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Case Report

CASE REPORT

Ochronotic arthropathy—a rare clinical case

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Abstract

Ochronotic arthropathy is a rare condition found in patients with alkaptonuria that results from the accumulation of ochronotic pigment. We present the case of a 65-year-old woman who presented for medical evaluation due to hip and knee chronic pain. The physical and radiographic findings were compatible with an end-stage hip osteoarthritis and knee osteoarthritis. During total hip arthroplasty it was noticed that the articular capsule and the cartilage of the femoral head were black. In the postoperative period she was diagnosed with alkaptonuria. Later, a total knee arthroplasty was performed and once more the presence of black cartilage was noted. Alkaptonuria usually appears after age 30 and is usually asymptomatic until the involvement of the spine, hip, knee and shoulder joints. Therefore, orthopaedic surgeons must be suspicious of an atypical arthropathy in order to not be overwhelmed during surgery with the presence of darkened cartilage.

INTRODUCTION

Alkaptonuria, also known as AKU or Black Bone Disease, was first described as one of the four inborn errors of metabolism by Sir Archibald Garrod in 1902 Garrod and was also the first disease recognized to follow the classic Mendelian recessive inheritance [1]. It has an estimated prevalence ranging from 1:200 000 to 1:1.000 000 live births worldwide; is more common in certain areas of Slovakia and in the Dominican Republic [1, 2]

It is an ultra-rare autosomal-recessive metabolic disease due to an autosomal recessive mutation mapped in chromosome 3 between regions 3q21 and q23, the site of the homogentisate 1,2-dioxygenase (HGD) gene [2, 3]. More than 80 mutations in the HGD gene have been identified in people with the disease.

This enzyme, predominantly produced by liver and kidney, is responsible for the turnover of homogentisic acid (HGA) into maleylacetoacetic acid; its absence leads to HGA accumulation (more than 2000 times the normal rate) in different parts of the body [2, 4, 5].

Some of HGA excess is excreted through the urine which turns dark when exposed to oxygen; alkalization can also occurs leading to homogentisic aciduria. The accumulated HA initially oxidizes and then deposits inside the connective tissue; subsequently, it turns into an irreversibly melanin-like pigment known as ochronosis; this blue-black pigmentation usually appears after age 30 and, over time, leads to black and brittle bones and cartilage, and early onset osteoarthritis [3–5].

The disease progresses from simple benign alkaptonuria to alkaptonuric ochronosis, leading to ochronotic arthropathy (OA) that is the most severe symptom [4]. Pigment is deposited in the chondrocytes and matrix of articular cartilage, as well as in ligaments and elastic cartilages, causing tissue degeneration [5].

Clinical symptoms of OA typically begin with stiffness and pain in the thoracolumbar spine; the subsequent articular degeneration is most often observed in knee, hip and shoulder joints [1]. Additional manifestations are related to HGA accumulation in hyaline cartilage, tendons, ligaments, sclera, skin, heart valves, nose and ears cartilage, renal tubule epithelial cells, pancreas, central nervous system, endocrine organs, respiratory organs and arteries [2, 4].

The diagnosis of alkaptonuria may be confirmed by an accurate physical examination and quantifying the HGA in urine.

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Currently, there is still no approved effective treatment for alkaptonuria; in OA the treatment is symptomatic and similarly to a normal arthropathy. However, surgical treatment may be necessary in cases of significant degenerative arthropathy [2, 6].

CASE REPORT

A 65-year-old Caucasian woman presented for evaluation after a 2-year history of left hip and knee pain. On physical examination, the left knee presented with a mild effusion, tenderness and with stiffness and decreased mobility. The hip showed a true capsular pattern of limitation and pain with internal rotation of the hip. Radiographically, the left knee showed degenerative osteophytic changes and osteophytes in all compartments of knees and mild to moderate narrowing of the joint space. In case of the left hip, radiographic evaluation showed also advanced osteoarthritic changes.

Since the physical examination and radiographic findings were compatible with the diagnosis of an end-stage hip osteoarthritis and knee osteoarthritis, the patient was first listed for a cementless total hip arthroplasty (THA) (Fig. 1), followed by a cemented total knee arthroplasty (TKA) (Fig. 2).

During surgical dissection it was noticed that the articular capsule and the cartilage of the femoral head were black (Figs 3 and 4). Histological sections of bone and soft tissue demonstrated classic findings of ochronosis, including multiple pigmented areas by deposition of ochre-coloured granules, reactive giant cells, hyaline cartilage degeneration and a thickened and inflamed synovium. The case was discussed intraoperatively with the Senior Surgeon: the macroscopic evaluation of bone quality seemed reasonable and the OA diagnostic was the most consensual between the team. We maintained our initial plan and finished the cementless THA.

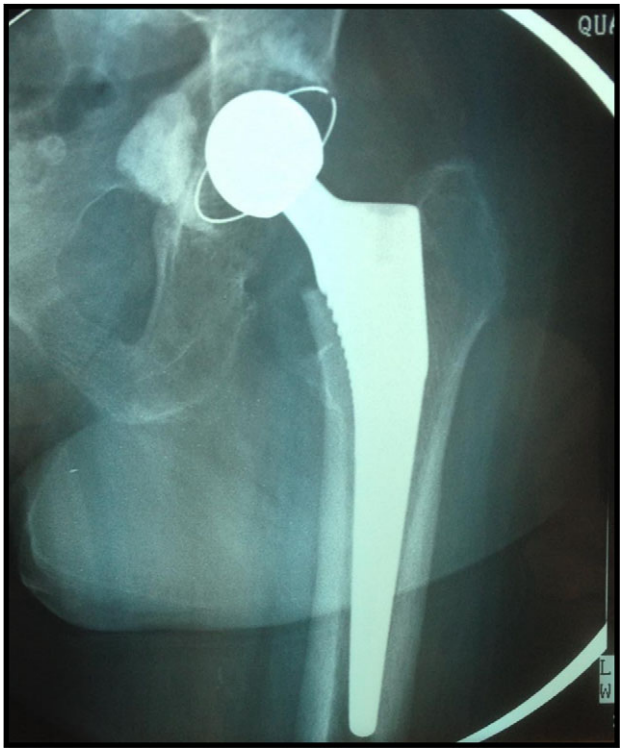

Figure 1: Total hip arthroplasty

After surgery she confirmed that was never diagnosed with alkaptonuria in her past. She was re-examined and we found black ochronotic pigmentation in sclera and ear cartilage (Fig. 5), as well as dark urine. A high level of HA was also found in the urine. She was evaluated by a senior rheumatologist and progressed favourably without any complications.

Eight months later she was treated for her left end-stage knee osteoarthritis and we noticed again the presence of black cartilages (Fig. 6). On follow-up examination (36 months) the patient progressed well, with a good range of motion and no reported hip or knee pain.

DISCUSSION

Alkaptonuria can be detected in children, as young as a few months of age by the presence of dark spots in the diapers or

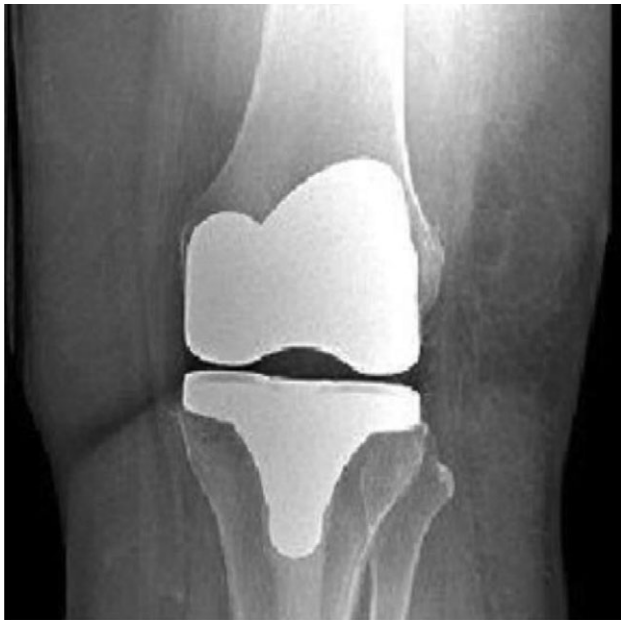

Figure 2: Total knee arthroplasty

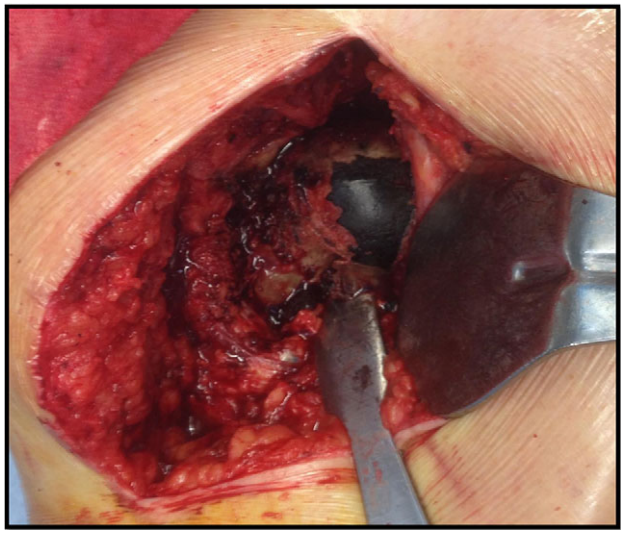

Figure 3: Intraoperatively, hip arthroplasty

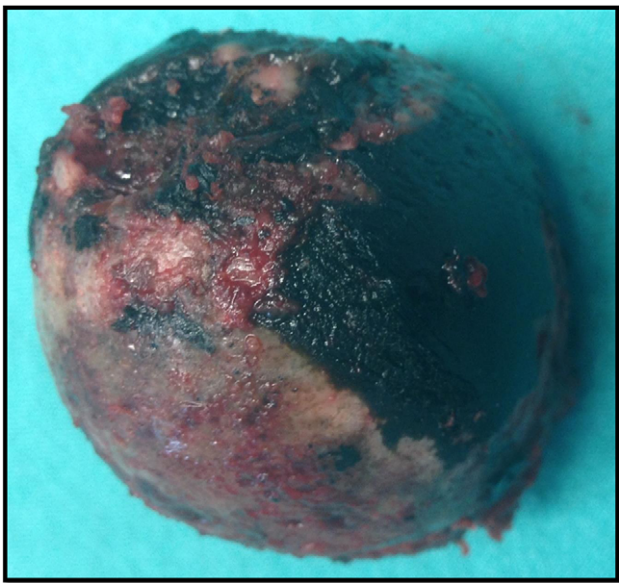

Figure 4: Intraoperatively resected head of the femur

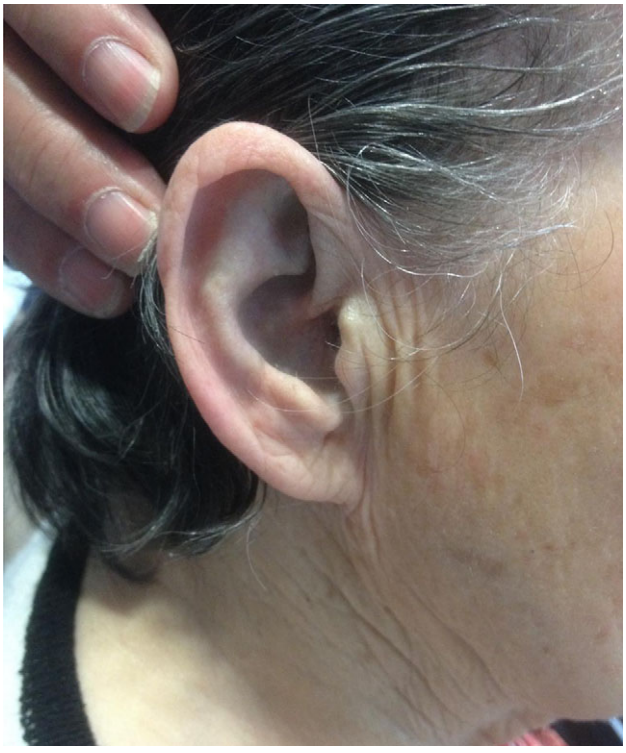

Figure 5: Black ochronotic pigmentation in ear cartilage

underwear, but patients are usually asymptomatic until arthropathy develops, after the fourth decade of life [1, 6, 7]. A plausible explanation for that is the renal tubular excretion of HGA: is very effective in the early years but becomes less so with age [7].

Although the symptoms appear later in life, connective tissue degeneration can be rapid and aggressive, often leading to the need for joint replacement [1].

Early involvement of the intervertebral discs at the thoracic and lumbar levels is very common (approximately in 50% of affected individuals). The large joints (knee, hip and shoulder)

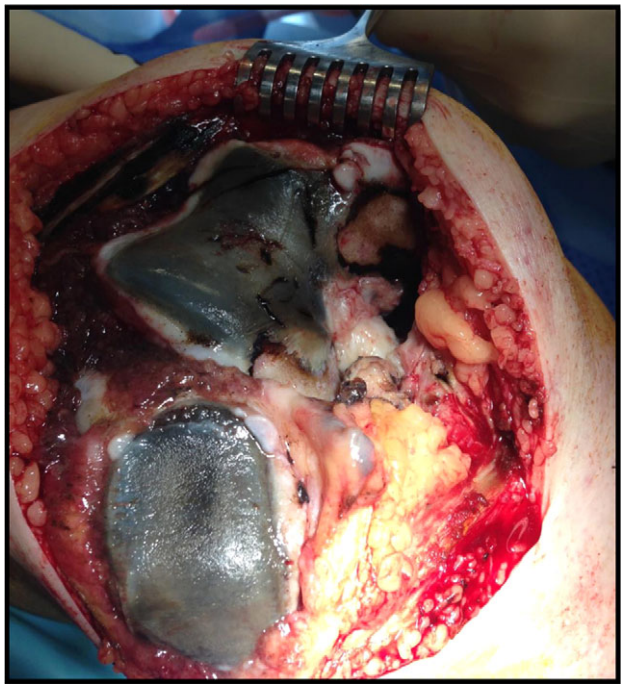

Figure 6: Intraoperatively, the joint surfaces of the ochronotic knee

are very frequently involved [8]. In tendons, the ochronotic pigment deposition can lead to their thickening and rupture, as well as muscle tears resulting from minimal trauma [1, 8].

Diagnosis can be confirmed using gas liquid chromatography, thin-layer chromatography or a enzymatic spectrophotometry to analyse the amount of HGA in urine [1]. Because of the rarity of the disease and paucity of clinical symptoms until middle age, the diagnosis of alkaptonuria is occasionally made just intraoperatively [1].

Currently, there is no proven therapy or prophylactic treatment for alkaptonuria. Whereby, the treatment is generally symptomatic and aimed at preventing or minimizing the effects of OA [1, 2]. Measures like restriction of foods containing phenylalanine and tyrosine have been shown to be effective in limiting symptoms of ochronotic arthritis. However, it is controversial, because despite having been shown to limit HGA excretion in children, the data showed less success in adolescents and adults [1, 9]. Supplementation with vitamin C is recommended for older children and adults, because the mild antioxidant nature of ascorbic acid helps retard the process of conversion of homogentisate to the polymeric material that is deposited [7, 9]. The drug nitisinone is being researched as the first potential treatment for alkaptonuria; in previous research has shown to reduce the levels of HGA by up to 95% [10]. Although management of OA is usually conservative, surgery can be necessary and it can include synovectomy, arthroscopic debridement or even arthroplasty [2, 9].

Life expectancy is globally normal; however, the morbidity can be significant [8]. Further research is necessary.

This is a rare case report of a total hip and knee arthroplasty performed in a patient with Alkaptonuria suffering from OA: after 36 months of follow-up, our clinical result suggest that this treatment procedure is an safe and effective option to treat OA [1]. Orthopaedic surgeons must be suspicious of an atypical arthropathy in order to not be overwhelmed during surgery with the presence of darkened cartilage.

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None.

CONFLICT OF INTEREST STATEMENT

All authors have no conflict of interest to report.

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ETHICAL APPROVAL

This study was conducted with ethical approval.

CONSENT

A written patient consent and permission to publish have been obtained.

GUARANTOR

André Couto.

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