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ALKAPTONURIA A CASE REPORT

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ABSTRACT Alkaptonuria is a rare inborn disease of error in metabolism with autosomal recessive inheritance. This occurs due to mutation of homogentisate 1, 2-dioxygenase which leads to deposition of homogentisic acid in connective tissues resulting in ochronosis. A case report of 56 year old male patient referred to out- patient department for Rheumatological evaluation with complaints of pain and stiffness in the lower back, hip and knee joint for the past 20 years and loss of weight. The patient had brownish black ocular pigmentation. Radiographs of thoracolumbar spine showed intervertebral disc calcification. Based on the clinical and Xray findings the presumptive diagnosis of Alkaptonuria was made. There is no specific treatment for Alkaptonuria, Vitamin C in the dose of 1g/day is recommended for older children and adults as it hinders the accumulation and deposition of homogentisic acid. Management is mainly advice on low protein diet and this will reduce tyrosine and phenyalanine in the body. Physiotherapy will help to reduce weight and improve posture.

KEYWORDS : Alkaptonuria; Homogentisic acid; homogentisate 1, 2 dioxygenase, Ochronosis

INTRODUCTION

Alkaptonuria is a rare inborn error of metabolism with autosomal recessive disease with autosomal recessive inheritance[1].It was first described by Sir Archibald Garrod as an "inborn error of metabolism"[1] in 1901 in London, UK[2]. The global prevalence of alkaptonuria is 1 per 100,000 to 250,000. This occurs due to mutation homogentisate 1, 2 dioxygenase (HGD). HGD enzyme catalyzes the conversion of homogentistic acid to maleylacetoacetic acid[1,2]. This prevents the complete breakdown of tyrosine and phenylalanine and leads to deposition of homogentisic acid in connective tissues called ochronosis. Homogentistic acid is excreted in urine which on exposure to air is oxidized to form a pigment-like polymeric material and this is responsible for the urine turning black color on standing[2] .When this polymer deposits in the cartilage it becomes blue and this ultimately becomes apparent on the skin overlying the cartilage[2]. This blue-black pigmentation usually appears after the age of 30 years.

Apart from cartilage homogentisic acid is deposited in other connective tissue including tendons and ligaments and even bone in later stages. Eventually the tissue that is affected becomes discolored, brittle and susceptible to rupture[2]. Enduring alkaptonuria leads to chronic joint pain and inflammation (arthritis), mainly in the spine and large joints (ochronotic spondylo-arthropathy). Ankylosis occurs due to stiffening or immobility of affected joints secondary to fusion of vertebrae or other bones[4]. Ochronosis causes osteoarthritis of major joints like knee.

Homogentisic acid less commonly deposits in aortic or mitral valves causing their stenosis and calcification. Homogentisic acid deposition in blood vessel leads to generalized accelerated atherosclerosis and myocardial infarction is a common cause of death. The deposition of HGA in kidney causes renal calculi and with associated complications of infection and obstruction leads to renal failure[1,2].

Case Report

A 56 old male patient was referred to our out- patient department with chronic backache and stiffiess for evaluation. His chief complaints was pain and stiffness in the lower back, hip and knee joint for the past 20 years and loss of weight with increased appetite for 6 months.

He gave history of bluish black discoloration of his undergarments for the past 14 years and a known case of hypothyroid on thyroid replacement therapy. He has undergone surgery for patella tendon rapture following a trauma and surgical therapy for benign prostatic hypertrophy. On the general examination: He was thin built, moderately nourished with BMI- 23, posture was skewed up with kyphosis and brownish black ocular pigmentation present outer side of palpable conjunctiva.

Fig: 1; showing brownish black ocular pigmentation on macroscopic examination of the patients urine revealed dark colour transformation after 6 hours of standing.

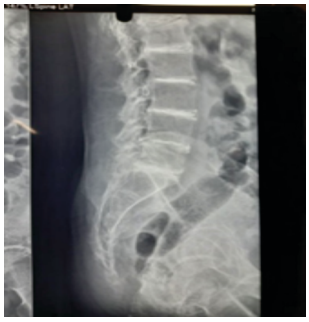

Fig:2. Xray lumbosacral spine lateral view showing intervertebral disc calcification at L2-L3,L3-L4& L4-L5

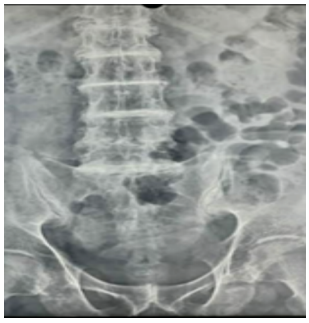

Fig:3. Xray Pelvis AP view showing intervertebral disc calcification at L1 –L5.

Systemic examination was normal. Rheumatological examination showed swelling of both knee joints and hip joint with painful restriction of all range of movements around the knee and hip joint. Chest expansion was reduced. Modified shobers test positive reflecting reduced forward flexion of the spine, left Knee crepitus was present with Genu-varus deformity and had evidence of carpo-metacarpal joint arthritis

Biochemical investigation: ESR 30, CRP 8, Thyroid function, liver function and renal function tests were normal. Urine was tested for homogentisic acid and it was positive.

Radiographs of chest was normal and the thoracolumbar spine showed intervertebral disc calcification, Vaccum phenomenon, knee joint showed bilateral medial compartment joint space narrowing with subchondral cyst (geodes jods) the largest one measuring 1.5cm in the lower end lower end femur. Based on the clinical, biochemical and X-ray findings the diagnosis of Alkaptonuria was made.

DISCUSSION:

Alkaptonuria is an autosomal recessive inherited disorder leading to excessive accumulation of homogentisic acid in the body and excreted in urine[4]. Homogentisic acid has great affinity towards alkali and hence accumulates in connective tissue of the skin, cartilage, sclera and joints[4]. All these reasons lead to the triad of homogentisic aciduria, ochronosis and arthritis[4]. The differential diagnosis includes acute intermittent porphyria, rheumatoid arthritis, ankylosing spondylitis and osteoarthritis.

The laboratory diagnosis is testing urine for the presence of homogentisic acid which is the gold standard test[4]. The quantification of homogentisic acid is done using gas chromatography-mass spectrometry (GC-MS) analysis of 24 hours urine. The amount of HGA excreted per day in Alkaptonuria is 1 to 8 grams[4].

There is no specific treatment for Alkaptonuria, Vitamin C in the dose of 1 g/day is recommended for older children and adults as hinders the accumulation and deposition of homogentisic acid but long-term use still proves to be ineffective[4]. The research in use of Nitisinone is promising and studies are going on because it has the ability to reduce the level of homogentisic acid in the body[4]. Management is mainly advice on low protein diet and this will reduce tyrosine and phenyalanine in the body. Physiotherapy will help to reduce weight and improve posture. Surgical therapy in Ochronotic arthropathy necessitates even joint replacement therapies[4].

Conflicts of interest: none

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