Original Research Paper

Volume-9 | Issue-4 | April-2019 | PRINT ISSN No 2249-555X

Paediatrics

ALKAPTONURIA

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ABSTRACT Alkaptonuria is a rare disorder of tyrosine catabolism. A 6 year old male child presented with history of generalized swelling . The urine when kept in a sterile container for a few hours turned black. Urine examination showed massive amounts of homogentisic acid, urine albumin 4+. Patient was diagnosed as nephrotic syndrome with alkaptonuria

KEYWORDS : Alkaptonuria, Nephrotic Syndrome , Homogentic Acid Oxidase

INTRODUCTION

This rare (with an incidence of approximately 1 in 250,000 live births) Autosomal recessive disorder is caused by a deficiency of homogentisic acid oxidase (homogentisate 1,2-dioxigenase). In alkaptonuria, large amounts of homogentisic acid are formed , which are excreted in urine or deposited in tissues.

The main **clinical manifestations** of alkaptonuria consist of ochronosis and arthritis in adulthood. The only sign in children is a blackening of the urine on standing, caused by oxidation and polymerization of homogentisic acid. A history of gray- or black-stained diapers should suggest the diagnosis. This sign may never be noted; hence, diagnosis is often delayed until adulthood. *Ochronosis,* which is seen clinically as dark spots on the sclera or ear cartilage, results from the accumulation of the black polymer of homogentisic acid. *Arthritis* is another result of this deposition and can be disabling with advancing age..

The gene for homogentisic acid oxidase *(HGD)* maps to chromosome 3q13.3. Several disease-causing mutations have been identified. Alkaptonuria is commonest in the Dominican Republic and Slovakia.

The **diagnosis** is confirmed by finding massive excretion of homogentisic acid on urine organic acid testing. Tyrosine levels are normal.The enzyme is expressed only in the liver and kidneys.

CASE REPORT

A 6-year-old male child of a first-degree consanguineous couple presented to out-patient services with history of Generalized swelling periorbital swelling more during morning relieved by evening . The child had no other complaints. on physical examination periorbital swelling , ascites ,scrotal edema were present. vitals normal.no organomegaly The child was made to void and it was noticed that the urine appeared normal at the time of voiding . However the urine turned dark after exposure to atmosphere within a few hours .

LABORAOTARY INVESTIGATIONS :

Urine albumin ++++, urine p/c ratio : 4.2 , serum cholesterol: 346 mg/dl serum creatinine : 0.6 mg/dl, serum albumin : 1.6mg/dl. skeletal x-rays showed no obvious bony changes. The urine gas chromatography/mass spectrometry (GC/MS) showed a massive amount of homogentisic acid. Routine laboratory investigations were with in normal limits.

Child was treated for nephrotic syndrome , started on vitamin c 500mg the patient is under regular follow up

Fresh urine sample . Dark discoloration of urine when left standing.

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. Pediatric patients with alkaptonuria are usually asymptomatic , in this child as urine is collected for routine monitoring and for laboratory assessment it was noticed to darken. 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.2 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.

Conclusion

Even a rare disorder high index of suspicion regarding the complaint and examination of dark coloured urine helps in early identication , early initiation of dietary restriction of tyrosine and phenylalnine and early initiation of treatment.

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