be found in medications and home remedies because of its antimicrobial properties. True blue urine comes to be very uncommon, presumably because blue pigments interact with urochrome, the primary contributor to urine's regular yellow hue, to produce a green color prior to urine's elimination [14].

Medications commonly associated with green urine are phenol-containing groups, including promethazine, thymol, and propofol, which are widely used for induction and maintenance of general anesthesia [14]. Propofol is mainly metabolized and conjugated in the liver, whereas the presence of phenolic metabolites is responsible for the green color of urine, and the intensity of the green color is dosage dependent. Green urine generated by propofol, on the other hand, is a recognized non-nephrotoxic condition that does not modify or depict renal function [15, 16]. Green urine can also be caused by dyes such as indigo blue, indigo carmine, carbolic acid, flavin derivatives, or food coloring additives; likewise, food dye and color blue no. 1, which is absorbed through the gastrointestinal tract, may result in dark green urine [17]. Sometimes called "verdoglobinuria", green urine could also be caused by a prescribed cyclic antidepressant amitriptyline, consumed over long periods [18]. Herbicide ingestion with components of mefenacet and imazosulfuron is also detected through spectrophotometric analysis [19]. Green urine has also been correlated with prokinetic drugs, namely metoclopramide, as an iatrogenic cause [20].

Flupirtine, a muscle-related analgesic that is neither an opioid nor a nonsteroidal anti-inflammatory drug, was discovered as a causative agent in two cases, either in a suicide attempt or in an adolescent, through gas chromatography with subsequent mass spectroscopy. The drug is still sold in some Asian countries, though it is currently not available on the European market [21, 22].

The bacteria that cause *Pseudomonas* infection generate the pigments pyocyanin and pyoverdin, which can cause green urine was addressed in an article published almost 40 years ago [23, 24]. Bile pigments, such as biliverdin, an oxidation product of bilirubin, are an uncommon and problematic discovery in locating the leak [25]. One such source of bile is described in a case report of an enterovesical fistula produced by pelvic radiation treatment. Certain medical disorders can also cause blue or green urine similarly problems with tryptophan absorption and blue urine in diapers are symptoms of an uncommon genetic illness termed familial benign hypercalcemia [26] and Hartnup disease [27]. Other potential etiologies for the manifestation of a blue-green urine hue have been collated and are presented in Table 1.

Methylene blue has several clinical uses, such as as a bacteriostatic genitourinary antiseptic, a topical agent (0.1% solution), in combination with vitamin C for the management of chronic urolithiasis, and as an indicator dye, such as in colonoscopic polypectomy [28]. Ingestion of methylene blue is likely to be harmless, although there are still several adverse effects that are mild, self-limiting, and show a dose-related trend [29].

One in vivo study [30] found that the preadministration of methylene blue has the potential to hinder the endothelial relaxation induced by *Panax ginseng*. Despite our thorough investigation, we did not find any human studies that provide insight into this specific interaction.

Methylene blue was suspected to be the cause of the discoloration in this case due to its widespread use and distinctive blue-green color. Several traditional medications also contain methylene blue due to its antimicrobial properties [5, 14]. The results of the urinalysis indicated

Page 4 of 5

Medications/drugs	Dyes/pigments	Diseases/infections	Miscellaneous
Amitripyline [18] Anthraquinone Arbutin Azuresin Blutene Bromoforium Cimetidine Clioquinol Flupirtine [21, 22] Flutamide Guaiacol Indomethacin Iodochlorhydroxyquin Magnesium salicylate Methocarbamol Metoclopramide [20] Metronidazole Mitoxantrone Phenyl butazone Phenyl salicylate Phenol Promethazine Propofol [15, 16] Resorcinol Tetrahydronapthalene Thymol Tolonium Triamterene Zaleplon	Biliverdin [25] Boric Acid Carbolic acid Diagnex blue Evans blue FD&C blue no Indigo blue Indigo carmine Methylene blue [5] Toluidine blue	Blue diaper syndrome Bile via vesico-enteral Chronic obstructive jaundice Familial indicanuria [26] Hartnup disease [27] Meconium aspiration syndrome <i>Pseudomonas</i> infection [23, 24] Typhoid fever	Clorets (chlorophyll-containing breath mints) [27] Excessive use of mouthwash or deodorant Herbicides [19]

proteinuria, but in a similar situation, a blue-green hue might result in a false-positive reading of proteinuria. In addition, the results were still borderline and could have been brought on by physiological proteinuria [31]. In addition, there were no other ongoing medications aside from the traditional medicine, and the change in urine color started on the next day of traditional medicine consumption. Nonetheless, establishing causality is challenging.

Conclusions

We did not find any reports of discoloration attributable to *Panax ginseng, Strobilanthes crispus, Plantago major,* or *Orthosiphon stamineus* among the herbal extracts that have been identified. Conversely, methylene blue is recognized for inducing blue urine, as corroborated by extant literature on herbal medicine and home remedies. Despite the absence of concrete evidence linking the patient's herbal medicine to methylene blue, the prevailing hue of the urine strongly implies the probable presence of methylene blue in the aforementioned herbal medicine.

This case demonstrated a traditional medicine consumption history obtained through thorough history taking. Consideration of the patient's diet, current medications, and any medical conditions or diseases may aid in deducing the causality of urine discoloration. The clinician's awareness of the effects that would arise from certain medications, diseases, and conditions could merit a focused diagnosis while avoiding unnecessary and costly investigations.

Acknowledgements

Not applicable.

Author contributions

S.K.L. contributed to the conception of the work in addition to the acquisition of data, images, and in the writing of the paper. A.H. participated in the writing of the paper and supervision. S.P.H. participated in the writing of the paper. All authors read and approved the final manuscript.

Funding

Not applicable.

Availability of data and materials

All data generated or analyzed during this study are included in this published article [and its supplementary information files].

Declarations

Ethics approval and consent to participate

Consent was obtained from the patient for the publication of this case report.

Consent for publication

We have obtained consent for publication from the person involved in this case.

Competing interests

The authors declare that they have no competing interests.

Received: 29 September 2023 Accepted: 20 January 2024 Published online: 14 March 2024

References

- 1. Partin AW, Dmochowski RR, Kavoussi LR, Peters CA. Campbell-walsh-wein urology. 12th ed. Philadelphia: Elsevier; 2020.
- Raymond JR, Yarger WE. Abnormal urine color: differential diagnosis. South Med J. 1988;81:837–41. https://doi.org/10.1097/00007611-19880 7000-00008.
- Nisa U, Astana PRW, Triyono A, Ardiyanto D, Fitriani U, Zulkarnain Z, Novianto F, Jannah WDM. Ethnobotanical study of medicinal plants used for treating urinary tract problems in eastern Indonesia. IOP Conf Ser: Earth Environ Sci. 2021;905: 012119. https://doi.org/10.1088/1755-1315/905/1/ 012119.
- Prakash S, Saini S, Mullick P, Pawar M. Green urine: a cause for concern? J Anaesthesiol Clin Pharmacol. 2017;33:128–30. https://doi.org/10.4103/ 0970-9185.202190.
- Lam C-W, Wong SYJ. A case of green urine due to a traditional Chinese medicine containing methylene blue. N Z Med J. 2010;123:71–6.
- Alcaraz A, Rodríguez-Antolín A, Carballido-Rodríguez J, Castro-Díaz D, Medina-Polo J, Fernández-Gómez JM, Ficarra V, Palou J, de León P, Roca J, Angulo JC, Esteban-Fuertes M, Cózar-Olmo JM, Pérez-León N, Molero-García JM, Fernández-Pro Ledesma A, Brenes-Bermúdez FJ, Manasanch J. Efficacy and tolerability of the hexanic extract of Serenoa repens compared to tamsulosin in moderate-severe LUTS-BPH patients. Sci Rep. 2021;11:19401. https://doi.org/10.1038/s41598-021-98586-5.
- Kim D, Choi C, Ahn I, Ryu I, Choi M, Lee Y, Lee MS. Efficacy and safety of Baweidihuang-wan in women with overactive bladder: a randomized, double blind, placebo controlled trial. Int J Clin Exp Med. 2014;7:2744–53.
- Coon JT, Ernst E. Panax ginseng: a systematic review of adverse effects and drug interactions. Drug Saf. 2002;25:323–44. https://doi.org/10.2165/ 00002018-200225050-00003.
- Ghorbani Z, Mirghafourvand M, Farshbaf Khalili A, Javadzadeh Y, Shakouri SK, Dastranj Tabrizi A. The effect of Panax ginseng on genitourinary syndrome in postmenopausal women: a randomized, double-blind, placebo-controlled clinical trial. Complement Med Res. 2021;28:419–26. https://doi.org/10.1159/000514944.
- Kim SK, GyuKo I, Park HJ, Chung J-H, Cho KB, Kwon OY, Park KH, Ahn YS, Park CG, Kim YO. Effects of Panax ginseng on the nerve growth factor expression in testosterone induced benign prostatic hyperplasia. Saudi J Biol Sci. 2018;25:66–70. https://doi.org/10.1016/j.sjbs.2016.07.005.
- Endrini S, Rahmat A, Ismail P, Taufiq-Yap YH. Cytotoxic effect of γ-sitosterol from Kejibeling (Strobilanthes crispus) and its mechanism of action towards c-myc gene expression and apoptotic pathway. Med J Indonesia. 2014;23:203–8. https://doi.org/10.13181/mji.v23i4.1085.
- Chali BU, Hasho A, Koricha NB. Preference and practice of traditional medicine and associated factors in Jimma Town, Southwest Ethiopia. Evid Based Complement Alternat Med. 2021;2021:9962892. https://doi.org/10. 1155/2021/9962892.
- 13. Viswanathan S. Urine bag as a modern day matula. ISRN Nephrol. 2013;2013: 215690. https://doi.org/10.5402/2013/215690.
- 14. Aycock RD, Kass DA. Abnormal urine color. South Med J. 2012;105:43–7. https://doi.org/10.1097/smj.0b013e31823c413e.
- Rawal G, Yadav S. Green urine due to propofol: a case report with review of literature. J Clin Diagn Res. 2015;9:OD03–4. https://doi.org/10.7860/ JCDR/2015/15681.6706.
- Fujii-Abe K, Kawahara H, Fukayama H. An analysis of green discoloration of urine caused by propofol infusion. J Clin Anesth. 2016;35:358–60. https://doi.org/10.1016/j.jclinane.2016.08.032.
- Carpenito G, Kurtz I. Green urine in a critically ill patient. Am J Kidney Dis. 2002;39:E20. https://doi.org/10.1053/ajkd.2002.32013.
- Greenberg M. Verdoglobinuria. Clin Toxicol (Phila). 2008;46:485–6. https:// doi.org/10.1080/15563650701874629.

Page 5 of 5

- Shim Y-S, Gil H-W, Yang J-O, Lee E-Y, Kim S-H, Hong S-Y. A case of green urine after ingestion of herbicides. Korean J Intern Med. 2008;23:42–4. https://doi.org/10.3904/kjim.2008.23.1.42.
- 20. Pak F. Green urine: an association with metoclopramide. Nephrol Dial Transplant. 2004;19:2677. https://doi.org/10.1093/ndt/gfh359.
- Vilela M, Fernandes D, Salazar T, Duarte A. Hulk-like urine: a case of green urine caused by flupirtine intoxication. Cureus. 2020;12: e12333. https:// doi.org/10.7759/cureus.12333.
- Maier A, Liu Y, Scholze A, Westhoff TH, Tepel M. Green urine following exposure to flupirtine. Am J Kidney Dis. 2010;56:1014–5. https://doi.org/ 10.1053/j.ajkd.2010.08.012.
- Stone HH, Martin JDJ, Graber CD. Verdoglobinuria: an ominous sign of pseudomonas septicemia in burns. Ann Surg. 1964;159:991. https://doi. org/10.1097/0000658-196406000-00016.
- Moussa M, Chakra MA, Papatsoris AG, Dellis A. Green urine due to Pseudomonas urinary tract infection: An unusual occurence. Am J Emerg Med. 2022;52:249–50. https://doi.org/10.1016/j.ajem.2021.03.089.
- 25. Pinto MPB. Green urine—understanding its importance. J Lab Med. 2018;42:213–4. https://doi.org/10.1515/labmed-2018-0108.
- Foley TP, Harrison HC, Arnaud CD, Harrison HE. Familial benign hypercalcemia. J Pediatr. 1972;81:1060–7. https://doi.org/10.1016/s0022-3476(72) 80232-4.
- Elkoundi A, Bensghir M, Balkhi H, Lalaoui SJ. Green urine in the operating room: the 'cloret sign'. QJM Int J Med. 2018;111:265–6. https://doi.org/10. 1093/qjmed/hcx219.
- Hadi HIA, Williamson JS, Bhowmick AK. Green urine in a postoperative patient. Case Rep. 2014:bcr2014204986. https://doi.org/10.1136/ bcr-2014-204986
- Tariq B, Simon SR, Pilz W, Maxim A, Kremer B, Baijens LWJ. Evaluating the safety of oral methylene blue during swallowing assessment: a systematic review. Eur Arch Otorhinolaryngol. 2021;278:3155–69. https://doi. org/10.1007/s00405-020-06509-3.
- Choi YD, Xin ZC, Choi HK. Effect of Korean red ginseng on the rabbit corpus cavernosal smooth muscle. Int J Impot Res. 1998;10:37–43. https:// doi.org/10.1038/sj.ijir.3900300.
- Poloni JAT, de Moraes Sassi MG, de Oliveira TF, Rotta LN, Perazella MA. Blue-green discoloration of urine and false nephrotic range proteinuria at dipstick urinalysis. Clin Chim Acta. 2018;482:74–7. https://doi.org/10. 1016/j.cca.2018.03.036.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.