

**ALKAPTONURIA DIAGNOSED IN A 72 YEAR OLD FEMALE AFTER  
TOTAL KNEE REPLACEMENT**

Wael Zaabout

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## ALKAPTONURIA DIAGNOSED IN A 72 YEAR OLD FEMALE AFTER TOTAL KNEE REPLACEMENT

### Abstract

Alkaptonuria is a rare autosomal recessive disorder of metabolism caused by deficiency of homogentisic acid oxidase and resulting in accumulation of homogentisic acid in collagenous structures. It is characterized by homogentisic aciduria, bluish-black discoloration of connective tissues (ochronosis) and arthropathy of large joints. Less common manifestations include cardiovascular abnormalities, renal, urethral and prostate calculi. Bone fractures are unusual in ochronosis. In this report, we describe a woman, 72 years of age, with a history of severe arthropathy requiring total joint replacement in both of her hips and left Knee. During the Left Total Knee Replacement, an intra operative observation of a bluish-black discoloration of the knee joint and the surrounding soft tissue raised the diagnosis of Alkaptonuria. We review the etiology, pathogenesis, clinical presentation, diagnosis and treatment of alkaptonuric ochronosis. Early detection is important for prevention and treatment of multiple systems.

### Keywords

Alkaptonuria, homogentisic acid, ochronosis, osteoarthritis, ochronotic arthropathy

## 1. INTRODUCTION

Aromatic acids as Tyrosine and Phenylalanine, contained in foods and metabolized by our body, are important in the synthesis of multiple hormones. Any defect in specific step of the catabolism of tyrosine will result in specific genetic disorders. One of these rare disorders is known as Alkaptonuria. Alkaptonuria is an autosomal recessive trait on chromosome 3q21-23 caused by the deficiency in homogentisic acid 1, 2 deoxygenase (HGD), an important enzyme in the pathway of catabolism of tyrosine (Mistry et al., 2013).

The prevalence of the disease is 1:250,000-1,000,000 cases. Only 950 cases were reported throughout 40 countries. It is characterized by an increase in the deposition of homogentisic acid in the connective tissues of the body resulting in ochronosis; a bluish-black discoloration of the connective tissues, especially in the articular surfaces of big joints. Moreover, the excess homogentisic acid in the urine causes it to turn dark in color. (Mistry et al., 2013, Craide et al., 2012). In pediatric age group the diagnosis is missed since the only presentation is urine discoloration of the diaper and urine is usually exposed to alkalization after air exposure on diaper. By the third decade, patients present with symptoms mimicking osteoarthritis, and ankylosing spondylitis which later progress to be complicated with ochronosis. (Mistry et al., 2013, Adamopoulos et al., 2016)

Clinical presentation of Alkaptonuria is sufficient for diagnosis. Homogentisic acid is increased in the accumulated fluids and tissue. Finally, gas liquid chromatography on urine is done to confirm the diagnosis (Khatu et al., 2015). Symptomatic treatment is the only identified therapy in Alkaptonuria with main objective to prevent further complications and multiple surgeries. Multivitamin supplementation, especially Vitamin D, could be added to improve the quality of the bone damaged and preserved. (Alajoulin et al., 2015). We present a case of 72-years old female who was diagnosed with Alkaptonuria only during total knee replacement.

## 2. CASE REPORT

A 72-year-old female non-smoker, known to have osteoarthritis, osteoporosis and rheumatoid arthritis admitted to our hospital for elective left total knee replacement for severe knee osteoarthritis. Patient was diagnosed with rheumatoid arthritis and severe osteoporosis at an early age (40 years). Following this diagnosis, the patient was maintained on anti-inflammatory, vitamin D and Calcium supplements with no reported treatment for rheumatoid arthritis

At the age of 52, the patient underwent left total hip replacement for severe left hip osteoarthritis. 3 years later following her surgery, the patient was readmitted to our hospital for right total hip replacement secondary to severe right hip osteoarthritis. At that time, the patient was concomitantly suffering from intermittent bilateral knee pain, and lower back pain. During the investigations, radiological report showed severe degenerative osteoarthritis of the right hip, narrowing of the joint space, and severe L3, 4, 5-disc space narrowing. (Figure 1)

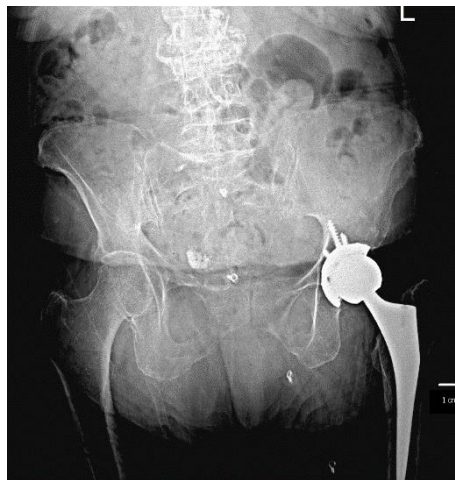


Fig.1: osteoarthritis of the right hip, narrowing of the joint space, and severe L3, 4, 5-disc space narrowing. Left Total Hip prosthesis.

Subsequent to her right total hip replacement, the operative note with the gross and the histological pathology report revealed femoral head deformity and edge discoloration but the diagnosis remained as severe osteoarthritis.

In 2019, the patient was readmitted for elective left total knee replacement for severe knee osteoarthritis diagnosed by X-ray (Figure 2).



Fig.2: Right knee osteoarthritis, joint space narrowing, degeneration of the articular surface. Left Total Knee prosthesis

During the surgery, a bluish-black discoloration of the quadriceps tendon and the patellar tendon along with the articular surfaces of the femur, tibia and patellae, and the surrounding soft tissue was surprisingly observed. The patellar tendon was very fragile causing worrisome about a possible avulsion. (Figure 3)

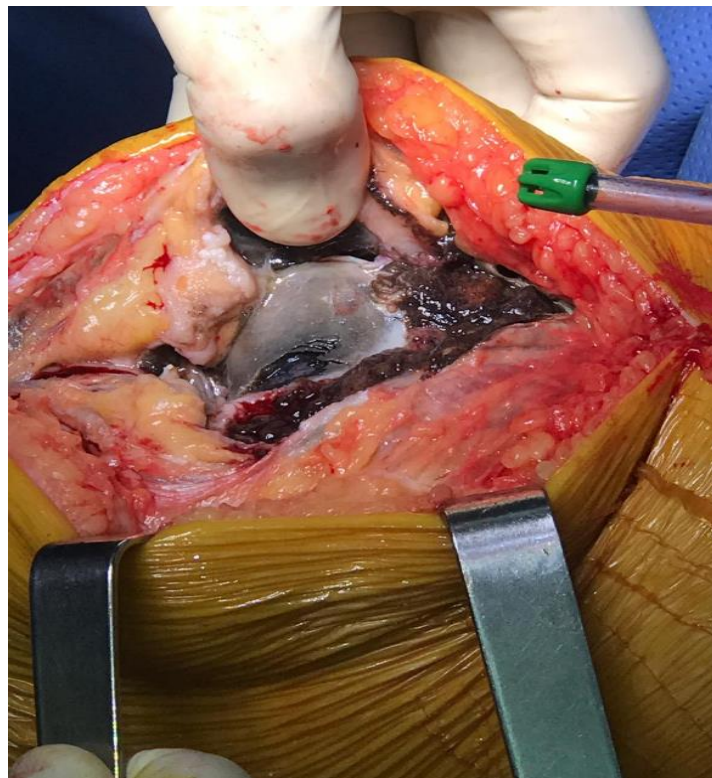


Fig.3: bluish-black discoloration of the quadriceps tendon and the patellar tendon along with the articular surfaces of the femur, tibia and patellae, and the surrounding soft tissue.

A tentative diagnosis of Alkaptonuria was made. Following the operation, the patient was examined physically and found to have a bluish black discoloration of the sclera and the cartilage of the ear. (Figure 4 and 5)



(4)

Fig.4: bluish black discoloration of the sclera.



(5)

Fig.5: bluish black discoloration of the cartilage of the ear.

The patient was finally diagnosed with Alkaptonuria based on her past medical history and present complaint and findings intra-operatively. She was referred to a rheumatologist and prescribed symptomatic treatment to prevent further complication.

### 3. DISCUSSION

Osteoarthritis is the most common degenerative disease affecting more than 25% of the population (Chen et al., 2016). Survival with the disease can last up to 30 years with a median age of diagnosis at 55 (Charlesworth et al., 2019). Our 72-year-old patient is presented with a previous diagnosis of osteoarthritis at the age of 40.

The knee is most frequently affected by articular surface disease as osteoarthritis and ochronosis due to the repetitive stress it is exposed to and the load it carries (Mora et al., 2018). In accord, our patient had previous history of repair surgeries of the hip and knee and was currently presenting for right knee replacement due to osteoarthritis.

Osteoarthritis typically presents with stiffness, instability and radiographic changes in which these symptoms are nonspecific (Chen et al., 2016)). It is previously mentioned that Alkaptonuria can be mistaken for osteoarthritis if no onchronosis was found (Adamopoulos et al., 2016). The metabolic enzyme system of the cartilage is inhibited in Alkaptonuria by the deposition of the pigments that acts like a chemical irritant, resulting in fragility and disintegration of the structure affected (Collins, 2005), thus leading to similar clinical symptoms with other diseases. Ochronosis is a bluish-black discoloration of the connective tissues, especially in the articular surfaces of big joints such as the hips and knees resulting from the accumulation of homogentisic acid (Collins, 2005). Our patient was diagnosed for osteoarthritis due to the recurrent presentation of diffuse pain in joints (knee and hip) with restricted movement and stiffness. During her hip replacement, incidental pigmentation on the joint was discovered with irregularity of femoral head surface indicating to onchronosis but no further investigations were done. Within her current surgery, the report along with the macroscopic appearance clearly showed bluish-black pigmentation on the edges of the cartilage.

Deposition in other areas of the body might be involved such as the skin, ears, eyes and heart (Alajoulin et al., 2015). Noting that after the surgery a complete proper physical exam was done revealing pigmentation on other sites. The clinical presentation of Alkaptonuria is sufficient for the diagnosis in addition to the finding of homogentisic acid accumulated in urine (Khatu et

al., 2015). No further urinary analysis or tests were done to confirm the diagnosis based on lab with our patient.

The patient was then referred to a rheumatologist for further investigations. She was also put on NSAID's as analgesics.

#### 4. LIMITATIONS

Limited number of cases reported in our country.

The patient was followed up for a short period of time after diagnosis.

No urinary tests were done to further confirm the diagnosis based on lab with our patient.

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