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Case Report

A Rare Cause of Hematuria in a Bangladeshi Infant: Hereditary Xanthinuria

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ABSTRACT

Background and Aim: Hematuria in an infant is not very uncommon. Nephrocalcinosis and renal stones frequently cause hematuria and urinary tract infections in early infancy. Furthermore, xanthinuria is a rare metabolic disorder that can lead to the abnormal accumulation of xanthine, resulting in nephrocalcinosis and the subsequent formation of renal stones. It is an autosomal recessive genetic disorder caused by a lack of xanthine dehydrogenase, which breaks down hypoxanthine and xanthine into uric acid in the final two steps of the purine degradation process. Only a few instances have been noted worldwide. Furthermore, pediatric xanthinuria has never been reported from Bangladesh.

Case Presentation: Herein, we discussed a 2-month-old male infant who had symptoms of excessive crying during micturition and microscopic hematuria, later diagnosed as a case of xanthinuria type 1.

Conclusion: Hereditary xanthinuria may present with hematuria and nephrocalcinosis. Confirmation by genetic testing is useful for identifying the type of hereditary xanthinuria and predicting the outcomes.

Keywords: Hematuria, Nephrocalcinosis, Hereditary, Xanthinuria

Introduction

Hematuria in children can have a wide range of causes, and the differential diagnosis may include infections, kidney and urinary tract abnormalities, vascular anomalies, such as nutcracker syndrome, malignancies, acute and chronic glomerular diseases, hypercalciuria, and stones. Nephrocalcinosis and renal stones may give rise to hematuria and urine infection in early infancy. Additionally, xanthinuria is a rare cause of nephrocalcinosis, and renal stones may present with these symptoms [1]. A deficiency of xanthine dehydrogenase/oxidase (XDH/OX) leads to decreased breakdown of hypoxanthine and xanthine into uric acid, resulting in the accumulation of these uric acid precursors and causing hereditary xanthinuria, which is inherited in an autosomal recessive manner [2]. Typically, type I xanthinuria is caused by a mutation in the *XDH/XO* gene, located on chromosome 2p23.1, while type II results from deficiencies in *XDH/OX* and aldehyde oxidase (AO). These deficiencies are due to mutations in the *MOCOS* gene, located on chromosome 18q12.2, which encodes the molybdenum cofactor sulfurase. Despite different mutations, these types are clinically indistinguishable [3, 4]. Most of the patients with classical

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xanthinuria are asymptomatic, and the onset of symptoms might happen at any age. Nearly 50% of patients with classical hereditary xanthinuria have urolithiasis, acute renal failure, renal colic, hematuria, and urinary tract infections. Additionally, arthropathy, myopathy, duodenal ulcers, and chronic kidney disease occur in a small percentage of patients [5, 6]. Herein, we discussed a 2-month-old infant who presented to us with excessive crying during micturition and hematuria, later diagnosed as a case of xanthinuria.

Case Presentation

A 2-month-old male infant, 1st born of consanguineous parents, weighing 5.6 kg, presented to our clinic with the complaint of excessive crying during micturition. He had no history of polyuria, weight loss, or neonatal seizure. The baby was delivered by lower segment cesarean section at term without any natal or postnatal complications. The mother was a primigravida and was undergoing regular antenatal check-ups. He had no history of gestational diabetes, hypertension, or TORCH infection. He also had no family history of any kidney disease.

On examination, there were no facial abnormalities, the eyes were free of cataracts, the ears, nose, and throat were normal, and vital signs were normal. His weight was 4.9 kg, his height was 55 cm, the occipito-frontal circumference (OFC) was 37 cm, and his reflexes were normal. Abdomen examination revealed no organomegaly and kidneys were not ballotable. Urine routine examination revealed the following results: Red blood cell (RBC): 10-12/hpf, White blood cell (WBC): 1-3/hpf, and albumin: Absent. Urine culture showed no growth. USG revealed multiple echo-dense areas and focal calcification in the left kidney (Figure 1). Thus, we did some blood tests. Provisionally, we diagnosed this case as a nephrocalcinosis due to idiopathic hypercalciuria and differentially think of other metabolic causes. His initial lab investigations are shown in Table 1.

Blood test revealed normal parathyroid hormone levels, serum calcium and phosphate levels were normal, the urinary calcium/creatinine ratio was 0.8 mmol/mmol and the urine oxalate creatinine ratio was normal. His renal function was found to be normal. ABG revealed a normal blood PH of 7.42. After genetic confirmation,

Table 1. Results of initial investigations

Variables	Patient Values	Ref. Values
Serum Na^+ (mmol/L)	142	135-145
Serum K^+ (mmol/L)	4.8	3.5-5.5
Serum Cl^- (mmol/L)	105	98-107
Blood PH	7.43	7.35-7.45
Serum magnesium (mmol/L)	0.8	0.7-1.0
Serum Ca^{2+} (mmol/L)	2.4	2.2-2.7
Serum PTH (pg/mL)	45.2	8.0-61
Serum PO_4 (mmol/L)	1.9	1.4-2.4
Serum creatinine(µmol/L)	45	27-62
Urine osmolarity (mOsm/kg)	297	50-750
Urine Ca/Cr (mmol/mmol)	0.8	0.09-2.2
Urine oxalate: creatinine (mmo:mmol)	0.09	0.06-0.17
Spot urine PCR (gm/mmol)	0.02	<0.05
Serum uric acid (mg/dL)*	1.9	2.5-5.5

Abbreviations: Na^+: Sodium; K^+: Potassium; Cl^-: Chloride; Ca^{2+}: Calcium; PTH: Parathyroid hormone; PO_4: Phosphate; Ca/Cr: Calcium/creatinine clearance ratio; PCR: Polymerase chain reaction.

*Serum uric acid level was low and all other parameters are within the normal range.

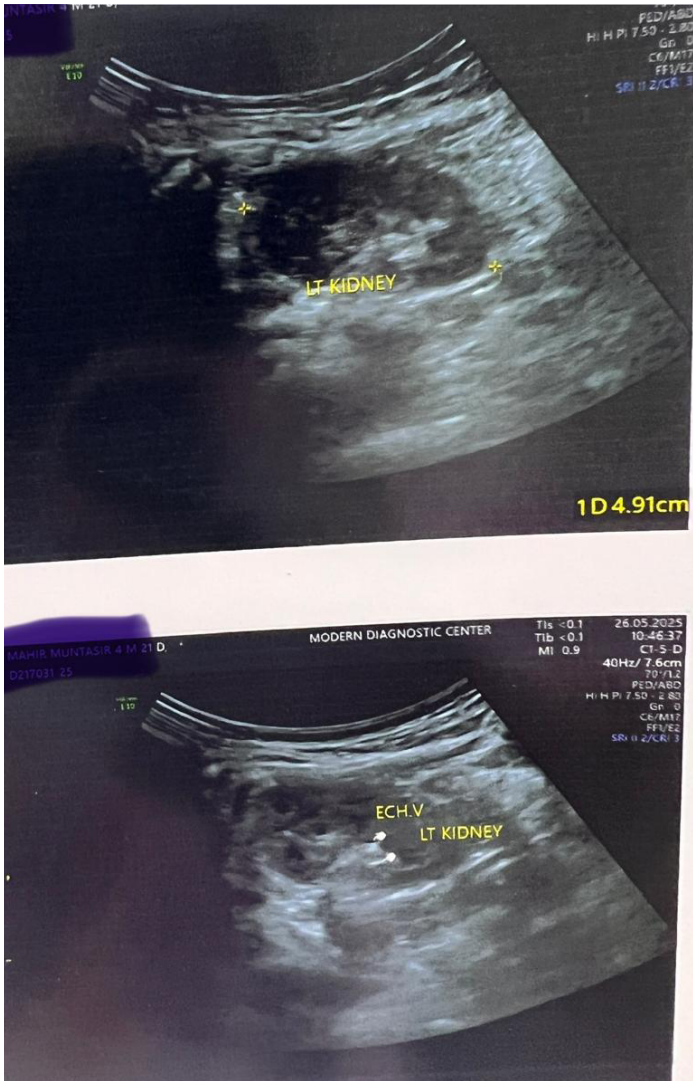

Figure 1. Ultrasound images of the kidneys

we also measured serum uric acid, which was found to be low (1.9 mg/dL). We started adding drinking water along with breast milk, as well as potassium citrate, after obtaining the USG report to minimize stone formation; however, once xanthinuria was confirmed genetically, we discontinued potassium citrate, as urine alkalinization does not prevent xanthine stone formation. We continue to follow up regularly with this patient. At one year of age, his urine report showed 1 to 5 RBCs per high-power microscopic field., and a recent ultrasonography revealed a single focal calcification in the left kidney. In addition, a surgical consultation was performed and it was recommended that conservative medical treatment be continued. For the publication of this case report, we obtained informed written consent from the parents.

Discussion

Classic xanthinuria occurs as a result of reduced or absent enzymatic activity of xanthine dehydrogenase (XDH), which is responsible for the final step of purine metabolism and leads to the conversion of xanthine and hypoxanthine to uric acid [7]. The onset of disease varies from infancy to adulthood. It may be asymptomatic or may present with hematuria, infections, nephrolithiasis, and colic [8]. Umair et al. reported an 18-month-old case presented with renal stone and hematuria [9]. Our patient presented at 2 months of age with symptoms of dysuria and nephrocalcinosis. The diagnosis may be made incidentally, by finding low serum uric acid or by analysis of stones after surgical removal of kidney or ureteral stones [8-10]. In the case of our patient, we found uric acid levels to be low as well. We confirmed our patient as a case of hereditary xanthinuria after the whole-exome sequencing revealed a mutation in the *XDH* gene.

Patients with xanthinuria are advised to follow a low-purine diet and drink a lot of water. Unlike individuals with uric acid lithiasis, urine alkalinization has no effect because xanthine's solubility is mostly independent of urine pH [11, 12]. We started adding drinking water at 2 months of age, which alleviated the symptoms of excessive crying during micturition. Additionally, although we initially started with potassium citrate, we stopped it at 6 months after genetic confirmation. We advised the mother to give the child complementary foods with a low-purine diet and to continue it.

Recently, a study identified in vitro inhibitors of xanthine crystallization that have the potential for inhibiting the formation of xanthine crystals in urine and preventing the development of renal calculi in patients with xanthinuria. Therefore, theobromine intake could protect xanthinuric patients from renal xanthine calculi. Clinical trials are needed to prove this effect in vivo and it is not available for treatment [11].

Conclusion

Hereditary xanthinuria may present with hematuria and nephrocalcinosis. All renal stones should be examined, and serum uric acid measurement may be done in suspected cases. Confirmation by genetic testing is useful for identifying the type of hereditary xanthinuria and predicting the outcomes.

Ethical Considerations

Compliance with ethical guidelines

This study was approved by the Ethics Committee of Dr. MR Khan Shishu Hospital & Institute of Child Health, Dhaka, Bangladesh.

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Authors' contributions

All authors equally contributed to preparing this article.

Conflict of interest

The authors declared no conflict of interest.

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References

[1] Park E, Kim SW, Kim SJ, Baek M, Ahn YH, Cho MH, et al. Hematuria in children: Causes and evaluation. Child Kidney Dis. 2024; 28(2):66-73. [DOI:10.3339/ckd.24.010]

[2] Mechler K, Mountford WK, Hoffmann GF, Ries M. Ultra-orphan diseases: A quantitative analysis of the natural history of molybdenum cofactor deficiency. Genet Med. 2015; 17(12):965-70. [DOI:10.1038/gim.2015.12] [PMID]

[3] Ichida K, Amaya Y, Okamoto K, Nishino T. Mutations associated with functional disorder of xanthine oxidoreductase and hereditary xanthinuria in humans. Int J Mol Sci 2012; 13(11):15475-95. [DOI:10.3390/ijms131115475] [PMID]

[4] Peretz H, Naamati MS, Levartovsky D, Lagziel A, Shani E, Horn I, et al. Identification and characterization- tion of the first mutation (Arg776Cys) in the C-terminal domain of the Human Molybdenum Cofactor Sul- furase (HMCS) associated with type II classical xanthinuria. Mol Genet Metab. 2007; 91(1):23-29. [DOI:10.1016/j.ymgme.2007.02.005] [PMID]

[5] Habbig S, Beck BB, Hoppe B. Nephrocalcinosis and urolithiasis in children. Kidney Int. 2011; 80(12):1278-91. DOI:10.1038/ki.2011.336] [PMID]

[6] Mateos FA, Puig JG, Jimenez ML, Fox IH. Hereditary xanthinuria: Evidence for enhanced hypoxanthine salvage. J Clin Invest. 1987; 79(3):847-52. [DOI:10.1172/JCI112893 PMID: 3818951] [PMID]

[7] Sawant S, Waydande A, Shinde A, Natha Mhaske S. Xanthinuria: A rare case report. Int J Sci Healthcare Res. 2023; 8(3):394-8. [DOI:10.52403/ijshr.20230353]

[8] Nagae A, Murakami E, Hiwada K, Sato Y, Kawachi M, Kono N. Asymptomatic hereditary xanthinuria: A case report. Jpn J Med. 1990; 29(3):287-91. [DOI:10.2169/internalmedicine1962.29.287] [PMID]

[9] Umair M, Hussain SZ, Khan A, Murtaza B, Rehman OF, Nawaz M. Pure xanthine pediatric urolithiasis: A cause of acute renal failure. Urol Case Rep. 2020; 34:101438. [DOI:10.1016/j.eucr.2020.101438] [PMID]

[10] Grases F, Costa-Bauza A, Roig J, Rodriguez A. Xanthine urolithiasis: Inhibitors of xanthine crystallization. Plos One. 2018; 13(8):e0198881 [DOI:10.1371/journal.pone.0198881] [PMID]

[11] López M, Hoppe B. History, epidemiology and regional diversities of urolithiasis. Pediatr Nephrol 2010; 25(1):49-59. [DOI:10.1007/s00467-008-0960-5] [PMID]

[12] Miake J, Hisatome I, Tomita K, Isoyama T, Sugihara S, Kuwabara M, et al. Impact of hyper- and hypo-uricemia on kidney function. Biomedicines. 2023; 11(5):1258. [DOI:10.3390/biomedicines11051258] [PMID]