Two Cases of Severe Ochronotic Arthropathy
N Elmali, I Esenkaya, E Türkmen, E Hazneci

Citation

Abstract
Ochronotic spondylarthropathy, a long-term musculoskeletal manifestation of alkaptonuria and involvement of joints may lead to a radiographic appearance similar to that of degenerative joint disease. We report the cases of two siblings with progressive familial ochronotic arthropathy treated with total hip arthroplasty.

INTRODUCTION
Alkaptonuria is an extremely rare hereditary error of metabolism which has an estimated incidence of 1:250 000–1: 1 000 000 [1]. This disorder is transmitted as autosomal recessive trait and characterized by the absence of the enzyme homogentisic acid oxidase, which leads to the accumulation of homogentisic acid produced during normal metabolism of phenylalanine and tyrosine. As a result of the accumulation of homogentisic acid in connective tissues, it produces a multisystemic disorder with a characteristic bluish-black pigmentation of the skin and cartilage, termed ochronosis. Owing to the excretion of homogentisic acid in the urine pathognomonically urine turns black when exposed to air. The striking clinical feature of ochronosis is bluish-black pigmentation of the sclerae and auricles, which occurs in 70% of patients. In ochronotic arthropathy, a long-term musculoskeletal manifestation of alkaptonuria, intervertebral discs and cartilage of the joints are preferentially affected. Peripheral arthropathy in ochronosis involves large joints, namely, knee, hip, and shoulder. Involvement of joints may lead to a radiographic appearance similar to that of degenerative joint disease[2,3]. We report two cases of familial ochronotic spondylarthropathy with progressive destructive changes in the hip. Total hip arthroplasty was performed in both cases and resulted in a satisfactory outcome so that the patients regained their walking ability.

CASE REPORT
CASE 1
A 53 year old-man was admitted to our clinic with progressive pain in the right hip joint for one year. He had bilateral knee and left shoulder pain. He had a previous history of lower back pain and was treated with L3-4 and L4-5 bilateral laminectomy in another clinic 10 years ago. He had myocardial infarction 7 years ago and was treated by cardiac bypass. He denied dark urine during childhood. On retrospective analysis of the family history, no symptoms or joint complaints have been noted among their parents, children (3 daughter and one son) and another sibling. However, a sister was also positive for the disease and is presented here as case 2.

In his physical examination a reduction of some movement were noted for the entire length of the vertebral column. The right hip range of motion (ROM) was painful and limited. Homogentisic acid test was positive in urine. He had characteristic bluish black pigmentation of the hands and fingernails (Fig. 1).

Figure 1
The first roentgenographic examination of the right hip joint revealed osteoarthritic changes, but sphericity of femoral head was preserved. During the following 3 months, rapidly
destructive changes of the femoral head developed (Fig. 2 a,b).

**Figure 2**

Throughout the spinal column there were prominent spondylotic changes with narrowing of the intervertebral disk space and dense calcification of the discs (Fig. 3 a,b,c).

**Figure 3**

**Figure 4**

**Figure 5**
There were no abnormalities in results of hematologic and biochemical laboratory studies. Microscopically his dermis showed many irregular shaped pigment deposits (Fig. 4).

The clinical data and positive findings in his urine led to a diagnosis of alkaptonuria and the patient underwent right cementless total hip arthroplasty. The femoral head also showed the complete disappearance of the cartilage in the weight-bearing zone and a distinct black region marked the femoral head. Microscopy showed that the articular cartilage revealed bluish-black pigmentation and the spaces below the subchondral bone were occupied by pigmented fragments of degenerating cartilage (Fig. 5 a,b).

After 2 years, the patient's right hip joint was painless and he had a better walking function (Fig. 6).
CASE 2

This case reports a 63-year-old woman with familial ochronosis. On admission to our clinic she reported moderate complaints in her spine, right shoulder and both knees. The severe complaints in her left hip began 2 years previously and progressively increased. Her brother had already been successfully treated at our department by total hip replacement. Her medical history included cholecystectomy for cholecystolithiasis at the age of 56. Her family history was given in case 1. In addition, she had a healthy daughter and two sons.

During the physical examination the patient's right hip range of motion (ROM) was painful and limited. She had stiffness of the lumbodorsal spine with pain on flexion and extension, and the range of motion was also painful in the right shoulder and both knees. There was no discoloration of the fingernails and ear cartilage of the patient. Her system examination showed no abnormalities, nor did urinary ultrasonography or echocardiography. Although discoloration of the urine had not been noticed before, a homogentisic acid test was positive for her urine. There were no abnormalities in hematologic and biochemical laboratory studies. Roentgenographic examination revealed severe osteoarthritic changes in the left hip joint, right shoulder and both knees (Fig. 7a).

There was discal calcification, disc space narrowing with maximal involvement of entire thoracic and lumbar spine. These clinical data and family history confirmed ochronotic spondylarthropathy. Because of severe hip pain and an inability to walk, hybrid total hip arthroplasty was performed. During hip replacement surgery the synovia and the cartilage of the femoral head were stained with a black pigmentation ring in the cartilage surrounding the eburnated area black. The postoperative 1-year course was uneventful (Figure 7b).
She was pain-free and adequate range of motion. The histopathology showed the same pattern as was seen in case 1.

DISCUSSION

The disease usually progresses from simple alkaptonuria to alkaptonuric ochronosis and finally to alkaptonuric arthropathy [4]. Patients with alkaptonuria are usually asymptomatic until symptomatic arthropathy develops after the fourth decade. However, pathogenesis of destructive ochronotic hip arthropathies is still unclear. In spinal involvement an inappropriate mechanical transfer to the hip joint may accelerate cartilage degeneration followed by fragmentation of the cartilage and active synovitis. Changes are otherwise similar to those in other degenerative diseases but ochronosis is characterized by severe changes and a rapid progression [5]. It may have devastating end results, as in described our cases. Since there has been no successful causal treatment to date, finally, arthroplasty of the hip may provide a solution, as two of our cases have demonstrated.

CORRESPONDENCE TO

Nurzat Elmali Inönü University Medical Faculty Turgut Ozal Tip Merkezi Ortopedi ve Travmatoloji, 44069, Malatya, Turkey E-mail: nelmali@hotmail.com Tel.: +90-422-3410660/5103 Fax: +90-422-3410610

References

Author Information

Nurzat Elmali
Associate Professor, Faculty of Orthopaedics and Traumatology, Inönü University

İrfan Esenkaya
Associate Professor, Faculty of Orthopaedics and Traumatology, Inönü University

Emine Türkmen
Specialist, Medical Faculty of Pathology, Inönü University

Ersoy Hazneci
Assistant Professor, Medical Faculty of Dermatology, Inönü University