Case Report

Sequential tendon ruptures in ochronosis: case report

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ABSTRACT

Alkaptonuria is a rare autosomal recessive disorder characterised by the absence of homogentisic acid oxidase, due to deficiency of an enzyme that degrades HGA in the tyrosine degradation pathway. Homogentisic acid (HGA) and its metabolites accumulate in the connective tissues leading to dark pigmentation of connective tissue in patients with alkaptonuria. HGA deposits in connective tissue causes weakness of the tendon and subsequent rupture, especially the large tendons in the body. Only few cases are reported in the literature with multiple tendon rupture but many case reports are available with isolated rupture of tendons. We report on a patient with sequential tendon ruptures in a patient. The case is reported for its rarity.

Keywords: Ochronosis, Multiple tendon ruptures, Medical prophylaxis in ochronosis

INTRODUCTION

Ochronosis is a rare autosomal recessive disorder of tyrosine metabolism. Ochronosis is the deposition of products of homogentisic acid (HGA) in the connective tissue resulting in bluish black discoloration of connective tissue. This is easily visible in the cartilage of the ear. The deficiency of the enzyme HGA 1,2-dioxygenase1, an enzyme in the tyrosine degradation pathway (Figure 1), results in accumulation of HGA. The HGA is oxidised to benzoquinones that polymerise and bind to connective tissue and cartilage. This leads to weakness and subsequent rupture of tendons, and early degeneration of articular cartilage. Accumulation of HGA in urine causes urine to darken on standing or on exposure to alkaline conditions. There are only a few reports in the literature of multiple rupture of the Achilles tendon.1-4 We report a case who had a rupture of the Achilles tendon, followed by rupture of the quadriceps tendon one year later.

CASE REPORT

A 37 year old male patient was admitted to hospital following a trivial tripping injury to the knee (Figure 2).
He felt a snap in the front of right knee. History revealed that he had surgery to the right ankle one year earlier for Achelles tendon rupture. Examination showed a palpable defect in quadriceps tendon. He also had dark pigmentation of sclera of both eyes and bilateral ear pinna (Figure 3-4). X ray showed a small lytic lesion superior pole of patella (Figure 5). MRI knee confirmed a rupture of the quadriceps tendon (Figure 6). The previous operation to the heel had healed and he had good function of the ankle. Clinically the Achilles tendon had healed (Figure 7).

Figure 2: Clinical presentation.

Figure 3: Greyish pigmentation of sclera.

Figure 4: Early pigmentation of pinna.

Figure 5: X ray knee lytic lesion on superior pole patella.

Figure 6: MRI showing quadriceps rupture.

Figure 7: Healed old surgical scar.

Figure 8: Dark pigmentation of quadriceps tendon and superior pole patella.
After discussing the treatment options, he was taken to theatre for open repair of the quadriceps tendon. The striking feature intraoperatively was that the soft tissue and the bone were stained black (Figure 8). The articular cartilage was greyish in colour (Figure 9). Specimens were taken for histopathology. The tendon ends were debrided, approximated and repaired with two anchor screw with fibre wire suture and a running nylon suture for the paratenon (Figure 10 and 11). He had an uneventful post-operative recovery. The histopathological study showed features of yellow brown pigment (ochre) deposited in the chondrocytes and the tendon, consistent with ochronosis. 24 hour urine sample turned to a dark colour and urine analysis showed elevated levels of HGA. Retrospectively we made the diagnosis of ochronosis as the cause of his sequential tendon ruptures.

**DISCUSSION**

Ochronosis is a very rare autosomal recessive disorder of tyrosine metabolism. It results from a deficiency of the enzyme HGA oxidise, which is involved in the degradation of tyrosine. This results in accumulation of HGA and its degradation products in the tissues. The prevalence is lower than 1:250000. The patients are usually asymptomatic till the third decade. By the second decade bluish grey pigmentation may appear in the sclera, cartilage of the ear, in the teeth, buccal mucosa and in the nails or skin. Our patient presented with the disease at 37 years of age.

The accumulation of HGA degradation products are responsible for the dark staining of the connective tissue, from which the term ochronosis is derived. Darkening of the urine is often the first sign, but is seldom reported by the patient. Sometimes mother may notice dark staining of diapers in children. Darkening of the sub-cutaneous cartilage, especially that of the ear is a very common clinical sign. This is however, not easily seen in dark-skinned individuals. Orthopaedic manifestations of the disease are caused by deposition of HGA in connective tissue. This weakens the connective tissue, leading to rupture of tendons and early degeneration of the cartilage. The most reported tendon rupture is the tendo-Achilles.

It causes back pain due to dystrophic calcification of the inter-vertebral disc. Arthritis involves mainly the large joints, like hip and knee. It is due to deposition of the HGA metabolites into the articular cartilage, meniscus and labrum causing early degeneration of the articular cartilage. X-ray knee joint of our patient did not show arthritis but cartilage was affected (Figure 3). Joint degeneration often manifests itself after the third to fourth decade.

Non-orthopaedic manifestations include deposition in the heart valves, causing dystrophic calcification of the valves, aortic stenosis, and coronary artery disease. Kidneys are also affected causing renal stones and deposition in ocular tissue leads to disturbances of vision. Treatment of the orthopaedic complications of alkaptonuria is repair of a tendon rupture, conservative treatment of osteoarthritis initially, up to total joint replacement. Isolated tendon rupture is commonly reported. Since ochronosis is a systemic disease other tendons are also involved and can rupture with time, as happened with this patient.

Prophylactic therapy in patients with tendon rupture in ochronosis is important to prevent subsequent tendon rupture. Cases of successful medical treatment have been
reported in the literature. Morava et al reported on a child with alkaptonuria where symptoms of joint pain, darkening of urine and radiologic signs of joint involvement were reversed by 1) putting the child on a diet that restricts the intake of tyrosine, and 2) adding a reducing agent, ascorbic acid. They recommend that patients with Alkaptonuria be put on a diet, restricting protein intake to 1.3 g/kg/day and take ascorbic acid at a dose of 0.5 to 1 g/day.

Another approach is by decreasing production of HGA by administration of nitisinone (2–nitro–4–trifluoronitril–1,3 cyclolexanediose), which is a compound that inhibits 4–hydroxy phenylpyruvic deoxygenase, the enzyme that produces HGA as shown in Figure 1. Nitnisinone has been used to decrease the formation of toxic oxidising metabolites in tyrosinaemia type I children and constitutes the treatment of choice in this otherwise fatal disease. Low-dose nitnisinone has been shown to reduce urinary excretion of HGA by 67% and more.

Although medical treatment is promising in the treatment and prevention of orthopaedic complications of ochronosis, further clinical trials required to support the routine use of medical treatment in this disease.

CONCLUSION

Ochronosis is a rare metabolic disease, leading to orthopaedic complications of tendon rupture, osteoarthritis and back pain. Prophylactic therapy may reduce the complications by a combination of protein restricting diet, ascorbic acid and nitnisinone. Clinical trials need to continue before these treatment modalities can be used routinely in this disease. The available medical evidence shows that medical treatment is the treatment of the future in this rare condition.

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