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A CASE OF OCHRONOSIS

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Abstract : Alkaptonuria (AKU) is an autosomal recessive disorder of tyrosine metabolism due to deficiency of the enzyme homogentisic acid dioxygenase. The description of alkaptonuria by Garrod in 1902 led to the concept of a single enzyme deficiency resulting in lifelong disease. The elevated levels of homogentisic acid (HGA) polymerises and gets de posited in connective tissues leading on to ochronosis. The usual presentation is with degenerative joint disease and hyperpigmentation of skin. We report a case of Alkaptonuria with Chronic kidney disease leading onto Secondary Hypertension and Spontaneous tendon ruptures in a young female for its rarity.

Keyword : ALKAPTONURIA, OCHRONOSIS, HOMOGENTISIC ACID

CASE REPORT:

•□□□□□□□ This 32-year-old female presented with complaints of giddiness of 2 months duration and low backache of 6 months duration. She had been noticing bluish discoloration of her palms for 2 months duration. Her past history revealed a surgery on her right foot for repair of spontaneous Achilles tendon rupture and left Achilles tendon injury that was conservatively managed. Her bladder habits were normal and voids normal colored urine. However she revealed that she had noticed her inner wears were getting stained black/brown especially when air-dried immediately after washing in soap water. She is being oligomenorrhic for the past 6 months. She was born out of a 3rd degree consanguineous marriage and one of her elder sibling had noticed the similar kind of inner wear staining. Her son and daughter are normal. On examination: Patient was short statured, thin built and anemic. Her PR was 80 /minute and BP 180/100 mm hg. She had bluish pigmentation diffusely over her palms and blackish discoloration of forehead, nose, ear cartilages and tympanic membrane (Figure -1). Musculoskeletal examination revealed a positive SLRT at 60 degrees. Her large and small joints were normal. Cardio vascular system revealed a systolic murmur in pulmonary area. Other systems were within the normal limits. Her investigations: Hb was 9.1g/dl, Urea 80 mg/dl, Creatinine 5.4. LFT was within the normal limits. Her urine color was normal on voiding but changed black at 16th hour (Figure -2) Urine routine was normal. Usg abdomen showed B/L contracted kidneys with loss of CMD. X -ray LS Spine showed classical intervertebral disc calcification (Figure – 3). ECHO was normal. Her serum uric acid level was normal, CRP negative. Calcium 8.9, phosphorus 6.4, PTH – 200 PG/ML. TSH 5.5. T4- 0.88. Peripheral Smear showed dimorphic anemia. USG NECK was normal. USG LEG showed features of chronic Achilles tendon rupture in left foot. Urine biochemistry was positive for homogentisic acid with quantitative levels of 40.33 (normal <33 mmol/mol of creatinine). Tyrosine levels were normal.

Treatment: Our patient was started on Anti-hypertensive, Iron, Calcium and Thyroxine supplementation. Physiotherapy was given. She was started on dialysis. Her Renal parameters improved and the patient was discharged with appropriate dietary advice.

Figure-1

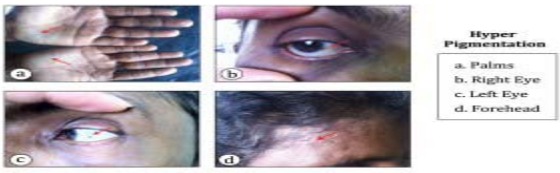


Figure-2

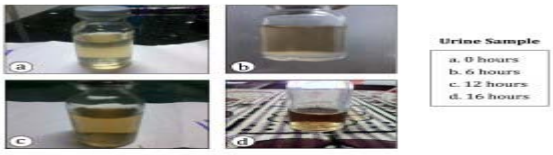
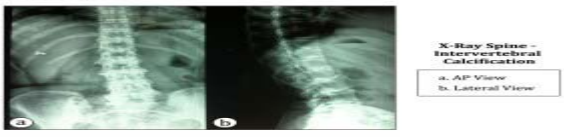


Figure-3



DISCUSSION:

INTRODUCTION:

Alkaptonuria (AKU), an autosomal recessive disorder resulting from the mutations in the gene encoding Homogentisic acid dioxygenase (HGD) has been mapped to chromosome 3q21-q23 and mutations identified in patients with AKU. (1, 2) The elevated levels of Homogentisic polymers bind with collagen and get deposited in the connective tissues, tendons and cartilages leading on to Ochronosis.

CLINICAL FEATURES :

Affected patients are asymptomatic in childhood. During the third decade, deposits of brownish or bluish pigments become apparent 1st in ear cartilage and sclera. Pigment deposits in large joints and spine are followed by calcification of intervertebral discs and ankylosis of spine (3). Deposition of pigments in heart valves, endocardium and coronary arteries can occur after 40 years of age (4). The renal involvement is characterized by formation of pigments stones. Cases of tubule interstitial diseases leading on to chronic renal failure (5) and renal failure aggravating ochronosis have been reported (6). Deposits of pigments leading on to rupture of Achilles and patellar tendon can occur.

DIAGNOSIS:

The disorder is characterized by excretion of urine that appears normal when fresh but turns black of standing or alkalinization. The dark color is due to the oxidation of homogentisic acid and hence the name black urine disease. Levels of HGA are increased in blood, urine and tissue samples. The diagnosis is confirmed by quantitative measurement of HGA in urine (7). Tyrosine levels are normal. The mean age of diagnosis of alkaptonuria is 29 yrs(3).

MANAGEMENT :

No effective management is available for AKU. Dietary restriction of tyrosine will reduce the excretion of HGA, although the clinical effect is limited (8). Ascorbic acid inhibits the enzyme that catalyses the oxidation of HGA to polymer and is being tried for ochronosis (8). Nitisinone, which inhibits the 2nd enzyme in tyrosine pathway – hydroxyphenyl pyruvate oxidase has been found to reduce urinary HGA levels (9). No modality is effective for established arthritis (10). Surgical joint replacement is done.

COURSE AND PROGNOSIS:

The severity of ochronosis increases with age and morbidity is increased, as no effective management is available. Majority of the patients end up with joint replacement for arthritis.

CONCLUSION:

Alkaptonuria and Ochronosis are not curable disorders. Our patient is currently on conservative line of management with diet, physio-therapy, Anti-hypertensives and Thyroxine supplementation.

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