Original Research Paper

Volume - 13 | Issue - 11 | November - 2023 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Pediatrics

# AN INFANT WITH DARK URINE: A BRIGHT DIAGNOSIS

| | |
|---|---|
| **Reshma Ramesh*** | M.D, Pediatrics, Registrar, Department of General Pediatrics and Neonatology Meenakshi Mission Hospital and Research Centre, Madurai, Tamil Nadu. *Corresponding Author |
| **Arun Priya** | DCH., DNB, Paeds, Associate Consultant, Department of General Pediatrics and Neonatology, Meenakshi Mission Hospital and Research Centre, Madurai, Tamil Nadu. |
| **Uma Muralidharan** | DCH.,DNB, Paeds., PGDDN, Senior Consultant, Department of General Pediatrics and Neonatology, Meenakshi Mission Hospital and Research Centre, Madurai, Tamil Nadu. |
| **Veena** | DNB Resident, Department of General Pediatrics and Neonatology, Meenakshi Mission Hospital and Research Centre, Madurai, Tamil Nadu |

**ABSTRACT** Alkaptonuria is an autosomal recessively inherited, rare genetic disorder of tyrosine metabolism with an overall reported incidence of 1 in 2,50,000 live births. Alkaptonuria is one of British physician Garrod's classic tetrad of Inborn Errors of Metabolism. The disorder is caused by the deficiency of Homogentisate 1,2-dioxygenase (HGD) enzyme, resulting in accumulation of Homogentisic acid and its metabolites in body fluids and tissues, resulting in ochronosis and ochronotic osteoarthropathy. The earliest and sole paediatric manifestation of the disease is darkening of urine. A one year old girl presented to the Pediatric Outpatient department with complaints of darkening of urine since neonatal period, with no other complaints. Urine quantitative analysis pointed towards Alkaptonuria. Currently, child is on regular follow up and is being treated with Vitamin C to delay the progression of the disease. Early diagnosis with prompt intervention can delay the onset of complications and preserves the quality of life of the child.

**KEYWORDS :**

## INTRODUCTION:

Alkaptonuria is a rare genetic disorder of tyrosine metabolism with an overall reported incidence of 1 in 2,50,000 live births[1]. Alkaptonuria is one of British physician Garrod's classic tetrad of Inborn Errors of Metabolism, proposed to have autosomal recessive mode of inheritance[2]. It is caused by the deficiency of Homogentisate 1,2-dioxygenase enzyme, resulting in excretion of large amounts of Homogentisic Acid (HGA) in urine. Accumulation of HGA and its metabolites - benzoquinone and melanin polymers in body fluids and tissues, results in blackish discolouration of urine, sweat and darkening of cartilage tissues of joints[1]. The earliest presenting feature of Alkaptonuria is blackish discolouration of urine, which also happens to be the sole manifestation of this condition in children, with only 21% being diagnosed before the age of 1. Sequelae such as arthritis, joint destruction and damage of cardiac valves occur only after the third decade[2]. We report a 1 year old girl baby, who presented with history of passing dark coloured urine since birth. A high index of suspicion is required in diagnosing this rare condition because it can be misdiagnosed as recurrent UTI by the unwary.

**Case Presentation**:

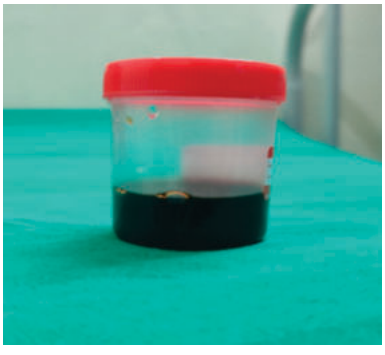
1 year old girl baby, first born to second degree consanguineous marriage was brought to the Paediatric Out patient department by her parents with complaints of darkening of urine on diapers and surfaces, few hours after voiding. This was noticed by the parents since birth. The child did not have recurrent history of fever, did not cry while voiding and had no history of double voiding. Multiple medical consultations were done in the past, before the child presented to us. The child had received multiple courses of antibiotics over the months, as recurrent urinary tract infection was considered the primary diagnosis, though concomitant symptoms were absent.

The Child was delivered at term by elective Lower Segment Caesarean section in view of failed induction. Her developmental milestones and nutritional status were age appropriate. There was no history of similar symptomatology in any of the family members. On general examination, she was active, alert, afebrile and had stable vitals and no other obvious abnormality on physical examination. Eye and ear examination were normal. No tenderness, swelling or deformity of joints were noted.

The child's fresh voided urine was collected in an open container and was observed for colour change. The colour of the urine appeared normal initially, however, after 3 hours turned dark, in concurrence with the history given by the parents.

Routine laboratory investigations were within normal limits. Urine for Homogentisic acid via gas chromatography-mass spectrometry (GC-MS) was positive for Homogentisic acid . Echo screening done was normal.

**Urine Immediately After Voiding**



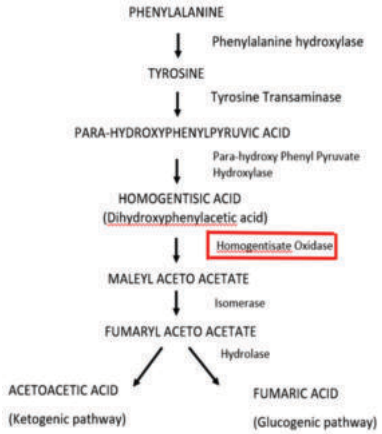
**Urine 3 Hours After Voiding**

**Management And Outcome:**

Considering the darkening of urine, porphyrias, hemoglobinuria, myoglobinuria and alkaptonuria were listed as differential diagnosis. A detailed history was elicited, including family, personal and drugs and examination was done. With urine for HGA being positive, we narrowed the diagnosis to alkaptonuria. Genetic testing for confirmation has been planned. As there is no recommendation for definite treatment, child was started on Oral Vitamin C 250mg once a day. Child is on regular follow up.

## DISCUSSION:

Alkaptonuria is a rare autosomal recessive disease, mapped to chromosome 3, between region 3q13.3. An inborn error of the catabolism of Phenylalanine and tyrosine, it is characterised by the inability to metabolise HGA. The enzyme HGD catalyses the conversion of HGA to Maleyl acetoacetate and fumaryl acetoacetate[3].




So alkaptonuria results in accumulation of HGA at about 2000 times the usual rate. Accumulated HGA gets oxidized to benzoquinones. Upon exposure to air, they form melanin pigment like polymeric material, responsible for the darkening of urine and tissues. The earliest manifestation is the dark staining of diapers, which is enhanced by an alkaline pH[3]. Daily excretion of homogentisic acid in the urine is usually around 4-8 grams/day and its quantification is also useful for monitoring of therapy. Diagnosis is usually delayed until adulthood when ochronosis or arthritis become apparent[5]. This is due to the rapid elimination of HGA by the kidneys, resulting in low blood levels of HGA. However with time, HGA gets accumulated in blood. The etiology behind ochronosis and osteoarthropathy is because the enzyme mediated conversion to the pigment like polymer occurs primarily in cartilaginous tissues. With time, the cartilaginous tissues lose their transparency and appear slate blue and black, usually by the 4 th decade. Other physical signs include scleral and limbal pigmentation and pigmentation of palms and fingers, which could lead to a misdiagnosis of Addison's disease. Despite significant associated morbidity, life expectancy remains normal. Typically, individuals start presenting with back pain due to the early involvement of intervertebral discs at the thoracic and lumbar level. The hallmark of this condition is arthritis, which occurs with advancing age, primarily involving the large joints such as hip, knee, spine and shoulder[7]. Cardiac involvement occurs in the form of valvulitis, involving the mitral and aortic valve leaflets. Calcification of coronary artery occurs in 50% of patients resulting in ischemic heart disease.

Medical therapy is used to alleviate the rate of pigment deposition. Restrictions on the dietary intake of Phenylalanine and tyrosine has reportedly reduced HGA excretion. Ascorbic acid, at a dose of upto 1gm/day is recommended for its antioxidant nature. It also retards the conversion of homogentisate to the pigment material. Nitisinone, an inhibitor of the 4-hydroxyphenylpyruvate dioxygenase which mediates formation of HGA, has been used with limited evidence[5].

## REFERENCES:

1. Datta A.K, Mandal S, Dasgupta A et al. Alkaptonuria diagnosed in a 4 month old baby girl: a case report. Cases Journal 1, 308 (2008).
2. Sangeetha G, Chandran S, Ganesan S, Jayaraj J. Alkaptonuria in an adolescent boy. BMJ Case Rep. 2021 Feb 4;14(2).
3. Damarla N, Linga P, Goyal M, Tadisina RS, Satyanarayana R, Bommisetti H. Alkaptonuria: a case report. Indian J Ophthalmol. 2017 Jun; 65(6):518-521.
4. Jemma B Mistry, Marwan Bukhari, Adam M Taylor et al. Alkaptonuria Rare Diseases
5. Sharma V, Nerli RB, Magdum PV, Mudegoudra A, Hiremath MB. Alkaptonuria in a 6 year old patient: case report. Urol Case Rep. 2015;3(6):188-189.
6. Craide FH, Fonseca JS, Mariano PC, Fernandez NM, Castro CG, Mene Y. Alkaptonuria: Case Report. An Bras Dermatol. 2014 Sep-Oct;89(5):799-801.
7. Kliegman, R. Nelson textbook of Pediatrics (Edition 21). Philadelphia, PA: Elsevier.