Diagnostic Odyssey in a Child with Red-Colored Urine and Proteinuria

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CASE DESCRIPTION

A 3-year-old female with no previous relevant medical history was referred to the nephrology clinic for evaluation of episodic red-brownish colored staining in her diaper and on the toilet seat. She was not prescribed any medications and had no exposure to hormonal creams, nor were there any obvious dietary factors. The patient initially presented to her primary care physician at 2½ years of age following the discovery of apparent blood on the toilet seat. Around this time, the child also visited the emergency room, where urinalysis was negative for blood, protein, or evidence of urinary infection. A renal-pelvic ultrasound was also unrevealing. Consultation with nephrology resulted in serial urinalyses, which were repeatedly negative for blood or protein, and urine microscopy was normal.

She was referred to endocrinology and gynecology for concerns of precocious puberty and vaginal bleeding, respectively. Endocrine assessment revealed that the child was Tanner stage 1 and had an appropriate bone age. Gynecological examination was positive for mild vulvovaginitis but was otherwise normal. In the interim period, she exhibited further episodes of pink/red splattering on the toilet. The patient was then referred to urology. Despite no outward cause of the episodes, the urologist recommended cystoscopy if symptoms persisted past 1 year.

Several months later, the child developed some periumbilical abdominal pain and was assessed by gastroenterology. At this visit, a family history (maternal great aunt) of acute intermittent porphyria was revealed. However, subsequent laboratory workup for acute intermittent porphyria, including urine porphobilinogen, coproporphyrins I and III, and uroporphyrin, was unremarkable. Approximately 1 year later, she developed proteinuria, which was noted on follow-up urinalysis screening by other providers (Table 1), triggering a referral back to nephrology. Despite persistently increased urine protein measurements over the following 5 months, other urine analyses, including albumin, β2- and α1-microglobulins, and protein electrophoresis, were all normal. A urine purine/pyrimidine panel was also negative, excluding the possibility of hyperuricosuria, a rare cause of orange-colored crystals in children's urine. The patient's serum albumin remained normal, and she had no edema. The nephrology service consulted the clinical laboratory regarding the ongoing apparent proteinuria without etiology that supported classic proteinuria. A chromogenic interference from the substance within the child's urine causing artifactually increased urine total protein determinations was strongly suspected.

QUESTIONS TO CONSIDER	
1.	What are the potential causes of pink- or red-colored urine?
2.	What could cause an apparent increased urine protein result in the context of otherwise normal urinalysis ?

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Table 1. Patient's urine analyses.

Component (urine)	Month 1	Month 1 follow-up	Month 2	Month 3	Month 4	Month 6	Reference interval
Protein[a]	1+	Negative				Negative	
Blood[a]	Negative	Negative				Negative	
Leukocytes[a]	Negative	Negative				Negative	
Nitrite[a]	Negative	Negative				Negative	
Urobilinogen[a]	Negative	Negative				Negative	
White cells[a]	3						0–2/hpf
Red cells[a]	4						0–3/hpf
Protein random (mg/dL)		92.0	159.0	129.0	270.0	153.0	0.0–12.0
Beta-2 microglobulin (µg/L)		63	43				0–300
Albumin		19	<12.0				

[a]Urinalysis performed using Bayer Multistix SG10 method.

Final Publication and Comments

The final published version with discussion and comments from the experts will appear in the January 2025 issue of *Clinical Chemistry*. To view the case and comments online, go to https://academic.oup.com/clinchem/issue/71/1 and follow the link to the Clinical Case Study and Commentaries.

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