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Ochronotic Spondyloarthropathy – A Case Report

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Abstract: ***Alkaptonuria is a disorder of tyrosine metabolism due to deficiency of homogentisic acid oxidase enzyme which results in accumulation of homogentisic acid[1]. Excess amounts of homogentisic acid gets oxidized and gets deposited in connective tissue leading to OCHRONOSIS. Characterstic features of ochronosis include blue black discoloration of connective tissues including sclera, cornea, articular cartilage, heart valves, auricular cartilage, tendons and ligaments. Alkaptonuric ochronosis particularly interesting because it can be detected based only on clinical signs and medical history. We herein present a patient with typical signs and symptoms such as darkening of urine, pigmentation of sclera, nails, ear cartilage and manifesting arthritis in the fourth decade.***

Keywords: Alkaptonuria , Arthritis, Homogentisic acid, Ochronosis, Spondyloarthropathy

1. Introduction

Alkaptonuria is a rare metabolic disorder due to deficiency of homogentisic acid oxidase resulting in triad of alkaptonuria, ochronosis and spondyloarthropathy. First described by Sir Archibold Garrod in 1902. Incidence of alkaptonuria is 1 in 2,50,000 to 1 million[2]. Life expectancy is usually normal. It is usually asymptomatic till third to fourth decades. The dominant and troublesome symptoms include severe arthropathy [3] which has detrimental influence on patient quality of life. Currently there is no specific and effective treatment available. Therefore symptomatic and supportive therapy is necessary to prevent further disability.

2. Case Report

A 50 year old male patient presented to us with complaints of low back ache and bilateral hip pain since 6 months. He had been suffering from low backache from 10 years. It is not associated with trauma, fever and no history of morning stiffness. On physical examination black discolouration of sclera was seen bilaterally, midway between the cornea and inner canthus and also between cornea and outer canthus, discolouration of pinna was present[**fig 1**]. The patient was short statured, decreased lumbar lordosis and increased thoracic kyphosis is noted. Decreased range of movements of spine and hip joints are noted. Chest expansion index was 5cm, modified schobers test was 4cm.

Radiological evaluation shows bilateral sacro ileiltis of both sacroiliac joints[**fig 2**]. Spine evaluation shows osteoarticular degenerative changes, with decreased disc space and disc calcification, vacuum phenomenon, ankylosis, and osteoporosis [**fig 3**]. Hip and knee xrays show arthritic changes[**fig 4**]. MRI of spine shows deforming spondylosis, degenerative changes, decreased spinal canal diameter, and narrowed disc space with disc calcification [**fig 5**]. 2D echocardiography show mitral regurgitation. Routine lab analysis such as complete blood picture, ESR, CRP, urea, creatinine, serum calcium and phosphate, LFT are assessed and were within normal limits. Rheumatoid factor and HLA B-27 was negative. Urine analysis shows large amounts of homogentisic acid. Finally the diagnosis of Ochronosis was made.

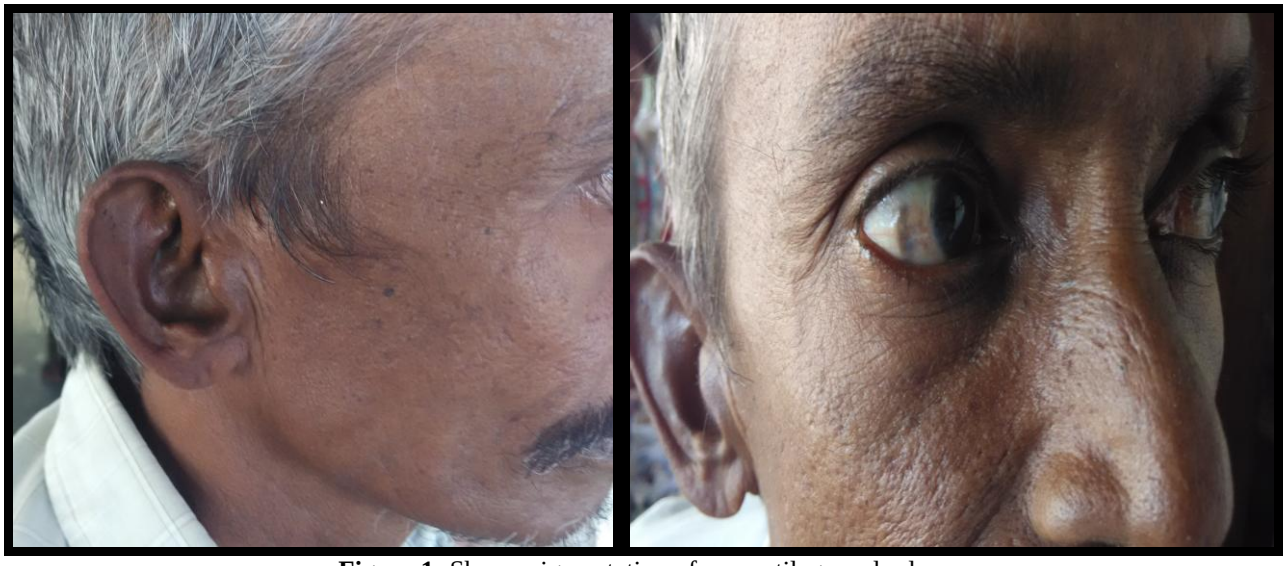

Figure 1: Shows pigmentation of ear cartilage and sclera

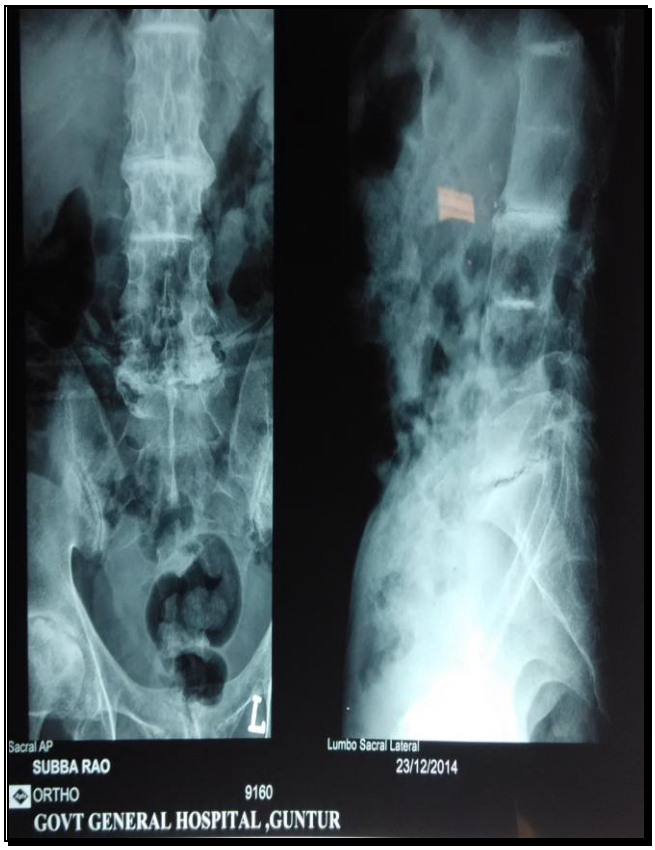

Figure 2: Shows degenerative changes of lumbar spine with disc space narrowing, disc calcification ,bilateral sacroileitis

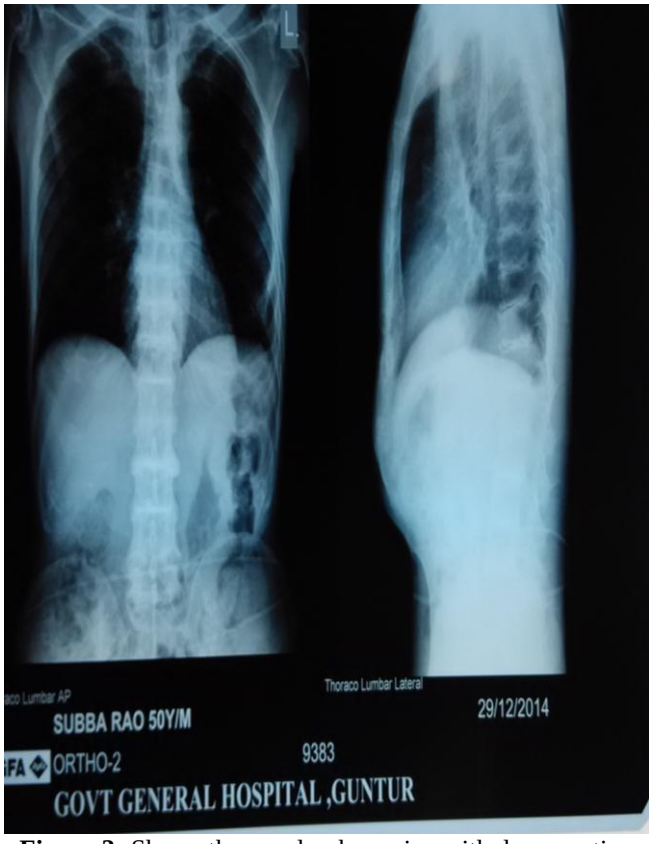

Figure 3: Shows thoraco-lumbar spine with degenerative changes, disc space narrowing and disc calcification

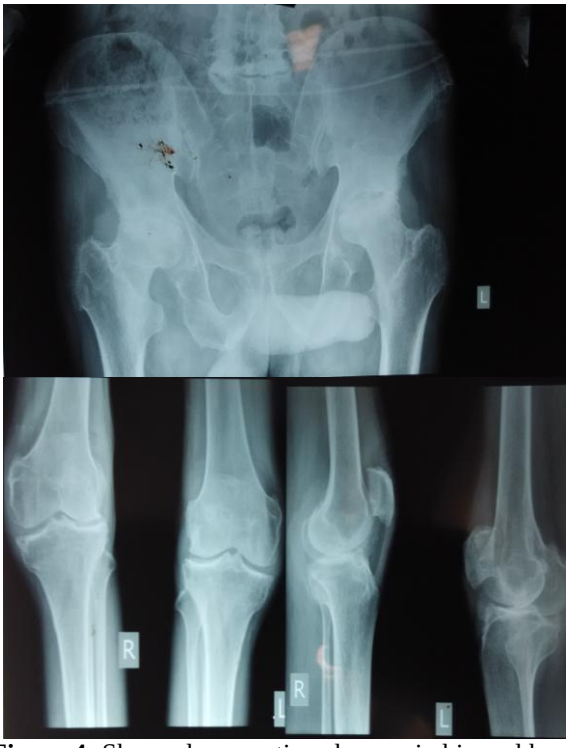

Figure 4: Shows degenerative changes in hip and knee joints

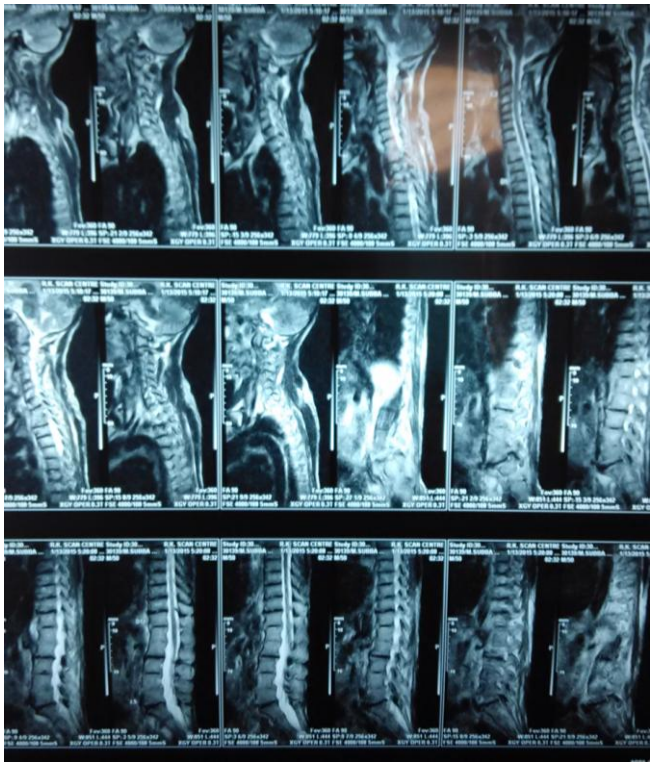

Figure 5: MRI of whole spine shows degenerative changes, narrowed disc space, decreased spinal canal diameter.

3. Discussion

Alkaptonuria is an autosomal recessive disorder was first described by Garrod in 1902[4]. In 1908 Garrod coined the term " Inborn error of metabolism" and proposed that alkaptonuria resulted from the deficiency of an enzyme that normally splits the aromatic ring of homogentisic acid. The enzyme was identified by *La Du et al. in 1958*[5].

Alkaptonuria is due to deficiency of homogentisic acid , resulting in accumulation of homogentisic acid, an intermediate metabolite of phenyl alanine and tyrosine metabolism. As homogentisic acid accumulates it gets oxidized which polymerises to form melanin like polymers, resulting in wide spread deposition in fibrous tissue and cartilage. Some of the homogentisic acid is deposited in urine. Since it has affinity to alkalis, it was named as alkapton and condition as alkaptonuria.

Alkaptonuria patients are usually asymptomatic until 3rd decade. Scleral pigmentation usually starts around the third decade . Skin pigmentation becomes obvious in the 4th decade. One of the first site involved is ear cartilage. There may discolouration of forehead ,cheeks ,axilla , palms, genitalia.

Ochronotic arthropathy starts around the 4th decade. Weight bearing joints like the hip, knee and intervertebral joints as well as the shoulder joints is involved, with narrowing of joint spaces and disc calcification. Arthritis is the only disabling effect of this condition and occurs in almost all patients as age advances. Ochronotic arthropathy can be so severe as to require joint replacement and decompressive surgery[6].

Aortic valvulitis, calcification of coronary arteries and atherosclerotic plaques are seen after the age of 50 years. Pigment deposits can form stones in the prostate , urethra and kidneys. The endocrine, CNS and teeth can also be affected.

The diagnosis is confirmed by the identification and quantification of homogentisic acid in urine using gas – liquid chromatography. The levels of homogentisic acid are increased in the blood, urine and tissues[7].

Acute surveillance for cardiac, renal and prostrate complications should be done after the 4th decade. No effective therapy is available for the treatment of ochronosis. Dietary restriction of phenylalanine and tyrosine play a limited role. Diet may prevent further progression of arthropathy.

Vitamin C (ascorbic acid) an antioxidant given in the dose of 500 mg twice daily, inhibits the polymerization of homogentisic acid and can be prescribed but its efficacy is not proven.

Nitisinone-a triketone herbicide, has shown to significantly reduce the excretion oh homogentisic acid by inhibiting the enzyme 4-hydroxy phenylpyruvate dioxygenase that is responsible for the synthesis of homogentisic acid. Side effects include elevated levels of tyrosine and corneal irritation. Long term studies are needed for its safety profile and efficacy[8].

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