



A child with green urine after a diagnostic enema: Answers

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Received: 20 February 2021 / Accepted: 25 February 2021 / Published online: 17 March 2021
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Keywords Child · Green urine · Recurrent cystitis · Autoimmune gastritis · Cystoscopy · Enema · Methylene blue

Answers

1. What is the differential diagnosis for a child with green urine?

The observation of green urine in this child raised further concerns about a recto-urethral fistula: however, this hypothesis was made unlikely by the lack of findings during cystoscopy, despite the irrigation of the rectum with a large amount of methylene blue. The differential diagnosis of green urine was therefore advocated. Congenital conditions potentially responsible for greenish discoloration of urine (namely, Hartnup disease, Blue diaper syndrome) were easily ruled out, based on the sudden occurrence of the phenomenon in adolescent age. Biliverdinuria and urinary tract infections were excluded by the normal urinalysis results. Among the different drugs potentially involved, propofol was taken into account: however, very low induction doses were used in this child, who separately had been sedated with propofol before, without displaying any similar findings. Finally, a dye-related urine discoloration was considered: based on previous reports, the occurrence of green urine in this child was attributed to the administration of methylene blue through a rectal enema. As expected, the urine discoloration eventually faded over few days. The history of recurrent cystitis was attributed to the severe constipation.

2. What diagnostic tests are useful to establish the diagnosis?

This refers to the article that can be found at <https://doi.org/10.1007/s00467-021-05028-5>.

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The diagnosis of dye-related urine discoloration is clinical and does not require any additional test. Urinalysis can assist the exclusion of urinary tract infections, potentially responsible for urine of greenish hue. The awareness of the benign nature of this condition prevented this child from undergoing further unnecessary invasive investigations.

3. How would you manage this patient?

Dye-related urine discoloration is self-limiting and does not require any additional treatment. The greenish hue tends to fade within a few days: patients must be reassured about the benign nature of the phenomenon.

Discussion

Abnormal urine discoloration is always alarming to the patient and intriguing to physicians. A bluish or greenish hue can arise from either endogenous or exogenous factors [1]. The former includes congenital conditions impairing amino acid absorption from the gastrointestinal tract (e.g., Hartnup disease, Blue diaper syndrome), biliverdinuria (resulting from obstructive jaundice or biliary leak), and urinary tract infections sustained by *Pseudomonas* (due to the formation of pyocyanin pigment [2]). Several drugs with phenolic green chromophore derivatives, conjugated in the liver and excreted by the kidney [2], can cause a dose-related, self-limiting urine greenish discoloration [3]: they include propofol, mostly after prolonged intravenous infusions [4, 5], cimetidine, and promethazine [6]; in addition, less frequently implicated, non-phenolic compounds are metoclopramide [7], amitriptyline [8], and indomethacin [9].

Dyes such as food coloring [10], indigo blue, and methylene blue can sometimes be responsible. Methylene blue is a water-soluble dye used to treat conditions such as methemoglobinemia and ifosfamide-induced encephalopathy [11] and as a diagnostic aid to assess the integrity and patency of either

the visceral walls or the intragastric balloons in bariatric surgery [12]. Moreover, it is often contained in several traditional Chinese medications, due to its antimicrobial properties [13]. After kidney filtration, blue pigments combine with urochrome, the major contributor to urine's normal yellow hue, discoloring urine green before elimination [1]. While the peak of excretion is between 2 and 6 h after administration, it can be detected in urine through chromatographic techniques until 24–48 h after administration. Methylene blue–related greenish urine discoloration has been reported after several modes of administration of the dye: these include both direct intravenous infusion [11] and systemic absorption after oral administration [14, 15], uterine filling during laparoscopic chromopertubation for infertility work-up [16], colon submucosal injections [17], irrigation of the bowel lumen [18], and manipulation of the paralytic ileum [19]. To date, only one case of urine discoloration after a methylene blue enema has been described in adults [20], and no similar reports exist in the pediatric literature.

Awareness of the benign and self-limiting nature of this condition can prevent children from undergoing unnecessary invasive investigations.

Author contribution All authors contributed to the study conception and design. The first draft of the manuscript was written by Luisa Cortellazzo Wiel, and all authors commented on the previous versions of the manuscript. All authors read and approved the final manuscript.

Funding Open access funding provided by Università degli Studi di Trieste within the CRUI-CARE Agreement.

Data availability Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

Code availability Not applicable.

Declarations

Ethics approval Not applicable.

Consent to participate Not applicable

Consent for publication Not applicable.

Competing interests The authors declare no competing interests.

Additional declarations for articles in life science journals that report the results of studies involving humans and/or animals Not applicable.

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References

1. Aycock RD, Kass DA (2012) Abnormal urine color. *South Med J* 105:43–47
2. Leclercq P, Loly C, Delanaye P, Garweg C, Lambermont B (2009) Green urine. *Lancet* 373:1462
3. Ku BD, Park KC, Yoon SS (2010) Dark green discoloration of the urine after prolonged propofol infusion: a case report. *J Clin Pharm Ther* 36:734Y736
4. Tirosh R, Barzilay Z, Almog S, Paret G (1996) Propofol and green urine. *Paediatr Anaesth* 6:244
5. Boshkovska Spaseski M, Spaseski D (2020) Green Urine. *N Engl J Med* 383:e128
6. Bowling P, Belliveau RR, Butler TJ (1981) Intravenous medications and green urine. *JAMA* 246:216
7. Pak F (2004) Green urine: an association with metoclopramide. *Nephrol Dial Transplant* 19:2677
8. Norfleet RG (1982) Green urine. *JAMA* 247:29
9. Gillett MJ, Burnett JR (2006) Medications and green urine. *Intern Med J* 36:64–66
10. Elkoundi A, Bensghir M, Balkhi H, Lalaoui SJ (2018) Green urine in the operating room: the 'Cloret Sign'. *QJM* 111:265–266
11. Miri-Aliabad G (2014) Green urine secondary to methylene blue. *Indian J Pediatr* 81:1255–1256
12. Bernante P, Francini F, Zangrandi F, Menegon P, Toniato A, Feltracco P, Pelizzo MR (2003) Green urine after intragastric balloon placement for the treatment of morbid obesity. *Obes Surg* 13: 951–953
13. Lam CW, Wong SYJ (2010) A case of green urine due to a traditional Chinese medicine containing methylene blue. *N Z Med J* 123:71–76
14. Peter C, Hongwan D, Kupfer A, Lauterburg BH (2000) Pharmacokinetic and organ distribution of intravenous and oral methylene blue. *Eur J Clin Pharmacol* 56:247–250
15. Koratala A, Leghrouz M (2017) Green urine. *Clin Case Rep* 5:549–550
16. Szkodziak P, Woźniak A, Szkodziak F, Buszewicz G, Czuczwar P, Woźniak S (2020) Green urine sign after laparoscopic chromopertubation as an effect of severe contrast intravasation: a report of three cases. *J Int Med Res* 48:300060520942083
17. Sun D, Huang SS (2018) Green urine. *CMAJ* 190:E224
18. Hadi HIA, Williamson JS, Bhowmick AK (2014) Green urine in a postoperative patient. *BMJ Case Rep* 2014:bcr2014204986
19. Morell-Garcia D, Bauça JM, García-Suquía A, Robles J, Barceló B, Fernández-Ballina A, Carlos-Vicente JC (2016) Green urine: A bezoar effect. *J Clin Anesth* 33:306–308
20. Deshmukh AS, Bansal NK, Kropp KA (1977) Use of methylene blue in suspected colovesical fistula. *J Urol* 118:819–820

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