



Case report

Total knee replacement for ochronotic arthritis: A rare case report

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ABSTRACT

Introduction and importance: Total knee replacement (TKR) is commonly performed for managing advanced osteoarthritis. There are several causative factors of osteoarthritis, from degenerative processes associated with age to rare genetic disorders correlated with a rare course of disease and remained undetected even until adulthood. Herein, we present a case of ochronotic arthritis characterized by black discoloration of the articular cartilage, meniscus, and soft tissue surrounding the right knee, which was detected during TKR, in a patient with alkaptonuria. This is a rare case and managing the patient require conscientious approach.

Case presentation: For the past four years, a 64-year-old man had been experiencing chronic right knee pain. During admission, the patient was limping and unable to bear weight on the affected knee. The right knee was swollen, with limited range of motion and audible crepitation during flexion. Radiography revealed narrowing of the joint space and osteophytes on the articular surface. Further investigation showed that the patient was previously diagnosed with alkaptonuria and was scheduled for TKR. Intraoperatively, we found that the articular cartilage, meniscal surface, and soft tissue surrounding the knee had black discoloration. Thus, additional debridement of soft tissues was required.

Clinical discussion: Alkaptonuria may increase the risk of osteoarthritis in the knee joint. Ochronosis correlated with alkaptonuria. Diagnosis can be conducted with physical examination, synovial fluid exam and complete urinalysis to avoid misdiagnose of this disease.

Conclusion: In our study, TKR for ochronotic arthritis had good outcomes, with a knee score of 95 and a function score of 90. The patient received routine treatment for alkaptonuria at the Urology Department.

1. Introduction and importance

Alkaptonuria is a rare autosomal recessive metabolic disorder caused by a deficiency in homogentisic acid oxidase, resulting in the accumulation of homogentisic acid in collagenous structures [1,2]. This causes the classic clinical triad of homogentisic aciduria (blackening of the urine after standing when oxidized or alkalinized); eumelanin-like pigmentation of the skin, sclera, cartilages, and other organs; and degenerative ochronotic arthropathies commonly appearing in the fourth decade of life [3]. Articular cartilage may experience mild discoloration due to aging. However, in some cases such as ochronotic arthritis, pathological tissue pigmentation can occur. Matsumoto et al. reported black discoloration in the knee articular cartilage due to deposition of hemosiderin and lipofuscin caused by recurrent

hemarthrosis [1,2]. In this case report, we present a case of ochronotic arthritis managed by TKR. The surgery was performed in a teaching hospital and also a government-owned tertiary care center.

This case report was written with SCARE 2020 criteria [12].

2. Case presentation

A 64-year-old-man with a chief complaint of chronic pain in the right knee for approximately 4 years ago presented to the emergency room. The pain gradually worsened over 1 year. Moreover, low back pain was observed approximately 10 years back. At the time of presentation, the patient was limping, and the pain was severe when standing on the right leg. He was not able to stand for long periods of time, and the pain worsened when climbing stairs and walking at longer distances. The

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pain subsided when sitting. Moreover, the patient complained of dark colored urine approximately 8 years back. However, there was no history of kidney disease, bladder trauma, diabetes, and hypertension before admission. Approximately 8 years back, he was diagnosed with alkaptonuria. Nevertheless, no previous family history of other diseases were observed.

Based on the physical examination of the right knee, redness and swelling were noted. The right knee was tender to touch. Crepitation was noted during active movement of the knee. The range of movement of the right knee was slightly limited, with 110° flexion. The patient was subjected to additional examinations. His complete blood count, renal and liver function, and blood coagulation marker levels were normal. Urinalysis revealed a dark brown urine color; other urine parameters were within normal ranges. Moreover, no blood cells or leukocytes were observed in the urine. Further radiography of the right knee was performed, and osteophytes on the meniscal surface of the right knee were discovered (Fig. 1).

Based on the history taking and physical and other supporting examinations, the patient was diagnosed with osteoarthritis of the right knee (grade IV based on the Kellgren–Lawrence classification system). The patient then underwent total knee arthroplasty. During surgery, black discoloration of the right knee was incidentally discovered. Additional debridement of soft tissues surrounding the knee was performed. The surgery was uneventful, and the patient was treated with antibiotics and analgesics (Fig. 2).

Post operative radiograph was taken one day after the surgery (Fig. 3). The patient performed isometric exercise on the first day and isokinetic exercise on the third day after surgery. Thereafter, he began walking with a walker. On the fifth day after surgery, the patient again performed isokinetic exercise, and he began walking with a walker. The patient was discharged a week after the surgery, and he could walk without using an assistive device. The patient was scheduled for routine postoperative rehabilitation to improve muscle and joint function. After 1 year, the patient could walk pain free without using mobility aids, with a knee range of motion of 0°–110°. Outcome assessment using the Knee Society Score (KSS) revealed a satisfactory outcome, with a knee score of 95 and a function score of 90. The patient received routine treatment for alkaptonuria at the Urology Department.

3. Clinical discussion

Alkaptonuria is an autosomal recessive metabolic disease affecting 1 in 250,000–1 million people worldwide [2,4]. Homogentisic acid oxidase enzyme deficiency leads to the accumulation of homogentisic acid

polymers [2]. This condition results in darkening of the urine, pigmentation of connective tissues, and pathologic changes in other internal organs [2,5]. Patients with this disease are commonly asymptomatic, and complaints are observed after the fourth decade of life [6]. There is no previous data about the prevalence of this condition due to undiagnosis [3]. Herein, we report a patient diagnosed with the disease prior to surgery. However, he had no significant history of symptoms other than low back pain due to spondylolisthesis. Ochronotic arthropathy was diagnosed incidentally during TKR, with initial indication for osteoarthritis management, which was similar to a previous case by Harun et al.

Alkaptonuria is systematic disease caused by homogentisic acid accumulation [4]. In patients with alkaptonuria, the initial characteristics of ochronosis in the musculoskeletal system are likely spinal arthropathy and tendinopathy. Eventually, osteopenia and osteoporosis are observed. However, they may not always occur in this sequence [4]. Arthropathy of the spine and peripheral joint is associated with pain, which causes limited range of motion, swelling, and stiffness. The accumulation of homogentisic acid on the cartilage leads to fragility and loss of cartilage elasticity, thereby causing fragmentation and formation of loose bodies. The cartilage fragments may adhere to the synovial membrane and may cause fibrosis or chondromatosis. Osteophytes or subchondral cysts may cause clinical signs including pain and limited range of motion [7]. Deposition of homogentisic acid and its correlation with ochronotic arthropathy are yet to be explained, and further research must be performed.

In our case, right knee pain was most likely caused by alkaptonuria-related arthropathy. After detecting the discolored meniscal surface on the right knee during TKR, several hypotheses were considered. After alkalization, his urine turned brown. The qualitative evaluation of organic acids in the urine is required to confirm alkaptonuria [4,7]. The urine of patients with alkaptonuria will turn black if sodium hydroxide is added and green for a brief period of time if ferric chloride is added. The amount of homogentisic acid in the urine can be determined via gas liquid chromatography, thin-layer chromatography, and enzymatic spectrophotometry [3,7]. In our case, a confirmatory diagnosis was not obtained via chromatography or urine alkalization.

The accumulation of homogentisic acid in the circulation causes increasing oxidative products. Patients with alkaptonuria experience accumulation of homogentisic acid and acid deposit in collagen-rich connective tissues in some cases [5,8]. Nag et al. reported a 30-year-old woman with prior undiagnosed alkaptonuria characterized by right knee pain and occasional locking of the knee joint. The patient was treated with knee debridement using arthroscopy [9]. However, joint symptoms in individuals with ochronotic arthropathy commonly appear at the age of 40–50 years [6]. The proportion of male patients with this condition was higher than that of female patients. The synovial and intervertebral joints may be involved. Other than the non-specific clinical manifestation of joint pain, limited range of motion, and stiffness, oxidized homogentisic acid on the deeper layers of the articular cartilage may manifest as a dark discoloration in the surface cartilage [3,5,7]. Excessive accumulation and subsequent oxidation of homogentisic acid lead to inflammatory and degenerative processes, resulting in decreased structural integrity. One hypothesis is that ochronotic pigment acts as a chemical irritant causing inflammation and joint degeneration [5,10]. The oxidative stress of polymerizing homogentisic acid can lead to protein oxidation, lipid peroxidation, thiol depletion, and tissue inflammation [11].

Due to manifestations in the musculoskeletal system, the morbidity and mortality of patients with ochronotic arthropathy may be dependent on clinical manifestation and location [2]. Medical treatment to prevent this disease is limited, as in some cases correlated with arthropathy. However, improved preoperative preparation during surgery may prevent intraoperative complications [7]. In our case, ochronosis of the joints might be observed in the right knee (visual confirmation of blackening of meniscus in the right knee, which was incidentally

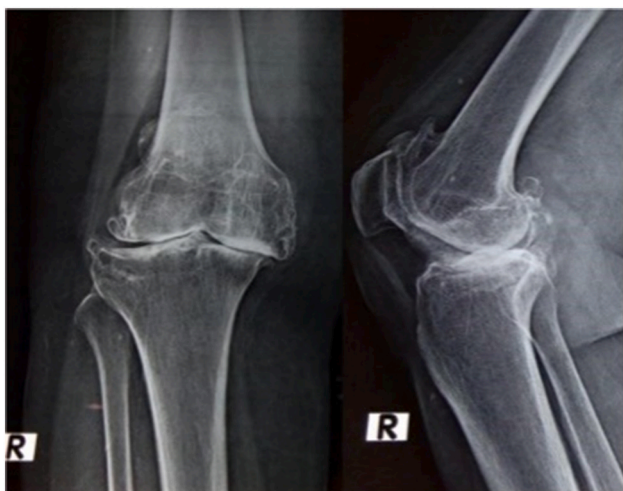


Fig. 1. Lateral and anterior view of both knees in (preoperative) conventional radiography.

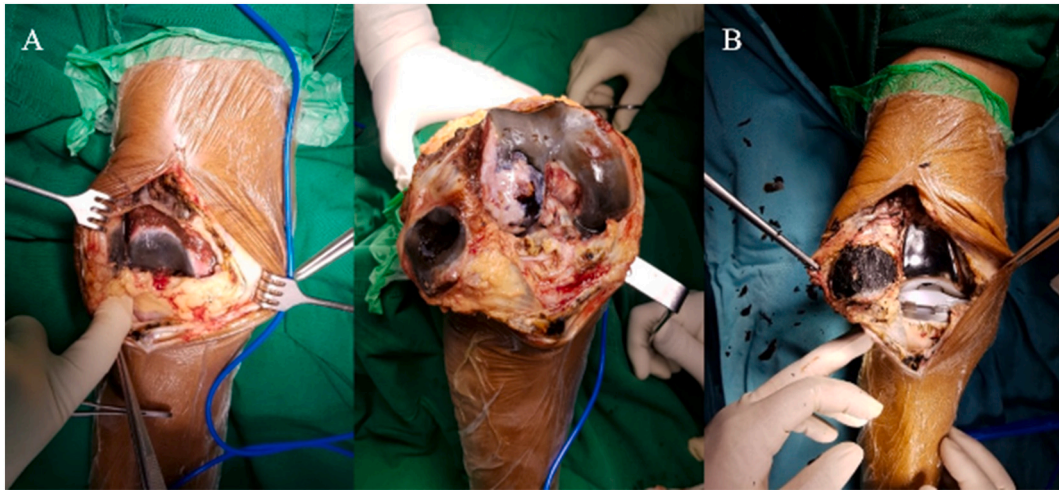


Fig. 2. A. During the TKR surgery, a dark staining of the right cartilage and meniscus was discovered by coincidence. B. Post TKR surgery, debridement was also done to remove all of the devitalized tissue.

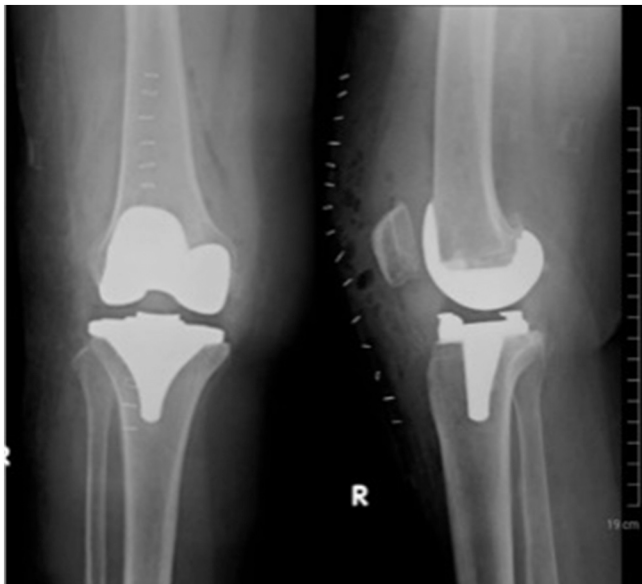


Fig. 3. Anterior and lateral radiographs of the knee after TKR surgery showed a good correction of the alignment.

identified during TKR). The patient had good prognosis based on better physical activity and painless knee.

4. Conclusion

Alkaptonuria is a rare condition caused by toxicity caused by the lack of homogentisate 1,2 dioxygenase activity, which results in the accumulation of homogentisic acid. The buildup of the material in the musculoskeletal system can start as a degenerative process, resulting in joint arthrosis or pain, and reduced range of motion in the affected joint. Ochronotic arthropathy is occasionally identified during surgery. In such circumstances, perioperative management may necessitate thorough inquiry into the disorder's associated comorbidities. In our study, TKR for ochronotic arthritis had good outcomes, with a knee score of 95 and a function score of 90. The patient received routine treatment for alkaptonuria at the Urology Department.

Additional information

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

The work has been reported in line with SCARE 2020 criteria [12].

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Ethical approval

This study was approved under the local committee of ethics in Hasan Sadikin Hospital Bandung. The ethics approval form is available on request.

Consent

This study already obtained permission from the patient for publication. The consent form from the patient is available on request.

Registration of research studies

1. Name of the registry: www.researchregistry.com
2. Unique identifying number or registration ID: researchregistry7978
3. Hyperlink to your specific registration (must be publicly accessible and will be checked): <https://www.researchregistry.com/register-now#user-researchregistry/registerresearchdetails/629cdbcbce7422001e1e1a61/>

Guarantor

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CRediT authorship contribution statement

1. Dicky Mulyadi, M.D.: Surgeon of this cases, conceptualization the idea, writing the paper
2. R. M. Satrio Nugroho Magetsari, M.D.: Assistant Surgeon of the patient, writing, supervision
3. Nucki Nursjamsi Hidajat, M.D.: Supervision, Conceptualization

4. Atar Trengginas Asmarantaka, M.D.: Assistant, Editor (helping the first and second author to revise format)
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Declaration of competing interest

There is no any conflict of interest from all author related on process of writing this paper.

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