Bang Med J Khulna 2016; 49 : 37-39

CASE REPORT

Alkaptonuria

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Abstract

Alkaptonuria is a rare metabolic autosomal recessive disorder. It occurs due to lack of an enzyme that results in deposition of homogentisic acid in various tissues. A male patient of 45 years presented with back pain for 20 years and multiple joint pain for 10 years. Patient has multiple nodules in both pinnae and pigmentation in both sclerae. His urine turns black upon standing. These findings are compatible with the diagnosis of Alkaptonuria..

Introduction

Generally, Alkaptonuria, also called ochronosis refers to the systemic deposition of ochre-colored pigment within the cartilage and collagenous tissues. It is a rare metabolic autosomal recessive disorder. Incidence of this disease is 1 in 250,000.1

This was the first human disorder found to conform to the principles of Mendelian autosomal recessive inheritance. Alkaptonuria usually occurs in adults, starting after the age of 30.2 It is a condition which is present at birth but is associated with morbidity years later.3

The disease is caused by an inborn error of tyrosine metabolism due to lack of the homogentisic acid (HGA) oxidase enzyme, which is normally highly expressed in hepatocytes.4 As a result excess homogentisic acid is deposited mainly in cartilaginous tissue, mucosa, skin, bone and heart, as well as excreted in urine, sweat, semen etc. The main complications are valvular calcifications and osteoarthritis mainly in the joints of spine and also dark pigmentation of skin, cartilage, sclerae and other connective tissue.

We report a case of alkaptonuria so that new cases can be diagnosed easily and early detection of complication and adequate management of the complication can be done. The detection of this disorder is beneficial for the affected individual as the administration of unnecessary drugs can be avoided.

Case Report

A male patient, 45 years old, complained of progressive back pain for 20 years. The pain was increased after activity and decreased in rest with no radiation. He also complained of multiple joint pain for 10 years. Knee joints were the most affected. The patient consulted several physicians and was diagnosed as a case of osteoarthritis and was treated with analgesics, anti-inflammatory drugs, muscle relaxants etc. He is a smoker, normotensive and non diabetic. There was no history of consanguinity.

Previously he was diagnosed as a case of nephrolithiasis and his renal stone was removed surgically. He was also hospitalized for acute coronary syndrome and conservative management was given.

General examination of this patient reveals normal body built and well nourished having no anaemia, cyanosis, jaundice or oedema of the feet. His pulse, B.P. was normal. There was multiple painless hard nodules in both pinnae and there was hyperpigmentation of both sclerae. (Fig. 1)

Examination of locomotor system reveals that there is kyphoscoliosis and movement of spine is restricted in all directions. Both knee joints were swollen, tender with restriction of both active and passive movements. Examination of other system reveals no abnormality.

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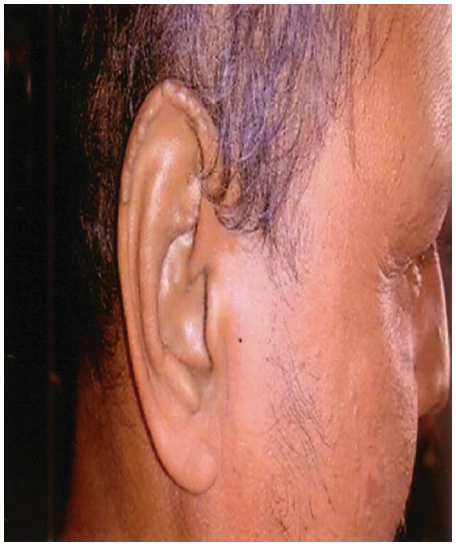

Fig 1: Patient with Alkaptonuria showing multiple nodule in pinnae

His haemoglobin was 12 gm/dl, total leucocyte count was 8200/cmm., with Polymorphs 67%, Lymphocyte 30%, Monocyte 1% and Eosinophil 2%. Serum uric acid was 3.5 mg/dl; E.S.R.13 mm in the Ist hour; Random blood sugar 88 mg/dl.

X ray of Lumbosacral Spine shows destruction of intervertebral discs with calcification causing reduction of joint spaces. There is also osteophyte and syndesmophyte formation. (Fig. 2)

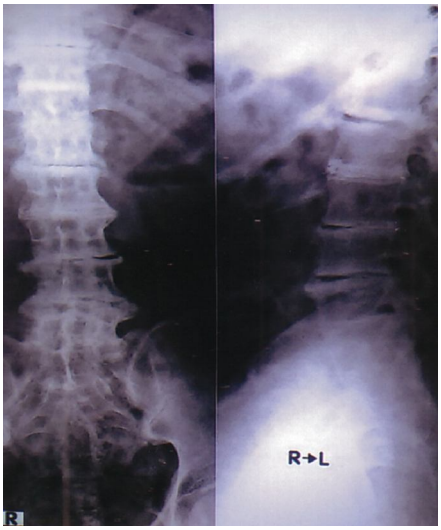

Fig 2: X-ray lumbosacral spine showing reduced disc spacewith calcification; osteophyte & syndesmophyte

Patient's urine was left standing for several hours and then it turns into black (Fig. 3). When Benedict's solution was added to urine it instantly turns black (Fig. 4). These findings were compatible with endogenous ochronosis or Alkaptonuria.

Patient was treated with NSAIDs for back pain and joint pain. He also received vitamin C 500 mg twice a day. The patient was advised to avoid diet rich in phenylalanine, tyrosine and protein such as cheese, soyabeans, beef, nuts, eggs, dairy, beans etc. He was advised for physiotherapy.

Fig 3: Urine turns into black when left standing

By taking these treatment pain was decreased and there was improvement of range of movement of spine and knee. He was discharged from hospital and advised for follow up visit.

Fig 4: Black urine after adding Benedict's solution

Discussion

Endogenous ochronosis is a rare metabolic autosomal recessive disorder with total deficiency of homogentisic acid oxidase enzyme. The homogentisic acid is part of the metabolic pathway of phenylalanine and tyrosine. The deficiency of the enzyme that metabolizes it (homogentisic acid oxidase) leads to its accumulation, that will be polymerized in a melanin like pigment that presents high affinity for connective tissue especially cartilage resulting in an ocher color (for this reason it carries the name of ochronosis).

When uine containing HGA is exposed to oxygen and is allowed to stand, it gradually turns dark. This process also can be hastened by alkaline conditions (e.g. Benedicts solution). In children, its main symptom is the darkening of the urine after a long period of rest or 'in contact with the environmental air or as blackened spots in baby's diaper. Whereas in adults after the fourth decade of life the main manifestation is osteoarthritis, followed by changes in eyes, ears, skin and in the genitourinary, cardiovascular and musculoskeletal system.

The deposition of pigment in alkaptonuria is observed in joints that offer great pressure like in the lumbar column and in large articulations. However, the lumbar spine is the most common region affected.4 Deposition occurs because the ochronosis pigment has high affinity for the collagen fibers of articulations. The diagnosis of Alkaptonuria is done through the clinical history, and from changes in coloration of urine in environmental air or in alkali. And confirmed by dosage of homogentisic acid in urine, winch is the gold standard.

Currently no effective cure is available. High doses of ascorbic acid may prevent deposition of the polymerized ochronotic pigment and may therefore prevent or delay subsequent symptoms.5 Low protein diet especially low in phenylalanine and tyrosine is advocated in combination with ascorbic acid.5 A new medicine Nitisinone that inhibits the enzyme, which produces HGA is on trial for the evaluation of long term therapy.6

For the articular lesions the use of NSAIDs is recommended, associated with the practice of physical therapy and exercises. In some cases joint replacement surgery will be necessary.

This metabolic disorder occurs worldwide, with the highest frequency seen 'in the Czech Republic and Santo Domingo, in which the prevalence approaches 1 case per 25,000 inhabitants.7 Cases have also been reported from USA, UK, Germany, Lebanon, Sudan, Saudi Arabia, Pakistan, Turkey and other parts of the world.8 There are isolated cases reported sporadically from India.

Alkaptonuria. is frequently a subdiagnosed disease. However, in recent time case reporting & research about alkaptonuria is increasing. Early diagnosis and management will decrease the sufferings of the patient.

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