CASE REPORT

Alkaptonuria: A Case of Familial Inheritance from Hangarki Village in Dharwad District of Karnataka

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Abstract Alkaptonuria is a genetic disorder, unknown to the general public and ignored by general physicians due to lack of awareness of its high prevalence. Increasing incidences of familial inheritance are recorded. A 41 years 8 months male with the swollen knee, chronic mechanical pain, restricted limping walk and tingling sensation in the limb. Also, has a complaint of the stiffness of back in the morning, which gets relieved by movement. Mild hyper pigmentation of pinna and sclera of eye. X-ray report reveals osteoarthritis of the knee and thoracic kyphosis. After considering clinical finding, report of radiological investigation and Biochemical test results, patient was diagnosed as a case of Alkaptonuria. Screening of entire family revealed a typical case of familial inheritance. Hidden familial inheritance can be disclosed by mass screening of families and medical awareness.

Keywords Alkaptonuria · Homogentisic acid · Black urine · Familial inheritance

Introduction

Alkaptonuria (AKU) is unknown to the general public [1] who suffer from black discoloration of ear, nose along with joint pain of unidentified cause. It is ignored and treated as any other pain by many general physicians due to lack of awareness about the high prevalence of this rare autosomal genetic disease. A defective tyrosine metabolism if carefully correlated, exhibit cardinal triad of idiopathic arthropathy, Ochronosis and black colour urine on standing. Congenital deficiency or mutation affecting Homogentisate 1,2-dioxygenase enzyme is a root cause of this disease [2, 3].

Though few scattered cases have been reported from India, but this seems to be a tip of the iceberg for the prevalence of this disease in India [4–9]. We report a second case of the AKU Family from Hangarki village of Dharwad District having multiple sufferers due to inheritance.

Case Presentation

A 41 years and 8 months old male visited the Orthopedic Department of SDM College of Medical Sciences and Hospital, Dharwad. Complains presented were swollen knee with chronic mechanical knee pain, more in right knee, with a restricted limping walk and tingling sensation in the limb. Also, he has a complaint about the stiffness of back in the morning, which gets relieved by movement. From last 5 months knee pain progressively aggravated. It is more severe and unbearable form last month. The patient has a history of analgesic and anti-inflammatory medication prescribed by a general physician, but without much relief.

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On General Examination

Tenderness over lower thoracic and lumbar vertebra, restricted joint movement were noted. Mild hyper pigmentation of pinna and sclera of eye were visible, which may have been missed by others due to dark complexion. No neurological defect.

Radiological and Laboratory Results

X-ray report reveals osteoarthritis of the knee and thoracic kyphosis. Routine biochemical parameters within the normal reference range. R.A test was negative. Hematology investigations, complete blood count and hemoglobin were in normal range. ESR –15 mm/1 h.

Freshly voided urine sample was analysed in biochemistry department to look for suspected case of AKU. Biochemical tests like 1. Benedict's test for reducing sugar 2. Alkaline Urine test (5 % NaOH) 3. Ammoniacal silver nitrate reduction test 4. Ferric Chloride test 5. *N*-butanol extraction test and 6. Thin layer Chromatography was performed on urine, all above biochemical tests exhibited positive results [10, 11], Table 1.

After considering clinical finding, report of radiological investigation and Biochemical test results, patient was diagnosed as a case of Alkaptonuria.

Alkaptonuria is usually autosomal recessive. Earlier studies and our experience of family screening have detected multiple members affected in families. However, other individuals were asymptomatic; we looked for the screening of an entire family for the possibility of AKU in other members after taking their consent and explaining the importance.

Screening of Family Members

As shown in pedigree Fig. 1, we screened both sides, maternal and paternal relatives of our patient. We found there were no consanguineous marriages in the family, which could have been a possible cause of AKU. An entire family of patient's maternal side relative exhibited negative biochemical test for urine, thus indicating absence of this

disease. Among Patient's paternal side relatives, the patient's father who expired last year had suffered from cardiac disease. Homogentisic acid has an affinity for blood vessels and heart valve tissue; when it gets deposited it hardens the tissue which can cause cardiovascular disorders [12].

Patient's Grandfather who is 80 plus male, complain of chronic back pain, but as per his understanding farm work (labour) produces pain during the morning which subsides once the body becomes hot; hence he has ignored. On examination, he exhibited fewer psychological symptoms. His urine has shown biochemical tests for AKU positive.

Patient's first brother, who expired 8 years back due to some psychological complications. Whose detailed history was not available.

Patient's Second brother, 38 years, his urine sample shows biochemical tests for AKU positive. O/H he revealed complains about low back stiffness and wrist joint pains during the morning. He expressed black stains in cloths but did not put much mind. He practices and believes that a glass of water with the juice of one lemon early morning reduces the pain. Lemon is rich source of ascorbic acid (Vit C), which may act as antioxidant and delay the process of oxidative polymerization of Homogentisate when taken in mega dose. Though it need to be evaluated, but this is in disparity to similar clinical study results reported by Wolff JA (1989) "Vitamin C does not have any significant benefit in Alkaptonuric patients" [13, 14]. Patient's sister, has no complaints of pain or any physical symptoms but she has no child even after 8 years of marriage.

Patient's third Brother, is 30 years has no signs or symptoms of AKU and urine sample on analysis turned out to be normal.

The Patient has two female children, Out of two daughters, the one who is 3 years 5 months old, demonstrated mild colour for biochemical test expressing early case of alkaptonuria. Presently she is asymptomatic. The urine sample from Second daughter and the mother remained negative for biochemical test of AKU.

Patient's second brother, has two male children, first son who is 4 years 6 months turned out as normal but, second 3 years son, detected positive for AKU.

Table 1 The results of various biochemical tests performed to detect AKU on patient's family members (n = 25)

Test result	Benedict's test	Ferric chloride test	5 % NaOH test	Ammoniacal silver nitrate test	Butanol extraction test	Thin layer chromatography
Negative	18	20	20	20	20	20
Positive	7	5	5	5	5	5

Fig. 1 Typical pattern of non-consanguineous, hereditary alkaptonuria in farmer family of Hangarki village of Dharwad

Discussion

AKU is an inborn error. However, with the exception of black urine, disease remains silent till second or third decade of life. The reasons for this is unclear, and requires for detailed systematic study. A possible reason may be a gradual accumulation process reaching to expressive limit at this age of life. This was our second AKU family having multiple sufferers detected as part of our mass screening. Though as we know the prevalence is low, but Similar multiple cases have been reported from the Indian community in South India [15]. Numbers of reported cases are increasing year after year, which is the result of improved diagnostic facilities, increased medical awareness and better coverage. In this case our strange finding of lemon juice as palliative treatment needs further research. Due to lack of genetic study setup we could not do further investigations. High prevalence in our area has forced me to think for a genetic lab setup.

Acknowledgments This study is purely a self funded study, approved by the institutional ethical committee. The sample used for the study was Urine, which was collected from all the participants of the study after explaining and taking their consent.

Compliance with Ethical Standards

Conflict of interest The authors of this case report have declared that they have no conflict of interest.

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