MKÜ Tıp Dergisi 2019; 10(36): 25-26

The Probable Cause of Hypouricemia; Xanthinuria

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DOI: 10.17944/mkutfd.494816

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Bildirimler/Acknowledgement

Yazarlar bu makale ile ilgili herhangi bir çıkar çatışması bildirmemişlerdir.
The authors declare that they have no conflict of interests regarding content of this article.
Yazarlar bu makale ile ilgili herhangi bir finansal destek bildirmemişlerdir.
The Authors report no financial support regarding content of this article.

Geliş/Received: 10.12.2018
Kabul/Accepted: 05.03.2019

e-ISSN: 2149-3103
Web: http://dergipark.gov.tr/mkutfd

Öz

Hipoüriseminin Muhtemel Nedeni; Ksantinüri

Kalıtımsal hipoürisemiye genellikle ksantinüri ve herediter renal hipoürisemi yol açmaktadır. Hipoürisemi serum ürik asit seviyesinin 2mg/dl'den düşük olması olarak tanımlanmaktadır. Ksantinüri her yaşta, nadir görülen ve otozomal resesif geçen bir hatalıktır. Ksantin ve hipoksantin, enzim veya kofaktör eksikliği sonucu ürik asite dönüşümü olmaz ve kanda birikir, ayrıca idrar ile atılımı artar. Serum ve idrarda ürik asit seviyesi çok düşük saptanmaktadır. Biz bu makalede, hipoürisemi saptanan ve ksantinüri tanısı konulan yetmiş yedi yaşında kadın hasta litaratür eşliğinde tartışıldı.
Anahtar Kelimeler: Hipoürisemi, Ksantinüri, böbrek taşı

Abstract

The Probable Cause of Hypouricemia; Xanthinuria

Xanthinuria and hereditary renal hypouricemia usually leads to hereditary hypouricemia. Hypouricemia is defined as having serum uric acid level lower than 2 ml/dl. Xanthinuria is an autosomal recessive disease that can be occasionally seen in all ages. As a result of enzyme or cofactor deficiency, xanthine and hypoxanthine do not convert to uric acid and accumulate in the blood and increase the excretion in urine. The level of uric acid is detected very low either in serum or in urine. In this study, a case of a seventy-seven-year-old female patient in which hypouricemia was detected and who had the diagnosis of xanthinuria was discussed.
Keywords: Hypouricemia, Xanthinuria, renal calculus

INTRODUCTION

Hypouricemia is a benign status in which the plasma uric acid levels are less than 2.0 mg/dl. Hereditary hypouricemia is caused by hereditary renal hypouricemia and xanthinuria. Xanthinuria is occasionally autosomal recessively inherited. Xanthinuria is originated from the type-1 xanthine dehydrogenase/xanthine oxidase enzyme deficiency or insufficiency, on the other hand, type-II xanthinuria is originated from the combined deficiency of xanthine dehydrogenase and aldehyde oxidase. Third type is clinically different, and it is characterized by molybdenum cofactor deficiency, sulphite oxidase deficiency. In the molybdenum cofactor deficiency, the functions of xanthine dehydrogenase and aldehyde oxidase are affected with sulphite oxidase together (1-2).

It is important to emphasize that xanthinuria may occur in each age group. Xanthine is an extremely insoluble purine. It may lead to xanthine calculus in kidneys. Xanthine calculi are usually brownish orange and oval and, they are easily cut. The prevalence of hereditary xanthinuria is not known. Its annual incidence is estimated as 1/6000 and 1/69000 (2).

CASE

A female seventy-seven-year old female patient referred to our out-patient clinic due to the fact that blood urea nitrogen levels were found higher. In her medical history, there are osteoporosis, nephrolithiasis and she was operated two times for nephrolithiasis (she was using candesartan-hydrochlorothiazide and ibandronic acid). In physical examination, blood pressure was 130/60 mmHg, her body temperature was 37 °C and her other physical examinations were normal. Her laboratory findings were detected as 101 mg/dl (80 to 110) for glucose, as 43 mg/dl (7 to 28) for blood urea nitrogen, as 1 mg/dl (0.5 to 1.1) for serum creatinine, as 0.1 mg/dl (2.6 to 7.6) for serum

uric acid, 2.1 mg/dl (1.6 to 2.6) for magnesium, as 4.2 mg/dl (2.8 to 4.5) for phosphor, as 9.5 mg/dl (8.8 to 10.2) for calcium, 140 mmol/l (130 to 145) for sodium, as 5.2 mmol/L (3.5 to 5.5). Complete urine analysis was normal and, there was no proteinuria in the twenty-four urine and, uric acid was detected as 0.1 mg/dl and 1.4 mg/day. Fractional uric acid was computed as 2.6% percent. In renal ultrasound, a seven-millimeter calculus was detected at the lower pole in the left kidney. Since there was no reagent xanthine and hypoxanthine could not be studied in serum and in urine. Diagnosis of probable xanthinuria was established and hydration and a diet with poor purine were recommended.

DISCUSSION

The diagnosis of xanthinuria can be established by investigating the serum and urine uric acid, xanthine and hypoxanthine and moreover by studying genetic mutation. Serum uric acid can be lower as it cannot be detected in the xanthinuria patients. In xanthinuria patients, since xanthine and hypoxanthine cannot be converted into uric acid, uric acid is found as lower level as it cannot be detected. Furthermore, xanthine and hypoxanthine are detected higher (3).

Clinically, nonspecific characteristics such as hematuria, recurrent urinary infection, crystalluria, renal colic, acute renal injury and, chronic renal disease can be seen. Arthropathy, myopathy and duodenal ulcer related with the long-term accumulation of xanthine in soft tissues can be seen. Myopathy which is the most common among them emerges in the form of muscle pain and cramp following the exercise. It may be asymptomatic in twenty percent (20%) of the patients (4-5). Xanthinuria may be secondary to the use of allopurinol due to excessive production of uric acid. In Lesch-Nyhan syndrome or partial hypoxanthine guanine phosphoribosyl transferase deficiency, xanthine increases as a result of use of allopurinol. The increase in xanthine leads to xanthine stones and xanthine nephropathy (5). Xanthine crystals may induce acute gout arthritis and it has been demonstrated that rheumatoid arthritis occurs in hereditary xanthinuria (2, 6).

In order to distinguish type-I and type-II, allopurinol challenge test or since xanthine dehydrogenase/xanthine oxidase activity are only expressed in the small intestine and in the liver in humans, invasive bowel or liver biopsy are conventionally used. In allopurinol challenge test, serum oxypurinol is studied three hours after the administration of 10 mg/kg, maximum 300 mg allopurinol. In type-1, oxypurinol conversion occurs due to the presence of aldehyde oxidase in the deficiency of xanthine dehydrogenase and xanthine oxidase and while detecting oxypurinol in the serum, if this is type-2, no oxypurinol which is related with the deficiency of xanthine dehydrogenase, with the deficiency of xanthine oxidase and with the deficiency of aldehyde oxidase is detected in the serum. In hereditary renal hypouricemia, the fractional excretion of uric acid increases significantly in relation with the reduced tubular resorption being different form hereditary xanthinuria. Similarly, higher fractional uric acid excretion with hypouricemia (>10%) may accompany to renal Fanconi syndrome, to syndrome of inappropriate antidiuretic hormone secretion, to total parenteral nutrition, to Wilson's disease, to intravenous contrast agent administration, to several neoplasms, to salicylate and heavy metal intoxications. Hypouricemia with decreased fractional uric acid excretion is the conclusion of the administration of allopurinol or rasburicase, that of several neoplasms or that of the hepatic diseases (7-8). In the treatment of xanthinuria, hydration and a diet with poor purine are recommended.

In conclusion, xanthinuria can be seen in all age groups and, xanthinuria should be investigated in adults in which hypouricemia is detected. As a result, xanthinuria is one of the rare causes of hypouricemia. Xanthinuria can cause nephrolithiasis and acute renal injury. Hypouricemia should be considered in cases. After diagnosis, treatment diets suggestions should be made.

References

1. Grases F, Costa-Bauza A, Roig J, Rodriguez A. Xanthine urolithiasis: Inhibitors of xanthine crystallization. bioRxiv, 2018;335364.
2. Sebesta I, Stiburkova B, Krijt J. Hereditary xanthinuria is not so rare disorder of purine metabolism. Nucleosides Nucleotides Nucleic Acids. 2018; 3:1-5.
3. Raivio KO, Saksela M, Lapatto R. Xanthine oxidoreductase: role in human pathophysiology and in hereditary xanthinuria. In: Scriver CR, Beaudest AL, Sly WS, Valle D (Edds) The methabolic and molecular bases of inheredited diseases, 8th edn. New York. McGraw-Hill, 2001;2639-52.
4. Mraz M, Hurba O, Bartl J, Dolezel Z, Marinaki A, Fairbanks L, Stiburkova B. Modern diagnostic approach to hereditary xanthinuria. Urolithiasis, 2015;43(1), 61-67.;
5. Simmonds HA. Hereditary xanthinuria. Orphanet Encyclopedia. 2003.
6. Jurecka A, Stiburkova B, Krijt J, Gradowska W, Tylki-Szymanska A.Xanthine dehydrogenase deficiency with novel sequence variations presenting as rheumatoid arthritis in a 78-year-old patient.J Inherit Metab Dis. 2010;33(3):S21-4
7. Mraz M, Hurba O, Bartl J, Dolezel Z, Marinaki A, Fairbanks L, Stiburkova B. Modern diagnostic approach to hereditary xanthinuria. Urolithiasis. 2015;43(1):61-7.
8. Martín, N. Esparza, and V. García Nieto. "Hypouricemia and tubular transport of uric acid." Nefrologia 2011;31(1):44-50