Spontaneous Achilles Tendon Rupture in Alkaptonuria

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ABSTRACT

Alkaptonuria (AKU) is a rare genetic metabolic disorder caused by deficiency of homogentisic acid oxidase (HGO) enzyme leading to accumulation of homogentisic acid (HGA) in the body. HGA excreted and oxidized through urine causes its characteristic dark discoloration; however, once accumulated in bodily connective tissues, it causes characteristic dark pigmentation (ochronosis) of tissues, and in the long-term, it leads to degeneration of cartilage and tendons. In this case report, we present a patient who has had a unilateral spontaneous atraumatic rupture of the Achilles tendon. To our knowledge, such a case has not been previously reported in the French and Bahraini literature.

Keywords: Ochronosis, Alkaptonuria, Homogentisic Acid, Achilles Tendon

INTRODUCTION

Achilles tendon rupture is a common injury in orthopedic practice; it has been an incidence that ranges from 11 to 37 per 100,000 population, with men more than twice as likely to rupture their Achilles tendon than women[1]. This number reflects traumatic ruptures and re-ruptures, while atraumatic spontaneous ruptures remain very rare.

Alkaptonuria (AKU) is a rare autosomal recessive metabolic disorder with an estimated prevalence of 1:250,000-1,000,000[2]. A gene mutation on chromosome 3 (position 3q21-q23) that normally codes for the homogentisic acid oxidase (HGO) enzyme leads to the accumulation of homogentisic acid (HGA). The oxidation and/or alkalization of HGA in urine and tissues is responsible for their dark pigmentation. The first described case of AKU was the Egyptian mummy of Harwa 3500 years ago, when cartilage specimens recently confirmed HGA deposition[3]. HGA is deposited in the extra-cellular matrix (ECM) and the collagen present in intervertebral discs, tendons, and blood vessels. In articular cartilage, tendons, or ligaments, these depositions, along with their bonds with ECM, would alter the structure of these tissues and affect their biomechanical properties and resistance[4]. The ochronotic pigments can also cause chronic inflammatory reactions (acting as a foreign body) or acute inflammatory reactions manifesting as joint effusions with high cell counts[5].

The disease has three distinctive stages. Stage I (since birth) is when urine turns dark[6], stage 2 (20-30 years old) is when ochronosis of the ear and sclera are the main symptoms[7], and stage 3 (ochronotic lesions) is when such depositions lead to the biomechanical destruction of the spine, large joints, tendons, heart valves, kidney, and prostate[8,9]. The AKU diagnosis is made using gas chromatography-mass spectrometry analysis in urine and tissues.

CASE PRESENTATION

A 54-year-old female known to suffer from depression, anxiety, infantile psychosis, and long-standing left knee and back pain arrived at our facility following a history of hiking accidents. While normally walking on an even surface, she felt a dull pain at the back of her left ankle. She did not hear an audible snap or click. She could not bear weight immediately after and thus required assistance in seeking medical help. On arrival to our emergency department, clinical examination yielded a swollen left ankle and ecchymosis at the lateral border of the fifth metatarsal and lateral malleolus. She had a weak active plantar flexion. A palpable defect was appreciated at the mid substance of the Achilles tendon. The Summond-Thompson test was positive. On inspection, she had a bluish-gray tint on her ears and sclerae. Of note, the patient had undergone right Achilles tendon repair 10 years ago following a trivial trauma as described by herself. She takes cyamepromazine, paroxetine, oxazepam, and lercanidipine as regular medications. The patient lives in a center for adults with special needs. She had smoked 1.5 packets of cigarettes per day since she was 20 years old.

The patient opted and consented to surgical repair of the Achilles tendon. Under general anesthesia in a prone position, the skin was prepared with surgical scrub, and a tourniquet was placed at the proximal left thigh. A medial paratendinous incision was made centered over the site of Achilles tendon rupture. The tendon sheath was incised to reveal a complete Achilles tendon rupture at 3 cm from its calcaneal insertion. The stumps were of a particular consistency and color; they were irregular, tapered, black (ochronosis), clear zone of transition, hard, and retracted (Figures 1 and 2). The stumps were debrided and regularized; they were approximated and sutured using the Krackow technique. Samples were obtained for histopathological analysis.

Post-repair, Summond-Thompson was negative. The ankle was immobilized in a cast for a total of 8 weeks, the first 4 weeks being at 20° equinus and weeks 4-8 at 0° equinus. Progressive partial to complete weight-bearing was permitted after this period with the help of a certified physiotherapist. The patient was given an anticoagulant, Enoxaparin 4000 IU subcutaneously once daily, during the non-weight bearing stage. At the 3-month follow-up visit, the patient walked without aid, and the injury healed almost completely to allow her to do her activities of daily living.

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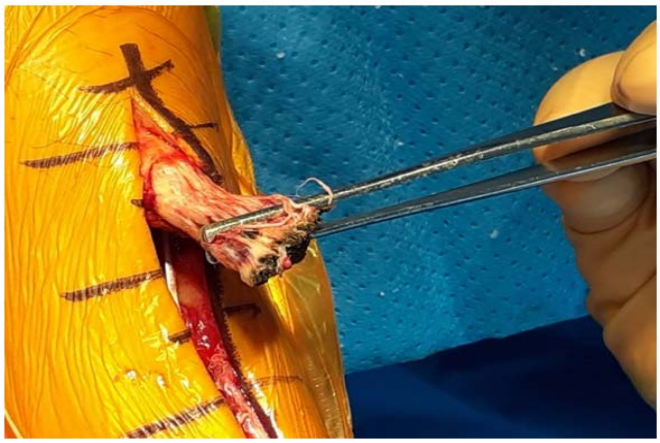

Figure 1: Ochronotic lesion depicted in mid-substance of the ruptured Achilles tendon

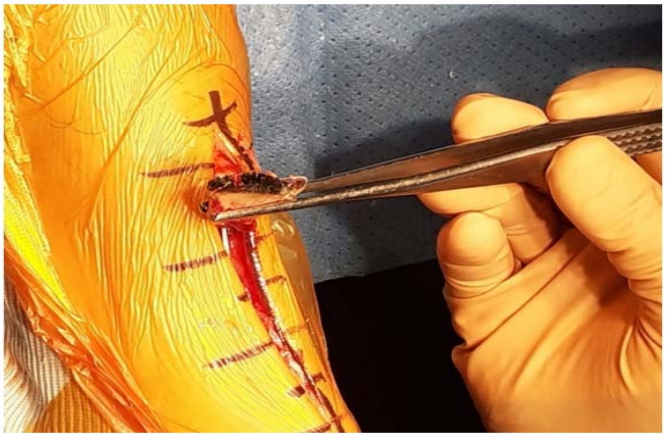

Figure 2: Degenerated tendon structure and consistency

On postoperative day 0, a urine sample was obtained after noticing the features mentioned above of AKU. The patient did not exhibit signs or symptoms of a urinary infection. It initially contained dark residue yet of normal color (Figure 3); however, when exposed to air, 36 h later, the urine turned black, confirming the diagnosis in question (AKU) (Figure 4).

Figure 3: Urine collected immediately post-op showed a dark-colored residue

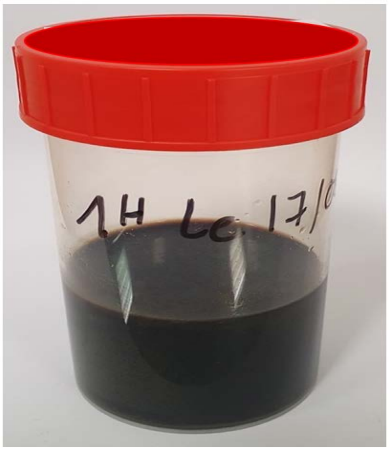

Figure 4: When exposed to air, HGA in urine is oxidized, turning urine black

DISCUSSION

The myriad of symptoms exhibited by the patient before the spontaneous rupture of the Achilles tendon went unnoticed. AKU is rare thus usually omitted from musculoskeletal differential diagnoses. Nevertheless, vigilance must be exercised when approaching a patient with visible and appreciable signs and symptoms of a disease. The patient complained of chronic lower back pain and moderate to severe knee pain that could be explained by ochronotic arthropathy[10].
Phornphutkul et al., in their paper published in 2002, found spondyloarthropathy in patients with AKU manifested clinically during middle age[6]. We demonstrate in our case report that even with suboptimal ruptured tendon stumps, the standard technique of tendon suturing (Krackow) could yield good results.

AKU has no proven implications on developmental delay, nor does it seem to affect lifespan[11]. The treatment is targeted to relieve the consequences of the disease, such as pain caused by arthritis. Perry et al., in their paper that included 53 AKU patients, concluded that almost 30% required a joint replacement, either knee, hip, or a shoulder[8]. Since ochronotic tendinopathy and arthropathy manifest earlier than age-related degenerative arthropathy, AKU patients' activity would be reduced if not addressed promptly.

Pain relief is a cornerstone of treatment, yet psychological support for depression and/or anxiety is equally important. No cure exists, yet physicians and surgeons can help tackle the consequences of such systemic disease. In addition, patients require physical and occupational therapy to maintain joint flexibility and strength when the diagnosis is made.

In 2000, the crystallographic structure of the HGO protein was reported[12]. This might have helped illustrate its exact functions and clinical implications. In 2001, nitisinone was approved by Food and Drug Administration (FDA) for tyrosinemia, yet it was shown to significantly reduce accumulations of homogentisic acid in individuals with AKU. However, more research is fundamental to determine if this investigational therapy is safe to use in young patients; profile its short- and long-term effects and its impact on the musculoskeletal burden of AKU.

CONCLUSION

Spontaneous Achilles tendon rupture is a rare entity in orthopedics. Collagen in tendons is prone to structural infiltration, degeneration, and

ultimately breakdown by a systemic manifestation of a genetic disease like AKU. Standard surgical repair techniques help restore tendon continuity and allow healing to occur, yielding a good functional outcome.

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