Endourology

Alkaptonuria in a 6 Year Old Patient: Case Report

Vikas Sharma a, Rajendra B. Nerli a,*, Prasad V. Magdum a, Abhijith Mudegoudra a, Murigendra B. Hiremath b

a KLES Kidney Foundation, KLES Dr. Prabhakar Kore Hospital and Medical Research Center, KLE University’s J. N. Medical College, Belgaum 590010, Karnataka, India
b Department of Biotechnology and Microbiology, Karnatak University, Dharwad, India

Abstract

Alkaptonuria is a rare disorder of tyrosine catabolism. A 6 year old male child presented with history of darkish staining of the toilet commode following voiding. The urine when kept in a sterile container for a few hours turned black. Urine examination showed massive amounts of homogentisic acid. Patient was diagnosed as alkaptonuria.

Keywords:
Alkaptonuria
Homogentisic acid
Dark urine
Ochronosis

Introduction

Alkaptonuria is a rare disorder of tyrosine catabolism in which deficiency of Homogentisic acid oxidase leads to excretion of large amount of Homogentisic Acid (HGA) in urine. HGA oxidizes to benzoquinones, which in turn forms melanin-like polymers in urine and tissues. Accumulation of HGA and its metabolites in tissues causes ochronosis, with darkening of cartilaginous tissues and bone. Alkaptonuria has possible consequences like arthritis, joint destruction, and deterioration of cardiac valves. We report a child who attended the pediatric urology OPD with complaints of dark staining of the toilet following voiding.

Case report

A 6-year-old male child of a first-degree consanguineous couple presented to out-patient services with history of darkish staining of the toilet commode following voiding. This was noticed by the mother of the child and was a matter of concern. The child had no other complaints. The child was moderately built and nourished. Genital examination revealed glanular hypospadiasis. No other obvious abnormality was noticed on physical examination. The child was made to void and it was noticed that the urine appeared normal at the time of voiding (Fig. 1a). However the urine turned dark after exposure to atmosphere within a few hours (Fig. 1b).

Routine laboratory investigations were within normal limits and skeletal x-rays showed no obvious bony changes. The urine gas chromatography/mass spectrometry (GC/MS) showed a massive amount of homogentisic acid. Child was started on Vitamin C 500 mg bid. The patient is under regular follow-up.

Discussion

The urine of an alkaptonuric individual is normal in appearance while voiding. However, it starts to darken when left standing. Darkening of urine occurs by oxidation and polymerization of the homogentisic acid, and its action is enhanced in an alkaline pH. Diagnosis may be delayed until adulthood, when arthritis or ochronosis occurs because acidic urine may not become dark even after many hours of standing. The diagnosis is confirmed by measurement of homogentisic acid in urine or by the high-pressure liquid chromatography method for the quantitation of homogentisic acid and its derivative benzoquinone acetic acid. Excretion of homogentisic acid in the urine is usually around 4–8 g daily and its measurement is also used for therapy monitoring.

Pediatric patients with alkaptonuria are usually asymptomatic. In our case the patient’s black-colored urine was discovered per chance by the mother because of presence of urine drops on the side of the Asian toilet where spillage occurs more commonly than in Western style toilets. Pigmentation of the sclera or the cartilage of the ear starts to appear in adulthood. Pigmentation may also be
seen in the teeth, buccal mucosa, and in the nails or the skin, giving these areas a dusty color, which is due to slow accumulation of the black polymer of homogentisic acid in the cartilage and other mesenchymal tissues.

Arthritis occurs in almost all patients with advancing age and it is the only disabling effect of this condition. It appears early in large weight bearing joints like hips, spine and knees. Cardiac involvement includes high incidence of heart disease, commonly due to mitral and aortic valvulitis. Ischemic heart disease with ultimate myocardial infarction is a common cause of death.

Treatment of alkaptonuric patients is a challenge. No treatment has been completely successful. Dietary restrictions on the intake of tyrosine and phenylalanine substantially reduce the excretion of homogentisic acid. Ascorbic acid prevents the effects of HGA on joints. Nitisinone has been proposed as potential therapy because it inhibits the enzyme that produces HGA but at present it is still under trial and use is limited to adult alkaptonuric patients.

Conflict of interest
The authors have no conflict of interest.

References
1. Phornphutkul C, Introne WJ, Perry MB, et al. Natural history of alkaptonuria. N Engl J Med. 2002 Dec 26;347(26):2111–2121.
2. Al Essa M, Al-Shamsan L, Rashed MS, Ozand PT. Alkaptonuria: case report and review of the literature. Ann Saudi Med. 1998;18(5):442–444.