Alkaptonuria: Spontaneous Achilles tendon rupture: Case report

Emre Baca, MD1, Alev Kural, MD2, Nezih Ziroglu, MD1, Cemal Kural, MD1

1Department of Orthopedics and Traumatology, Bakirköy Dr. Sadi Konuk Training and Research Hospital, İstanbul, Turkey
2Biochemistry Laboratory, Bakırköy Dr. Sadi Konuk Training and Research Hospital, İstanbul, Turkey

ABSTRACT

Alkaptonuria is an autosomal recessive disease caused by the accumulation of homogentisic acid (HGA) products in the ligament, cartilage, skin and various organs due to the lack of HGA oxidase enzyme. In this article, we present a 61-year-old male patient operated on due to a diagnosis of spontaneous Achilles tendon rupture and diagnosed as alkaptonuria due to the intraoperative color of the tissues and the subsequent examinations. We also reviewed alkaptonuria and its accompanying pathologies in light of the literature. Keywords: Achilles, alkaptonuria, ochronosis, rupture.

Alkaptonuria is a rare autosomal recessive metabolic disorder due to deficiency of the enzyme homogentisic acid (HGA) oxidase, which is involved in the metabolism of HGA, a metabolic product of the aromatic amino acids phenylalanine and tyrosine. Alkaptonuria has an estimated prevalence ranging from 1:200,000 to 1:1,000,000 live births worldwide, although an increased prevalence of disease of approximately one in 19,000 has been found in the Dominican Republic and within the Piestany region in Slovakia.[3] Blue-black pigmentation in tissues, degenerative arthritis with urinary color change to blue-black is defined as ochronosis. Ochronosis was first described by Virchow in 1866 on soil-colored pigmentation in different tissues in a necropsy material.[3] Arthropathic changes occur in approximately 30% of cases in the fourth-fifth decades of life.[3,4]

The HGA which accumulates is polymerized to form a dark pigment which is deposited in connective tissues.[3,4] These products are mainly deposited in sclera, cartilage, ligament, tendon, skin, nail, tooth and vessel intima.[3] Degenerative changes are mostly seen in the vertebral column and large joints.[4] Achilles tendon rupture is an uncommon clinical condition in patients with alkaptonuria like similar pathologies.[3] In the literature, few cases of spontaneous tendon rupture have been reported.[1,2,5,6] In this article, we report the case of a patient with a history of ambiguous joint complaints and spontaneous Achilles tendon rupture due to alkaptonuria.
rupture who was admitted to the emergency room and diagnosed with alkaptonuria as a result of further medical examinations.

**CASE REPORT**

A 61-year-old male patient was referred to the emergency department after falling from height. He had pain in the back of his right ankle. He was unable to walk. He was healthy, with no previous diagnosed systemic disease. When the detailed history was obtained, it was found that there was occasional joint pain in both knees and lower back.

On examination, he had diffuse swelling over the back of the ankle with a palpable defect over the Achilles tendon proximal to its insertion. There were no external injuries. The discontinuity of the Achilles tendon was confirmed clinically by the inability to stand on his toes and by the Thompson squeeze test. Magnetic resonance imaging revealed findings of total Achilles tendon rupture. A written informed consent was obtained from the patient.

He was operated on the same day receiving spinal anesthesia. The ruptured stumps of the tendon were found to have dark pigmentation, and both sides of the tendon were almost black in color (Figure 1).

Both ends of the rupture were highly fragmented. Fragmented tendon parts were excised, and sent for pathology with the suspicion of ochronosis. After debridement, there was a gap of 6 cm. Therefore, the tendon was repaired using the Lindholm’s double facial flap technique. After closure, leg cast was applied. A plaster cast was renewed every three weeks and its plaster was terminated at the ninth week.

Postoperatively, the patient was examined for alkaptonuria. His urine was kept outdoors. Color change occurred in 30 minutes. Urine qualitative ferric chloride test was found positive for HGA. Quantitative HGA level was found 2036.7 mg/g creatinine (normal, 0-14.8 mg/g creatinine) with gas-liquid chromatography. A high peak of HGA was detected when chromatogram of the study was inspected.

Detailed musculoskeletal and radiological examination showed contraction of the lateral compartment in each knee joint, synovial calcifications on the left knee joint, and intervertebral intervals of the thoracic and lumbar vertebrae were narrowed in the vertebral column and common degeneration findings (Figure 2a, b). No pathology was found in any other system examinations. It was learned that there was a discoloration of the urine residue in the underwear. The pathology report showed black pigmentation suspicious for alkaptonuria. Our patient was able to maintain his daily life without any skin problem with 20 degrees dorsiflexion and full plantar flexion on ankle in follow-up at 30 months postoperatively.

**DISCUSSION**

Alkaptonuria is usually asymptomatic until adulthood. Pigmentation in the eye sclera and the cartilage can be seen in the second decade. Color changes in teeth, nails and skin can follow these findings. Large joints such as the vertebrae and knee usually begin to show signs in the fourth decade. Less common findings are extraarticular involvement, heart valve involvement and obstruction in the urinary tract.

Homogentisic acid is widely deposited in connective tissue and such pigmentation must include tendons, which contain mainly type-I collagen. There are no specific findings for the diagnosis of ochronosis in soft tissues and tendons. In ultrasonography examination, small calcifications, decreased fibrillation and increased thickness are observed. Alkaptonuria usually affects large
Analyzing acetabular deficiency in Crowe type 2 hips

tendons (Achilles and patellar tendons), and their spontaneous rupture has been published in the literature in small numbers. In this pathology, HGA product accumulation leads to irreversible damage in the connective tissue polymerization and oxidation process. Calcification and rupture of the tendon may occur as a result of these events. One of the biggest problems in the treatment of Achilles tendon rupture, which is a common pathology in orthopedic surgery, is to repair the ends of the torn tendon ends after the debridement and to return to the old strength without rerupture. In our case, an adequate stability was achieved after debridement of the torn ends and the procedure of approximation and strengthening of the healthy tendon ends. However, the rehabilitation process included the conventional treatment plan for Achilles tendon rupture, which involved firstly slightly-flexed plaster cast, then gradual neutralization, partial load-bearing, and full range of motion.

When the literature is reviewed, the rupture of the Achilles tendon is present in approximately 12 cases mostly published in India. As in our case, the majority of the cases of tendon rupture were not diagnosed and they were followed with a diagnosis of alkaptonuria; the majority of the cases were diagnosed as alkaptonuria as a result of advanced investigations in the urine, due to suspected black-brown macroscopic appearance of the tendons during spontaneous rupture. The blackening of the urine sample with the addition of sodium hydroxide is an important diagnostic tool. Diagnosis is confirmed by gas liquid chromatography, thin-layer chromatography or enzyme spectrophotometry and by measuring the amount of HGA in urine. Intraoperative macroscopic color appearance, detailed urine analysis and degenerative changes in other major joints as well as detection of skin-cartilage discoloration have supported our recognition of alkaptonuria.

The prophylactic and definitive treatment of this disease has not been found yet. There are some treatment approaches for minimizing only ochronotic arthropathy and other findings. For patients with large joint involvement; resting, analgesia and physiotherapy may be useful in early periods. Joint debridement or arthroplasty can be performed in joints with advanced degeneration. It is preferable to reduce the intake of foods containing phenylalanine and tyrosine, particularly in diets. Daily 1 g of vitamin C intake is recommended in adults and children. The mild antioxidant nature of ascorbic acid helps to retard the conversion of homogentisate to the polymeric material which is deposited in the cartilaginous tissues. In human and mouse experiments, it was observed that nitisinone changed the urinary HGA extraction significantly. Although it is recommended to use this drug in tyrosinemia type I, there is no significant information for its use in ochronosis patients. In patients with large joint involvement, such as the load-bearing knee joint, it was reported that the use of 400 mg chondrotin
sulfate and 1,500 mg glucosamine per day for four months reduced joint complaints.[11]

In conclusion, alkaptonuria is a metabolic disease resulting from an enzyme defect. Early detection and repair of the disorder in the relevant gene may enable treatment of this multi-organ disease.

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