Case Report

Hip arthroplasty for ochronosis

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ABSTRACT

Alkaptonuria is a metabolic disorder in which homogentisic acid oxidase is absent. Therefore, homogentisic acid accumulates in cartilage and connective tissues. We can diagnose ochronotic arthropathy, a manifestation of long standing alkaptonuria, through careful radiological, physical, and laboratory examination. In this report, we describe 4 cases of ochronotic arthropathy to which we applied cementless total hip prosthesis due to severe hip involvement.

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Alkaptonuria characterized by the absence of enzyme homogentisic acid oxidase, is a rare hereditary disorder of phenylalanine and tyrosine metabolism. Generally, it is transmitted by an autosomal recessive gene, but in some cases it is transmitted by an autosomal dominant gene.[1-4] It occurs in less than one in a million births.[4] Due to the homogentisic acid oxidase deficiency, homogentisic acid accumulates in cartilage, and connective tissues. This situation is called ochronosis. This term was first used by Virchow in 1866.[1] Homogentisic acid can be oxidized to an ochronotic pigment either by enzymatic action (homogentisic acid polyphenol oxidase) or by oxygen, and alkali.[1] Brownish-colored ochronotic pigment accumulates in the ears, sclerae, tendons, ligaments, axillary, and genital areas.[1,3,5] The accumulation of homogentisic acid in connective tissues leads to spondylopathy and arthropathy.[2] Ochronosis may be considered if a patient has multiple joint involvement and unrecovered complaints with medical, and physical therapy regimens, and a total hip arthroplasty can be performed for involved hip joints. Thus, we reported 4 cases of ochronosis with hip joint involvement. We applied cementless total hip prosthesis unilaterally to 3 patients and bilaterally to one patient.

Case Report. ***Patient 1.*** A 69-year-old woman with complaints of low back, hip, shoulder, and knee pain for 20 years was admitted to our clinic. Medical and physical therapy procedures had been performed several times. In her personal history, we noted that a total hip prosthesis had been applied to her 63-year-old sister 2 years ago. On physical examination, a dark blue pigmentation in the ears and sclerae was observed by inspection, and cardiac murmurs were found by auscultation. The shoulder, hip and knee motions were markedly limited, and painful in all ranges. Laboratory tests revealed homogentisic acid in urine. The patient was (human leukocyte antigen) HLA-B27 negative. In radiographs of the spine, intervertebral disc narrowing and calcification, vertebral squaring, osteoporosis of the thoracolumbar spines, narrowing of the intervertebral disc spaces and osteophytosis of the cervical spines were observed. Radiographs of the shoulders and knees showed narrowing of the joint spaces with moderate degenerative changes and sclerosis. The hip radiographs presented severe degenerative changes and sclerosis on the right side and with these findings, she was diagnosed as ochronosis. A cementless total hip prosthesis was

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applied to her right hip. We observed that the joint surfaces and neighboring ligaments were black in color with some black strips of residual cartilage tissues.

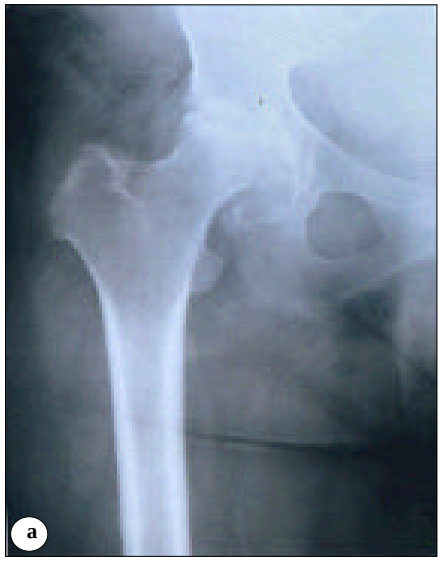
Patient 2. A 55-year-old woman with severe right hip, shoulder, and back pain for 10 years was admitted to our clinic. Physical therapy procedures had been performed before. None of the members of her family have these complaints. On clinical examination, neither sclerae pigmentation nor cardiac pathology were observed. Laboratory tests revealed homogentisic acid in urine. The HLA-B27 was negative. Her radiographs were compatible with ochronosis. A cementless total hip prosthesis was applied due to complaints of her right hip. Intraoperatively, discoloration of the femur head cartilage, and neighboring soft tissues were similar to the previous patient. **(Figure 1)**

Patient 3. A 56-year-old woman complained of the symptoms of sciatica, severe hip pain, back pain, and stiffness for 15 years. Medical and physical therapy regimens had been performed several times, but ineffective. In radiographs, pathological changes of ochronosis were observed. Laboratory tests revealed homogentisic acid in urine. The HLA-B27 was positive. Bilateral cementless total hip prosthesis was applied with 6 months interval.

Patient 4. A 72-year-old woman complained of the symptoms of severe hip, and back pain for 10 years. Her complaints continued in spite of medical treatment procedures. Her pelvis and spine radiographs had pathological changes of ochronosis as intervertebral disc narrowing, and calcification (wafer-like calcification), vertebral squaring, and osteophytosis. Homogentisic acid was present in urine. The HLA-B27 was negative. A cementless total hip prosthesis was applied to her right hip. **(Figures 2a & 2b)**

Discussion. Ochronosis is a rare pathological condition that transmits as an autosomal recessive trait. This disease commonly appears in the fourth and fifth decade of life. There is homogentisic acid deposition in connective tissue, skin, cardiovascular system, urinary tract, eyes, pulmonary system, big joints of extremities, and intervertebral discs. Ochronotic arthropathy is a manifestation of long-standing alkaptonuria, seen in less than one million births.[1] Ochronotic pigmentation appearing on sclerae, external ears, nose, axilla, and groin is observed over the age of 20 or 30 years.[1,6] Calcified aortic valve and aortic intima, renal stones, dysphagia and hoarseness are other manifestations of alkaptonuria.[7] Symptoms and signs of ochronotic arthropathy such as limited motion and pain in the hips, knees, shoulders, and spine usually first appear in the fourth decade of life. The first sign of alkaptonuria is often a change of urine color.[1] The

Figure 1 - Appearance of the extracted femoral head and joint capsule (black-white).



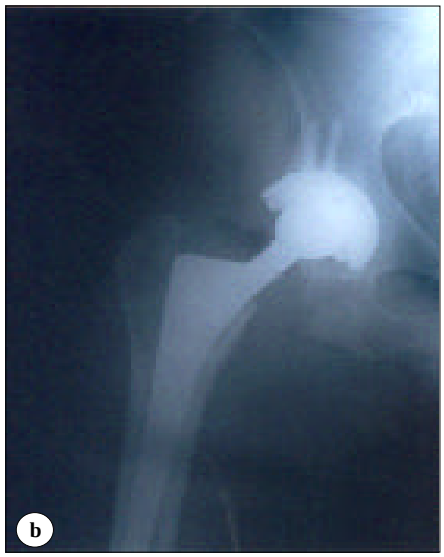


Figure 2 - Antero-posterior radiograph of the right hip showing **(a)** articular space narrowing, sclerosis **(b)** postoperative radiograph.

darkening of the urine and discoloration of the sclerae and external ears may be overlooked by patients and their parents. Thus, the diagnosis can be delayed until ochronosis has developed. Our patients ignored these symptoms.

The roentgenographic manifestations of skeletal involvement have been well outlined in ochronosis. We can divide these into spinal and extraspinal abnormalities. Spinal changes usually begin earlier.[1] Radiographic findings of ochronotic spondylosis are widespread discal calcification, disc space narrowing, small osteophytes, and vertebral osteoporosis.[1,8] Intervertebral disc calcification in ochronotic spondylosis is usually seen in the lumbar spine, but may appear in any segment of the vertebral column.[1,9] We saw spinal radiographic changes of ochronotic spondylosis in all patients, except cervical spine involvement of patient 3. Involvement of large joints usually occurs several years after spinal changes. The knee is the most common site of peripheral abnormality. Other sites of involvement are the hips, shoulders, sacroiliac joints, and symphysis pubis.[1] We determined the shoulder, hip, and knee involvements symmetrically in patients 1 & 2. At the symphysis pubis and sacroiliac articulations, we may see articular space narrowing, sclerosis, calcification, and bony eburnation in ochronosis.[1] We saw involvement of the symphysis pubis in patients 1 & 2, but only sacroiliac joint abnormalities in patient 1. Ochronotic patients usually have an unusual type of arthritis affecting the large weight-bearing joints, but not the small joints of the hands and feet.[1] Neither hand nor feet joints were involved in our patients. Hip changes may also be observed in ochronosis. Radiographic findings may be identical to changes of degenerative joint disease with articular space narrowing and sclerosis. Eburnation of both femoral head and acetabulum can be seen. In some patients with this disease, symmetric loss of joint space, severe destruction with fragmentation and formation of intra-articular cartilaginous and osseous bodies, and tendinous calcification and ossification permit differentiation from typical degenerative alterations.[1] Rapid destructive changes in hips can be seen in ochronosis.[5,10] Our patients had hip complaints for 2 or 3 years. In physical examination, we found that range of motion was decreased, and we observed severe degeneration and sclerosis in radiographs, and applied a cementless total hip prosthesis. We determined no complaints after the operation. During the operation, we observed black discoloration at the femur head cartilage, and capsule **(Figure 1).** Our patients' hip involvement progressed rapidly, so we think that destructive changes and sclerosis in hip develop rapidly.

A careful evaluation of the radiographs provides sufficient elements to distinguish ochronotic arthropathy from ankylosing spondylitis.[1,5] Broad band-like ossification of large segments of the intervertebral discs is seen in ochronosis. Thin and vertically oriented syndesmophytes, severe apophyseal facet joint involvement, erosion, and fusion of sacroiliac joints are typically associated with ankylosing spondylitis. Darkened urine when left standing and negativeness of HLA-B27 support the diagnosis of ochronosis.[5,11] The association of the disease with HLA-B27 is controversial in the literature.[1,6] In the present study, HLA-B27 was negative in 3 patients, and positive in one. The prevalence of HLA-B27 is 3-4.6% in our country.[6] The prevalence may be the reason of HLA-B27 positiveness in one patient. We think that possible association between alkaptonuria and HLA-B27 may be less common than the literature. All the patients had complaints for a long time. They applied to the hospital clinic several times, but the diagnosis of alkaptonuria was not established. Therefore, we should consider alkaptonuria in patients complaining of low back, hip, shoulder, and knee pain for a long time, and for patients that have unrecovered complaints with medical and physical therapy procedures. Patients who have destructive changes in hips due to ochronosis become comfortable after the total hip prosthesis.

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