

## Ochronosis or Alkaptonuric Arthropathy

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### Abstract

A rare case of Ochronotic arthropathy diagnosed on roentgen examination and confirmed by clinical history and urine examination is reported in this communication. To our knowledge this is the first ever case of this entity being reported from this region.

### Key Words

Alkaptonuria, Ochronosis, Arthropathy.

### Introduction

Alkaptonuria is a rare inborn error of amino-acid metabolism with an estimated incidence varying from one in five million to one in twenty two million (1). The disorder is inherited as a autosomal recessive trait. The basic error lies in the congenital absence of enzyme homogentisic acid oxidase, which is required for the normal metabolism of phenylalanine and tyrosine (2,3). In alkaptonuria, deposition of a polymer of homogentisic acid, a dark yellow pigment or 'Ochre' occurs in the cartilage and other connective tissues causing Ochronosis. While 50% of alkaptonurics are asymptomatic, the rest develop ochronotic arthropathy (4). Recently, we had an opportunity to diagnose this condition in one of our patients. This article presents the clinico-radiologic manifestations of the case with a brief review of the literature.

### Case Report

K.A., a 55-year old female was referred to us for x-ray of the lumbar spine with the clinical diagnosis of low back pain of more than 10 years duration.

Roentgenogram of the lumbar spine revealed loss of lumbar lordosis, gross narrowing of the disc spaces, dense calcification of all the discs, vacuum phenomenon at multiple levels and advanced osteoporotic and degenerative changes (Fig. 1). On the basis of these findings a confident radiological diagnosis of ochronotic spine was made, which was confirmed by detailed history, clinical examination and examination of the urine specimen.

On questioning, the patient admitted that her urine would become dark coloured on prolonged standing. She also admitted to having noticed brownish-black spots on her underwears. She had also recognised staining of the clothing at the axillae. On further questioning, she revealed that her brother had similar problem but none of her children had such complaints. However, her brother was not available for roentgen evaluation.

Physical examination revealed a middle aged woman of average built. Both pinnae of ears showed a few dark coloured spots. The pinnae were hard on palpation.

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Examination of the lumbar spine revealed decrease in lumbar lordosis with restricted movements of the lower back. The cervical spine showed no significant abnormality. Further, roentgen examination of dorsal and cervical spine revealed advanced degenerative changes with few calcified discs. The pinnae showed few patches of increased density. The patient's urine sample was collected. It turned dark brown on standing for two hours (Fig. 2). Chemical test of the urine confirmed the presence of homogentisic acid.



Fig. 1. X-ray lumbar spine (Lateral view) showing reduced disc spaces, advanced osteophyte formation, calcification of the discs and vacuum phenomenon in multiple discs.

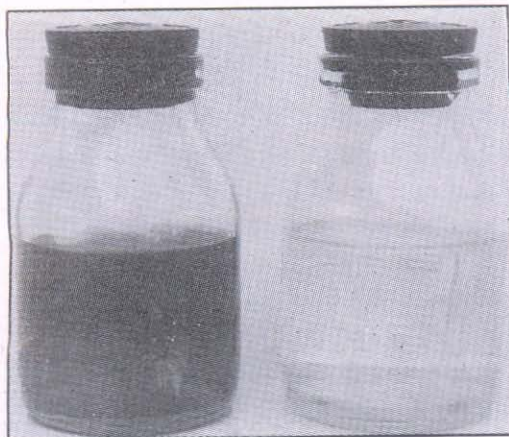


Fig. 2. A clear urine sample immediately after passing and change in colour to dark brown after two hours of exposure.

## Discussion

Ochronosis or Alkaptonuria is an autosomal recessive congenital metabolic error due to absence of enzyme homogentisic acid oxidase. In a normal amino-acid metabolic pathway, Tyrosine and Phenylalanine are oxidised to form homogentisic acid, which is further broken down in the presence of homogentisic acid oxidase to form fumaric acid and acetoacetic acid. In ochronosis, since further breakdown of homogentisic acid is not possible, it forms a polymer which is deposited in the body tissues. A part of homogentisic acid is excreted in urine and sweat. Thus urine of such patients turns dark on standing or when alkalinised, owing to the oxidation of homogentisic acid (4,5).

Patients with mild alkaptonuria may remain asymptomatic, the condition remaining unrecognized throughout the life. On the contrary, severe affection may manifest quite early, by observing that the infant's nappies become darkly stained on washing with an alkaline soap or on exposure to air (5,6). However, more commonly the cases are recognised in the fourth or fifth decades with a peak incidence in the fifth decade (1,7,8). Our patient had become symptomatic in the 4th decade of her life. Most of the cases are recognised in adult life, by observing the staining of clothes at the axillae and by the development of pigmentation in the pinnae, sclera or the skin (5,9). These pigmented patches are slate grey in colour and occur earliest in the concha and antihelix of ear. Later, they are seen in the tragus, antitragus, butterfly area of the face, sclera and in the skin (1).

Ochronotic arthropathy usually presents late in adult life, with symptoms worsening with progression of age. However, in severe cases arthropathy may occur much earlier (8). Spine is usually the first area to be affected, with patients complaining of stiffness and low back pain. Localised kyphosis or scoliosis may occur. Lordosis of



the lumbar and cervical spine is flattened. Occasionally, the patients present with sciatica, complaining of a root type of pain. (1).

Involvement of the urogenital system has also been reported with calculi in the renal pelvis, ureters, bladder and even in prostate (7,10). Biliary calculi and cardiac failure secondary to valve calcification may occur (1,11).

Radiologic changes sometimes precede the onset of patient's symptoms. In spine, the changes commence in the thoraco-lumbar region. Due to pigment deposition and subsequent calcification, the vertebral surfaces of the discs become increasingly radiodense, which is seen as 'doubling' of the outlines (5). The condition continues to progress with increase in the radiodensity of the discs. Intradiscal lucencies secondary to vacuum phenomenon may occur. The nucleus pulposus is the last part of the disc to become calcified. Vertebral osteoporosis occurs which may lead to kypho-scoliotic deformities secondary to compression fractures (1). Massive osteophyte formation, sub-chondral sclerosis, cyst formation and ultimately bony ankylosis may occur. (1,7). In knee joints, early change occurs in the form of meniscal calcification. Subchondral increased density occurs with scattered osteoporotic areas in the tibia and femoral condyles. Asymmetric joint space narrowing and marginal osteophytosis develops. Calcified loose bodies, subchondral cysts and sclerotic islands representing avascular necrosis may occur (1). Similar changes may develop in shoulders and hips, with flattening of the femoral and humeral heads (1,9).

Although ankylosing spondylitis, rheumatoid arthritis and age related degenerative spondylitis have been included in the differential diagnosis of ochronotic

spine, the roentgen changes seen in most of the cases are pathognomonic of the diagnosis and simple urine examination in these cases will confirm the diagnosis as in the case under report.

Ochronosis follows a progressive course and the treatment is aimed at providing symptomatic relief. Vitamin preparations are given because of the influence of vitamin C on tyrosine and phenylalanine metabolism (1). Corrective surgical procedures such as disc removal or decompression of the spinal cord have been successful in selected patients (12).

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