

Hypercalciuria: Common but Under-diagnosed Cause of Hematuria

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ABSTRACT

Hypercalciuria has been found to be the cause of unexplained asymptomatic macroscopic or microscopic hematuria among children in a substantial number of cases. It is more common than post-strept glomerulonephritis / IgA nephropathy or any other structural abnormality. Children with asymptomatic hematuria should be investigated and correctly treated for hypercalciuric as it can be easily misdiagnosed.

We report a case of hypercalciuria causing hematuria in a young teenager who was initially considered a case of glomerulonephritis. The patient had isolated gross hematuria, and was suspected of the case of glomerulonephritis and was being treated with immunosuppressants. The patient's family considered a second opinion with us before the earlier advised renal biopsy. The patient was found to have elevated urinary calcium causing hematuria. He was treated with diuretics, immunosuppressants were stopped and along with dietary restrictions, the patient became asymptomatic.

Keywords: Hypercalciuria, hematuria, immunosuppressants, red blood cells (RBCs), urinalysis, glomerulonephritis (GN), diltiazem, azathioprine.

INTRODUCTION

Hypercalciuria is considered one of the most important causes of unexplained asymptomatic macroscopic or microscopic hematuria among children. It is more common than glomerulonephritis or any other structural abnormality. Hematuria can easily be misinterpreted for renal stones, or glomerulonephritis leading to unnecessary procedures and unhelpful aggressive treatment to the patient. Children with asymptomatic hematuria should be investigated for urinary calcium excretion and if found hypercalciuric should be correctly treated with diuretics and proper dietary advice for complete resolution of their symptoms [1].

We report a case of a boy with isolated hematuria, who was thought to be the case of glomerulonephritis (GN) and was immediately treated with immunosuppressants, but he had hematuria secondary to hypercalciuria, which completely resolved after proper diagnosis and treatment along with the dietary restrictions.

CASE REPORT

CASE: A 13-year-old boy with no prior comorbid came for evaluation of hematuria. The patient had no previous history of renal stones, fever or flu-like symptoms, nasal bleed, oral ulcers and no skin rashes. The only history that the patient had was of diarrhea which occurred 6 months prior to presenting to us for which he was admitted in periphery history. The patient was first found to have RBCs during admission. He continued to have significant RBCs in his urinalysis. The patient followed the physician, he was vitally stable, with a weight of 39kg

and all other systemic examinations were clear. He was suspected to be the case of GN and was advised for renal biopsy and was started on diltiazem and azathioprine. The patient followed the physician after a month on immunosuppressants, with a complaint of reddish-tinged urine and significant RBCs in his urinalysis. He was advised to continue immunosuppressants and was again counseled for the need for a renal biopsy. After being on immunosuppressants for another month, with the unresolved complaint of reddish-tinged urine and significant RBCs in his urinalysis, he followed the nephrologist, who advised the patient for further investigations (**Table 1**), stopped azathioprine but continued diltiazem and counseled for the need of renal biopsy. The patient was very reluctant for invasive investigation and after another month on steroids, with similar complaints, the patient followed us. His steroids were tapered. Urine for dysmorphic cells was checked, which was negative. Spot urine for calcium (**Table 1**) was checked, which came 0.22. 24-hour urine calcium was checked which was significant at 184 mg/24 hours. He was started on thiazide diuretic and strict dietary restrictions were made with a decrease in his salt and protein intake with moderate calcium in his diet. After a week on treatment, significant decline in 24-hour urine calcium was seen from 184 mg/24 hours to 154 mg/24 hours. The patient's treatment was continued with a thiazide diuretic and dietary restrictions and follow-up were advised. After a month of treatment, his complaint was resolved and his 24-hour urine calcium had significantly declined from 154 mg/24 hours to 90 mg/24 hours and his urinalysis showed insignificant RBCs of 1 (**Table 2**). For academic purposes, he was followed after a year and a half. He had no complaints and his urinalysis showed insignificant RBCs of 2 (**Table 2**) and spot urine calcium/creatinine ratio was that of 0.1 with dietary restrictions alone without any other treatment.

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Table 1: Laboratory data.

Parameters	Results
Hemoglobin	14.7 g/dl
Total Leukocyte count TLC	9.5x 10 ⁹ /L
Platelet	346000/ μ l of blood
Urea	36 mg/dl
Creatinine	0.69 mg/dl
Sodium Na	142 mEq/L
Potassium K	4.7 mEq/L
Chloride	108 mEq/L
HCO ₃	36 mEq/L
Calcium	10.5 mg/dl
Phosphorous PO ₄	3.62 mg/dl
Albumin	4.0 g/dl
ESR	25
C3	1.38 g/l
C4	0.22 g/l
ANA	Negative
AMA	Negative
ASMA	Negative
AGPCA	Negative
Urine for Dysmorphic cells	Negative
Spot Calcium/Creatinine ratio (1st)	0.22
Spot Calcium/ Creatinine ratio (On long term follow up)	0.10
24-hour urine Calcium (1st)	184 mg/24 hours
24-hour urine Calcium (2nd) - 1 week on diuretics	154 mg/24 hours
24-hour urine Calcium (3rd) - 1 month on diuretics	90 mg/24 hours
Ultrasound	Right 10.8 cm *1.0 cm Left 9.3 cm *1.5 cm No evidence of renal calculus No hydronephrosis No calculus in the bladder

Table 2: Urinalysis.

Parameters	First Urinalysis	Urinalysis after Treatment with Diuretics and Dietary Restrictions	Urinalysis after 1½ Year on Dietary Restrictions Alone
pH	6	6.5	6.5
Protein	Nil	Nil	Nil
Glucose	Nil	Nil	Nil
Pus Cell	15-20	2	1
Rbc	30-40	1	2
Bact	Nil	Few	Nil
Cast	Nil	Nil	Nil
Crystals	Nil	Nil	Nil
Blood	Nil	Nil	Nil
Hb	Nil	Nil	Nil

DISCUSSION

Idiopathic hematuria can be misleading in many cases, especially in children. It can be misinterpreted for renal stones, glomerulonephritis, IgA nephropathy or any structural abnormality.

In the case discussed, a list of differential diagnoses could be made, but it needed careful exclusion of all to avoid unnecessary investigations especially invasive

investigations and the use of immunosuppressants. The renal stones were excluded as the patient had no associated symptoms like no flank pain, no other urinary symptoms, and no past or family history of renal stones. The possibility of the patient having renal stones secondary to renal tubular acidosis or renal tubular acidosis itself was excluded by normal electrolytes including normal potassium and serum bicarb. The patient's history did not include any history that could have hinted at the case of glomerulonephritis, there was no history of recent respiratory or skin infections, no history of oral ulcers, no history of frothy urine, and no skin lesions; also there was no proteinuria in the investigations that could have raised suspicion of GN.

There have been studies done to evaluate the importance of diagnostic evaluation in the cases of idiopathic hematuria among children. Among 342 children with microscopic hematuria, 16% were found to have hematuria due to hypercalciuria, and in 228 children with gross hematuria, 22% had hypercalciuria causing hematuria [2]. It has been found that in cases of microscopic hematuria not always extensive investigations are needed while in patients with gross hematuria investigations must be carried out since it can lead to urinary tract abnormalities. It was established that hypercalciuria was the most common cause of hematuria among patients with either microscopic or macroscopic hematuria [2].

Association of increased spot urinary calcium/creatinine ratio of ≥ 0.2 and hematuria (both macroscopic and microscopic) has been found in a significant number of cases [1]. Patient's symptoms have been observed to be resolving with the only conservative approach of dietary restrictions in the majority of the cases and not all patients required diuretics, but only those with a positive family history of renal stones, persistent hematuria, or markedly raised urinary calcium/creatinine ratio [2-6]. The study showed that among 96 patients with microscopic hematuria 82.3% of patients and 46 patients with gross hematuria 71.4% of patients had complete resolution of symptoms with these measures [1]. Most cases of idiopathic hypercalciuria, defined as 24-hour urine calcium excretion of 4mg/kg/24 hours, have been found prevalent in children with microscopic (54.9%) and macroscopic (53.6%) hematuria [3].

The dietary restrictions including low salt and protein intake with moderate calcium intake have been found to have an immense effect on hypercalciuria and the resolution of hematuria. It is observed that the reduction in sodium chloride intake of 100 mmol is found to cause a reduction of about 100 mg Ca/day [7-10]. The mechanism behind this is that in the distal segments of the renal tubule, sodium, and calcium compete for reabsorption; therefore, as the quantity of sodium arriving at the distal tubule increases, the calcium excretion also increases [11]. Another mechanism might be due to an excess of sodium chloride intake that can

lead to a state of subclinical metabolic acidosis leading to a release of bone calcium [12]. Protein restrictions of 0.8g/kg/day have also been found to decrease calcium excretion through reduced bone resorption and urinary calcium losses [13].

We suggest that in a patient with hematuria, hypercalciuria should be considered and immediate dietary restrictions should be made as that alone can cause resolution of the symptom, but in cases of persistent hematuria and increased urinary calcium, diuretics should be added along with the dietary restrictions. Particular caution must also be taken in suggesting and performing unnecessary invasive investigations and prescribing medications that could cause more harm than benefit to the patient.

CONCLUSION

Children presenting with asymptomatic microscopic or macroscopic hematuria can be misdiagnosed easily due to nonspecific symptoms, making delay in the proper diagnosis, and exposing the patients to unnecessary investigations and immunosuppressants. Patients with hematuria should be suspected and investigated for hypercalciuria and treated accordingly for complete recovery.

CONSENT FOR PUBLICATION

Consent for publication was taken from both patients after explaining the academic reason for publication and maintenance of confidentiality by not mentioning the personal information of patients in the final publication.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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Declared none.

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