

C A S E R E P O R T

Total Knee Replacement in alkaptonuric ochronosis

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Abstract. *Background and objective:* Alkaptonuria is a rare disease characterized by the accumulation of homogentisic acid (HGA). Over time, these patients may develop disabling ochronotic arthropathy. We present 2 cases of patients with end-stage arthropathy treated with total knee arthroplasty (TKA). *Methods:* Both patients complained of disabling knee pain and reported limited walking distance (200-300 m). One had a history of osteotomy for medial knee arthritis and ignored his underlying condition. The other presented with valgus gonoarthrosis and diagnosis of alkaptonuria. *Results:* Intraoperatively, the characteristic dark-blue color in the joint was observed. Both patients evolved favorably after TKA with excellent results according to the Knee Society Scores (KSS) at three years of follow-up. *Conclusion:* We believe TKA is the right treatment for patients with end-stage disease because it offers considerable relief from pain and allows patients to recover function. (www.actabiomedica.it)

Key words: alkaptonuria, ochronotic arthropathy, total knee replacement

Introduction

Alkaptonuria, also known as *black bone disease*, is a metabolic disorder with a very low prevalence originated by a mutation in chromosome 3 (3q21-q23). Patients with alkaptonuria suffer from a deficiency of homogentisic acid oxidase, the enzyme that converts homogentisic acid (HGA) into maleylacetoacetic acid (1-3).

Excess HGA is excreted in urine causing it to turn dark with oxidation. In addition to this, HGA deposits in connective tissues giving them a characteristic blue-black pigmentation (3-5). Over time, this HGA accumulation makes cartilage brittle, sometimes leading to ochronotic arthropathy (2-5). Here, we present 2 patients with arthropathy who were treated with TKA.

Case reports

Case 1

A 74-year-old male patient visited our center complaining of pain in his left knee. He had suffered

this pain for two years. His walking distance was limited to 200 meters. He had had an osteotomy for medial knee arthritis 7 years before this visit.

On the physical examination, he presented an eutrophic scar on the left proximal tibia and knee mobility in the range of 10-115° with varus-valgus stability. A radiograph taken in a single-leg weight bearing position showed degenerative changes consistent with varus gonoarthrosis (Ahlbäck IV) (Figure 1).

Left TKA was performed. A hemostatic tourniquet was used during the procedure. The proximal screws of the previous osteosynthesis were removed percutaneously. A standard anterior approach with medial parapatellar arthrotomy was used. At that point, the surgeon observed that both the joint capsule and the cartilage were blue-black (Figure 2) and decided to send a specimen to the anatomic pathology laboratory.

Soft tissues were then released and balanced to correct genu varum. A significant thickening of the patellar tendon was observed and, therefore, the patella was carefully mobilized to reduce tension on the

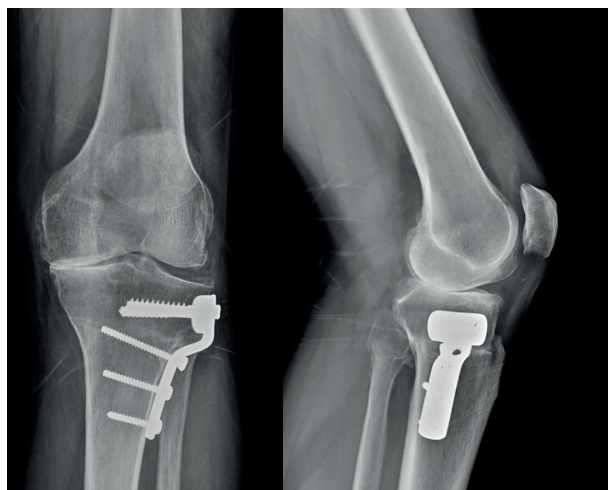


Figure 1. Preoperative radiograph taken in a single-leg weight bearing position showing varus malalignment and osteosynthesis material from prior osteotomy.

tendon. The usual cuts were performed, and prosthesis components were cemented. A Scorpio® posterior-stabilized prosthesis was used (Stryker®, NY, USA). The rehabilitation was similar to that of TKA patients with idiopathic osteoarthritis.

Anatomic pathology reports highlighted multiple pigmented areas with granular deposits of reactive giant cells, cartilage degeneration, and synovial hypertrophy.

The postoperative radiography showed proper component placement and femorotibial alignment (Figure 3).

An inter-consultation was held with the team of clinical medicine and rheumatology of our center and they confirmed the diagnosis after plasma and urine tests.

The patient progressed favorably. During the last follow-up visit, which took place 4 years after the surgery, he reported no walking limitations, was able to perform daily activities without assistance and felt no pain. His knee mobility was in the range of 0-115° and his knee and functional scores (KSS)⁶ were 90 and 88, respectively.

Case 2

A 60-year old male patient who had been diagnosed with alkaptonuria several years ago consulted for pain in his right knee. During the last year, pain had limited his walking distance to 300 meters and he needed a walking stick. The radiographic examination revealed right valgus gonarthrosis (Figure 4). On the physical examination,

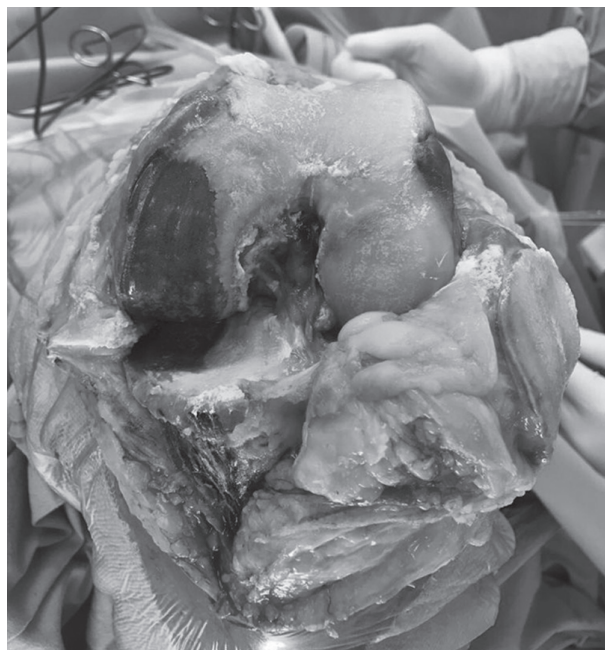


Figure 2. Intraoperative images. It is possible to observe a cartilage injury, the change in color to blue and black, and meniscal calcification.

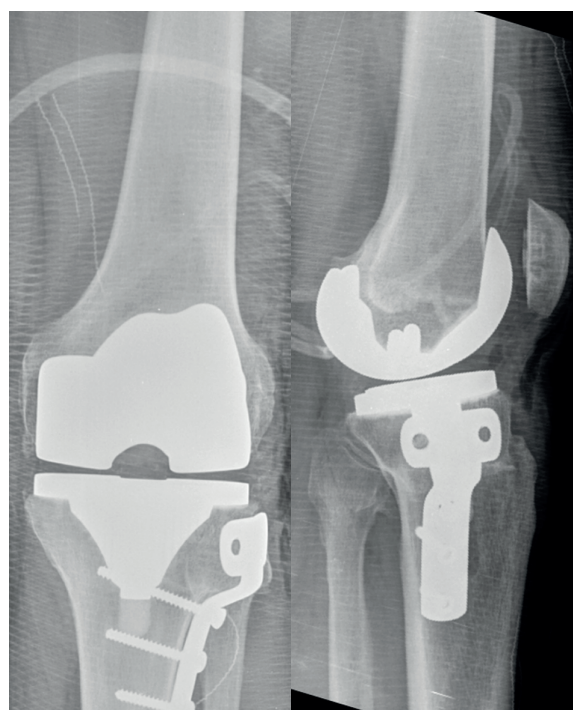


Figure 3. Follow-up x-ray. It is possible to observe prior osteosynthesis material—without the proximal screws, which were removed in the procedure. Proper alignment and placement of prosthesis components

the knee was stable with a 5-110° mobility. He presented pigment deposits in his ear cartilage and sclera.

During TKA, the surgeon removed samples of dark pigmented cartilage, joint capsule, and meniscus, which were sent to the anatomic pathology lab for analysis (Figure 5). The report was identical to that of the prior case.

The patient progressed favorably. 37 months after surgery, his knee and functional scores (KSS) were 94 and 89, respectively. During his last follow-up visit, his evolution was found to be good and the x-ray showed proper alignment with no signs of demarcation (Figure 6).

Discussion

Alkaptonuria was described in the early 20th century by Sir Archibald Garrod and was the first disease reported to follow Mendelian inheritance patterns (3,4).

Before the development of arthropathy (during the third-fourth decade of life) alkaptonuria is usually a silent condition - although it can be suspected in some children due to presence of small dark stains in their diapers or underwear (3,4,7).

The spine is affected in 50% of cases. In general, it begins as lumbar disc disease, but it may extend to all spinal cord segments. Hips and sacroiliac joints are affected in 35% of cases, shoulders in 43%, and knees in 64%. (5,8).

Tendons, especially the Achilles' and patellar tendons, tend to become thicker and a rupture might occur even with mild trauma (5,7). In addition to this, HGA deposits in nose and ear cartilage, ligaments, the sclera of the eye, skin, cardiac valves, epithelial cells of renal tubules, pancreas, CNS, arteries, etc. (4,8-12).

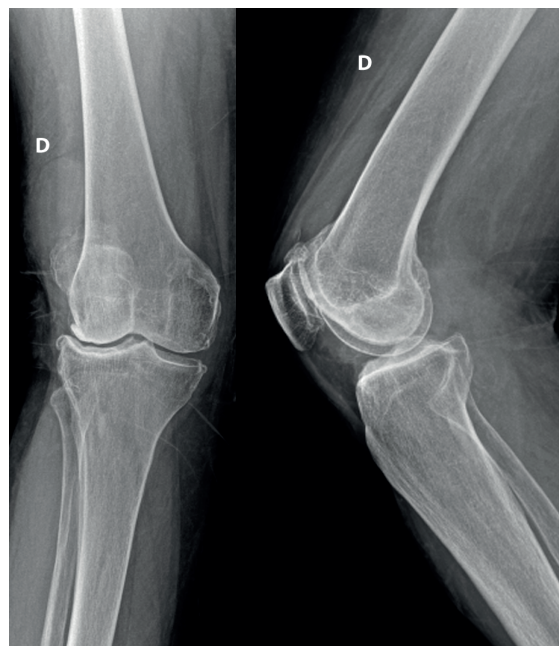


Figure 4. Preoperative radiograph taken in a single-leg weight bearing position showing right arthrosis genu valgum.

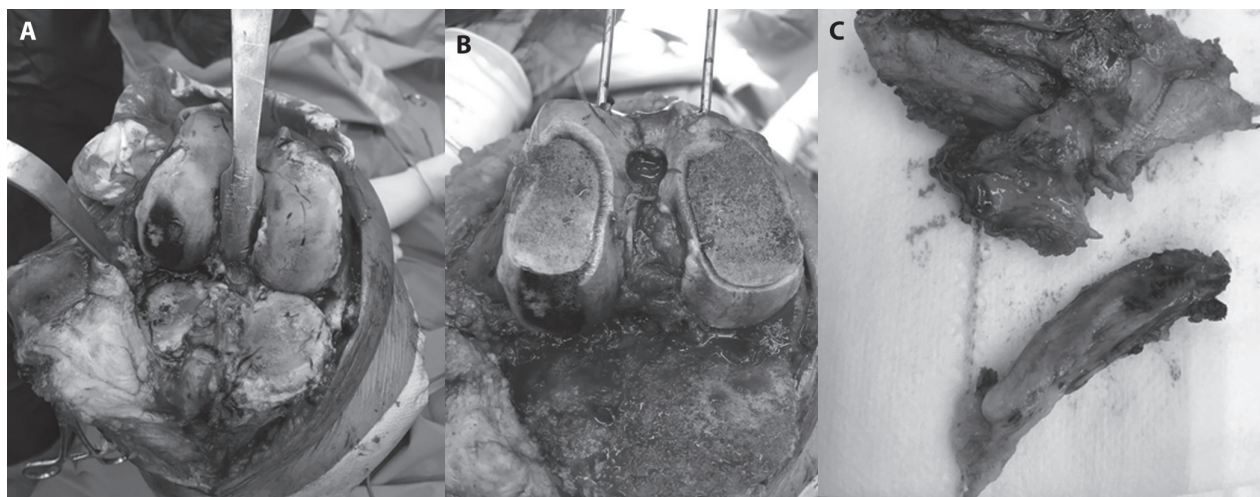


Figure 5. Intraoperative images. A-B: cartilage lesion and black color of cartilage tissue. Figure C: dark blue color of meniscus and joint capsule.



Figure 6. 3.7-year follow-up x-ray. Proper alignment and placement of prosthesis components with no signs of demarcation.

Even though this condition can be diagnosed through a urine test, in general, diagnosis is confirmed after joint surgery (5,8,9).

At present, there is no proven therapy or prophylactic treatment for alkaptonuria. Treatment is aimed at minimizing the effects of arthropathy. Available therapeutic options include non-steroidal anti-inflammatories, chondroitin sulphate, and hyaluronic acid or surgical procedures like arthroscopic debridement and arthroplasty (1,5,9-11).

With regard to prosthetic treatment for the knee, to the best of our knowledge, there are no series with a significant number of patients, just case reports or reviews on the subject (1,5, 8,13).

Karaoglu et al. reported a case of a 55-year old patient with knee osteoarthritis who underwent TKA with excellent results. Ochronosis was diagnosed intraoperatively (1). Couto et al. also published a case of TKA that progressed favorably after a 3-year follow-up (14). Spencer et al. reported 3 patients who underwent

11 arthroplasties (both in upper and lower extremities) due to degenerative ochronotic arthropathy with favorable results after a 12-year follow-up (15).

Recently, Rajkumar et al. (16) analyzed the functional and radiological outcomes of 16 patients who underwent 27 arthroplasties (15 Total Hip Arthroplasties and 12 TKAs). Both procedures resulted in a significant improvement in their functional scores and, in the case of TKA patients, there was no evidence of implant loosening at the end of follow-up.

In a systematic literature review, Lee et al. included 19 case reports published between 2000 and 2016 with 19 patients and 26 TKAs. They reported good results for all cases and no major complications. They also analyzed the types of prostheses used (non-cemented, cemented and with preservation of the posterior cruciate ligament). Like other authors, they concluded that, since ochronosis is an inflammatory condition that can reduce bone quality, cemented TKA using a posterior-stabilized prosthesis should be the prosthetic treatment of choice for this disease—as for patients with Rheumatoid Arthritis (17,18).

As for the surgical approach, unlike procedures for knee idiopathic osteoarthritis, the patella must be carefully mobilized to avoid injuring the knee extensor mechanism because patients might have thicker and stiffer tendons (19). This thickening was observed in one of the two cases presented in this report.

Just like with rheumatoid arthritis, the literature recommends patella replacement, because HGA deposits accumulated in cartilage as well as in patellar and quadriceps tendons could cause chemical irritation and inflammation (19,20).

Finally, it should be noted that these patients may present significant synovitis, which might cause bleeding—and result in longer surgeries—and/or make cementing of prosthetic components more difficult. For this reason, the use of a hemostatic tourniquet is recommended in TKA to minimize bleeding and achieve high-quality cementing (19).

In conclusion, as the underlying pathology is rare, diagnosis usually occurs after surgery (i.e. when surgeons observe the dark color of cartilage). Although information is scarce, TKA seems to be the treatment of choice for end-stage disease because it relieves pain and restores function.

Conflict of interest: Each author declares that she or he has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

References

1. Karaoglu S, Karaaslan F, Mermerkaya MU. Long-term result of arthroplasty in the treatment of a case of ochronotic arthropathy. *Acta Orthop Traumatol Turc* 2016;50:584–6.
2. Millucci L, Giorgetti G, Viti C, Ghezzi L, Gambassi S, Braconi D. Chondroptosis in alkaptonuric cartilage. *J Cell Physiol* 2015;230:1148–57.
3. Millucci L, Bernardini G, Spreafico A, Orlandini M, Braconi D, Laschi M. Histological and ultrastructural characterization of alkaptonuric tissues. *Calcif Tissue Int* 2017;101:50–6.
4. Li N, Tian W, Yuan Q, He D. Cervical spondylotic myelopathy due to the ochronotic arthropathy of the cervical spine. *J Korean Neurosurg Soc* 2016;59(1):65–68.
5. Gil JA, Wawrzynski J, Waryasz GR. Orthopedic manifestations of ochronosis: pathophysiology, presentation, diagnosis, and management. *Am J Med* 2016;129(5):536.e1–6.
6. Ewald FC. The knee society total knee arthroplasty roentgenographic evaluation and scoring system. *Clin Orthop Relat Res* 1989;248:9–12.
7. Harun M, Hayrettin Y, Serhat M, Cuneyt M, Fırat F, Ufuk O. A rare cause of arthropathy: an ochronotic patient with black joints. *Int J Surg Case Rep* 2014;5:554–7.
8. Drakoulakis E, Varvitsiotis D, Psarea G, Feroussis J. Ochronotic arthropathy: diagnosis and management - a critical review. *Am J Orthop* 2012;41:80–3.
9. Keller JM, Macaulay W, Nercessian OA, Jaffe IA. New developments in ochronosis: review of the literature. *Rheumatol Int*. 2005;25:81–85.
10. Raaijmakers M, Steenbrugge F, Dierckx C. Ochronosis, arthroscopy of a black knee: a case report and review of the literature. *Knee Surg Sports Traumatol Arthrosc*. 2008;16:182–184.
11. Laskar FH, Sargison KD. Ochronotic arthropathy. A review with four case reports. *J Bone Joint Surg*. 1970;52:653–666.
12. Damarla N, Linga P, Goyal M, Tadisina SR, Reddy GS, Bommisetti H. Alkaptonuria: a case report. *Indian J Ophthalmol* 2017;65:518–21.
13. Acar MA, Erkokak OF, Aydin BK, Altan E, Senaran H, Elmadag NM. Pacientes con cadera negra y rodilla negra debido a artropatía ocrónica: reporte de caso y revisión de la literatura. *Oman Med J*. 2013; 28(6): 448–9.
14. Couto A, Rodrigues A, Oliveira P, Seara M. Ochronotic arthropathy - a rare clinical case. *Oxf Med Case Reports* 2018;9:302–305.
15. Spencer JM, Gibbons CL, Sharp RJ, Carr AJ, Athanasou NA. Arthroplasty for ochronotic arthritis: no failure of 11 replacements in three patients followed for 6–12 years. *Acta Orthop Scand*. 2004;75:355–358.
16. Rajkumar N, Soundarajan D, Dhanasekaraja P, Rajasekaran S. Clinical and radiological outcomes of total joint arthroplasty in patients with ochronotic arthropathy. *Eur J Orthop Surg Traumatol* 2020;30(5):923–929.
17. Wu Chean Lee, Tong Leng Tan, Ying Ho Chan. Total Knee Arthroplasty in Ochronosis Arthropathy: A case Report and Systematic Review. *Case Reports Orthopedics*. 2019;2019:1–8.
18. Rodriguez JA, Saddler S, Edelman S, Ranawar CS. Long-term results of total knee arthroplasty in class 3 and 4 rheumatoid arthritis. *J Arthroplasty* 1996;11(2):141–145.
19. Ulucay C, Ozler T, Altintas F, Inan M, Onur A, et al. Arthroplasty in ochronosis “tips and pearls in surgery”: case series. *J Arthritis*. 2013;3;1–3.
20. Kajino A, Yoshino S, Kohda M, Nagashima S. Comparison of the results of bilateral total knee arthroplasty with and without patellar replacement for rheumatoid arthritis. A follow-up note. *J Bone Joint Surg. Am* 1997;79(4):570–574.

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