

*Case Report***Polyarticular Ochronotic Arthropathy: A Case Report**Anoop Hegde¹, Siddharth M Shetty², Arjun Ballal³, VikramShetty²¹Consultant Orthopaedic Surgeon, City Hospital, Mangalore-575004²Associate Professor, Department of Orthopaedics, K.S. Hegde Charitable Hospital, Mangalore-575018³Consultant orthopaedic Surgeon, Udupi-576101

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ABSTRACT

Alkaptonuria, a rare hereditary metabolic disorder, is characterized by accumulation of homogentisic acid in the connective tissues resulting from lack of the enzyme homogentisic acid oxidase. Ochronosis, dark pigmentation of connective tissues, is the musculoskeletal manifestation of alkaptonuria.

In this article, we report the case of a 53-year-old man who had ochronotic arthropathy and advanced degenerative changes in bilateral knee with calcification of the intervertebral discs and ochronotic pigment deposited in articular cartilage and cartilage of the ear and sclera.

Key words: alkaptonuria; homogentisic acid; metabolic disorder; ochronosis.

INTRODUCTION

The term ochronosis (from the Greek *okhros*, “significant yellow,” and *nosos*, “disease”) was used for the first time by Virchow in 1866. [1,2] Albrecht and Zdenek, in 1902, interrelated the terms alkaptonuria and ochronosis. [1]

Alkaptonuria is a hereditary disorder transmitted by an autosomal recessive gene. [3] However, on rare occasion, it is autosomal dominant. [4] Scribner, the first to describe alkaptonuria, in 1584, reported the case of a young boy whose urine turned black when exposed to the air. The true name of the disorder is attributed to Boediger, who in 1859 accelerated this reaction by alkalinizing urine (from the Arab *alqaliy*, “alkaline,” and the Latin *capere*, “take in”). [1,5]

In alkaptonuria, homogentisic acid (HA) accumulation leads to deposition of blue-black pigment in connective and cartilaginous tissues, which lose their elasticity and develop poor resistance to mechanical strain. [6] The sites most commonly affected are the earlobes, sclera, nose, axilla, and groin; the cardiovascular, genitourinary, and upper respiratory systems; the skin; the spine; and the articular surfaces of the large peripheral joints (knee, hip, shoulder). [4]

The incidence of alkaptonuria is 1 in 250,000 to 1 million persons, [7] and alkaptonuria occurs more often in Slovenian and Dominican populations. The male-female distribution is equal, [1] though affected males seem to have more disease manifestations than females do. [6]

Alkaptonuria causes progressive ochronotic arthropathy of the large weight bearing joints (knees, hips, shoulders, vertebrae). [6,8,9]

CASE REPORT

A 53-year-old gentleman, presented with severe pain in both shoulders (left more than right), restriction in movement, particularly during overhead activities, and pain in the right knee. The patient also reported occasional pain and stiffness in the lumbar spine. He had no family history of any similar complaints or any musculoskeletal disease.

Physical examination of the shoulders revealed pain around the joint,

stiffness, decreased range of motion (ROM), diffuse swelling and tenderness over the joints, and characteristic crepitus with movement. Physical examination of the bilateral knee revealed mild effusion and tenderness over the joint line, plus restriction of movements with fixed flexion deformity of 15° and varus deformity.

Findings on examination of the spine included rigidity of lumbar spine, decreased movement along entire length of vertebral column with thoracolumbar kyphosis, and flattened lumbar lordosis.

The examination also revealed dark pigmentation of ear cartilage and the characteristic grayish black sclera (Figures 1, 2).



Figure 1. Blue-black pigmentation of the external left ear. Figure 2: Grayish pigmentation of the sclera of both eyes.

Radiographs of the lumbosacral spine showed intervertebral disk narrowing and calcification, fusion of vertebral bodies with osteal bridges between 2 adjacent bodies, diffuse sclerosis of vertebral plates, mild lumbar scoliosis, and osteoporosis of vertebral bodies (Figure 3 and B).

A radiograph of bilateral knee showed mild to moderate narrowing of the joint space (lateral compartment), subchondral sclerosis, and peripheral osteophytosis (Figure 4).

The patient's urine turned dark when exposed to the air. The diagnosis of alkaptonuria was confirmed by the finding of HA in the urine. Other laboratory findings were within normal limits.

He was advised rehabilitation exercises for the spine with bilateral total knee arthroplasty. He refused any surgical intervention, hence knee rehabilitation and physiotherapy was begun for both knees. He improved functionally in a period of three months.



Figure 3 A



Figure 3B

Figures 3 Frontal (A) and lateral (B) radiographs of lumbosacral spine show narrowing and calcification of disk spaces and fusion of vertebral bodies.

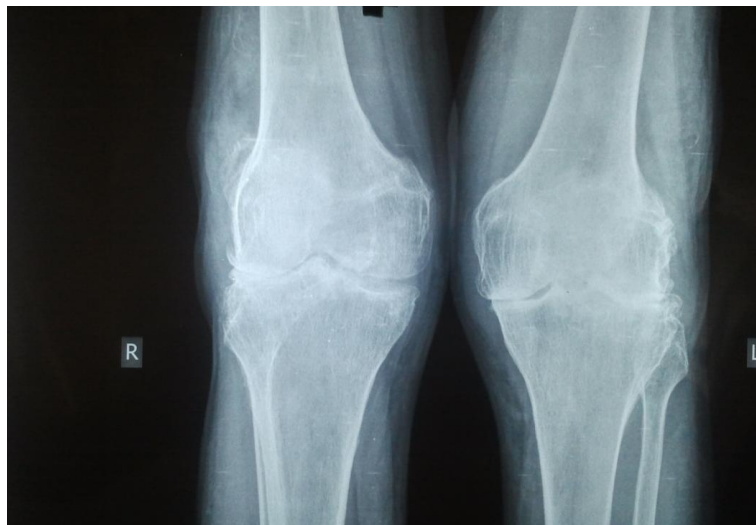


Figure 4. Standing anteroposterior radiograph of bilateral knees showing narrowing of the joint space (lateral compartment), subchondral sclerosis, and peripheral osteophytosis.

DISCUSSION

Homogentisic acid (HA) is the metabolic product of phenylalanine and tyrosine via the enzyme HA oxidase, which is active in the liver, kidneys, small bowel, colon, and prostate. [1,10] A defect on the long arm of chromosome 3 has been thought responsible for an inborn deficiency of HA oxidase, [7] leading to accumulation of HA in all connective tissues throughout the body, particularly the cartilage, resulting in pathologic blue-black pigmentation [7] and various systemic abnormalities. [1,5]

Increased accumulation of HA leads to decreased cross-linkage of collagen, increased vulnerability of articular cartilage to stress with subsequent cartilage failure, and degenerative changes. [5] Clinically, increased HA levels are characterized by presence of dark urine, degenerative joint arthritis, and ochronotic pigmentation. [5]

O'Brien and colleagues identify the knee as the most frequently affected joint, followed by the hip. [11] The intervertebral discs are also affected, with pigmentation and ossification of the nucleus pulposus, leading to degenerative changes. [6] Tendons

and ligaments also are heavily pigmented due to their collagen content. As a result, tendon inflammation, calcification, and rupture can develop. [12]

However, there have been case reports of ribs also being affected. Although the smaller joints do not appear to develop arthritis, the cartilage within these joints also demonstrates pigmentation. The build-up of deposited HGA that leads to brittle articular cartilage eventually becomes fragmented, creating loose shards and leading to joint deterioration and degenerative arthritis. The arthropathy is similar to an osteoarthritic pattern with a small inflammatory component; the shards cause synovial irritation, with an associated inflammatory response. [8]

Patients are usually asymptomatic until symptomatic arthropathy develops, after the fourth decade of life, with ochronotic pigmentation and urine changes. [4] A plausible explanation for this delay is renal tubular excretion of HA, which is very effective in the early years, but becomes less so with age. HA accumulation accelerates, resulting in increased pigment deposition on cartilage. [6] Ochronotic arthropathy must be distinguished from degenerative joint disease (small joints spared; osteophytes and subchondral cysts prominent at peripheral joints) and from ankylosing spondylitis (thin and vertical syndesmophytes, severe involvement of apophyseal facet joints, erosion and fusion of sacroiliac joints). [4]

Specific quantitative determination of HA in urine is available using gas chromatography and mass spectrometry. [2]

There is no specific management option for alkaptonuria. [2] Physical therapy and rehabilitation can help reduce loss of function and progression of symptoms. [1] Some authors have referred to the efficacy of using ascorbic acid because of its effect on oxidation and polymerization of HA in vitro, but that efficacy has not been

established. [2] Arthroscopic management involves debridement of destroyed tissues, removal of hypertrophic synovium and loose bodies, and smoothing of articular surfaces resulting in excellent pain relief, improved ROM, and, in most cases, delayed disease progression. However, the last solution remains arthroplasty. [10]

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