

Periprosthetic Femur Fracture on Alkaptonuric Patient: a Rare Case Report in Indonesia

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ABSTRACT

A 74-year-old male with alkaptonuria (AKU) was admitted to the emergency department with left distal femur pain and Rorabeck type 2 periprosthetic femur fracture following total knee arthroplasty (TKA). AKU is an autosomal recessive disorder characterized by homogentisic acid buildup in connective tissues and joints, leading to ochronosis and arthritis. Multiple joint replacements are common in AKU patients, and periprosthetic fractures may occur due to osteopenia. Rorabeck type 2 fracture is treated with intramedullary nailing or locked plating. The patient underwent internal fixation with locking plate and bone grafts using minimally invasive plate osteosynthesis (MIPO) procedure, resulting in good fracture healing. The case highlights the importance of considering AKU as a differential diagnosis in arthritis patients and managing periprosthetic fractures with care in AKU patients.

KEY WORDS: alkaptonuria, periprosthetic fracture, total knee arthroplasty, ochronosis, MIPO.

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INTRODUCTION

Alkaptonuria (AKU), also referred to as black bone disease, is a rare genetic disorder with a global estimated prevalence ranging from 1:200,000 to 1:1,000,000.⁽¹⁾ This autosomal recessive condition is caused by a deficiency of homogentisic acid dioxygenase (HGD), the third enzyme involved in tyrosine degradation.⁽²⁾ HGD deficiency leads to the accumulation of homogentisic acid (HGA), which can either be excreted in the urine or oxidize and polymerize to form an ochronotic pigment that deposits in the connective tissues (ochronosis).⁽²⁾ The ochronotic pigment can also deposit within the joints, causing ochronotic arthropathy that affects the axial and appendicular skeleton and eventually leads to arthritis of the spine and larger joints.⁽³⁾

The pathogenesis of AKU is the polymerization of deposited HGA, which discolors and weakens connective tissue, resulting in brittle tissue that is easily disrupted and resulting in chronic inflammation, degeneration, and osteoarthritis.⁽²⁾ While patients with AKU are typically asymptomatic, arthropathy usually develops in the fourth decade of life due to a decline in renal function with age.⁽⁴⁾

Most patients with AKU require multiple joint replacements in adulthood, with one survey indicating that the average age for joint surgery is between 50-55 years, and approximately half of all AKU patients undergo joint surgery before the age of 55.⁽⁵⁾ Total knee arthroplasty (TKA) is a common procedure for AKU patients⁽⁵⁾, but they are also at an increased risk of periprosthetic fractures due to osteopenia.⁽⁶⁾ Several conservative and surgical methods are currently applied to treat periprosthetic distal femur fractures following TKA.⁽⁶⁾

Rorabeck type II is the most common type of periprosthetic distal femur fracture in patients after TKA.⁽⁷⁾ Locked plating and intramedullary nailing are the most common treatments for Rorabeck type II.⁽⁷⁾ However, the rate of complications was lower for locked plating than for intramedullary nailing.⁽⁷⁾

CASE REPORT

A 74-year-old Caucasian male was transported by ambulance to our hospital's emergency room with complaints of pain and swelling in the left distal thigh to the knee area. He jumped from the edge of the swimming pool at a meter depth pool.

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The patient revealed that he was diagnosed with AKU at 20 in Melbourne, Australia. Since he was five, he noticed AKU signs beginning with discolored rashes on the backs of his hands and ears. Later, he was diagnosed with AKU after a urinalysis revealed a change in his urine color due to the presence of HGA deposits. His younger brother was also diagnosed with AKU at around the same age as him.

When the patient was 23 years old, he broke his right lower arm because of a ski accident and required a cast as the treatment. In his early 30s, he was already experiencing back, hip, and knee pain. Then, the patient was diagnosed with early arthritis during his 30s. He has had an active lifestyle as a professional football athlete from he was 20 years old to 32 years old. The primary cause he retired early from being a professional athlete was because he had severe arthritis. At age 40, he broke his cervical spine (C1) and received conservative treatment. The patient has not received any

medical management for his AKU. In his 50-60s, prior to joint replacement surgeries, he took some analgesics for arthritis pain relief. Due to his arthritis, he underwent total hip replacement on his left side ten years ago, total knee replacement on his left side eight years ago, total hip replacement on his right side six years ago, and total knee replacement on his right side four years ago. He also underwent heart valve surgery four years prior in Melbourne due to cardiac ochronosis.

On the physical examination, we discovered hyperpigmentation on both his backhands, sclera, auricular cartilage, and nails. We also discovered that his urine had a dark brown hue. To confirm the fracture, we performed anteroposterior pelvic and femur X-rays. Consequently, the patient's x-ray revealed a left periprosthetic femur fracture, specifically a Rorabeck type 2 fracture.

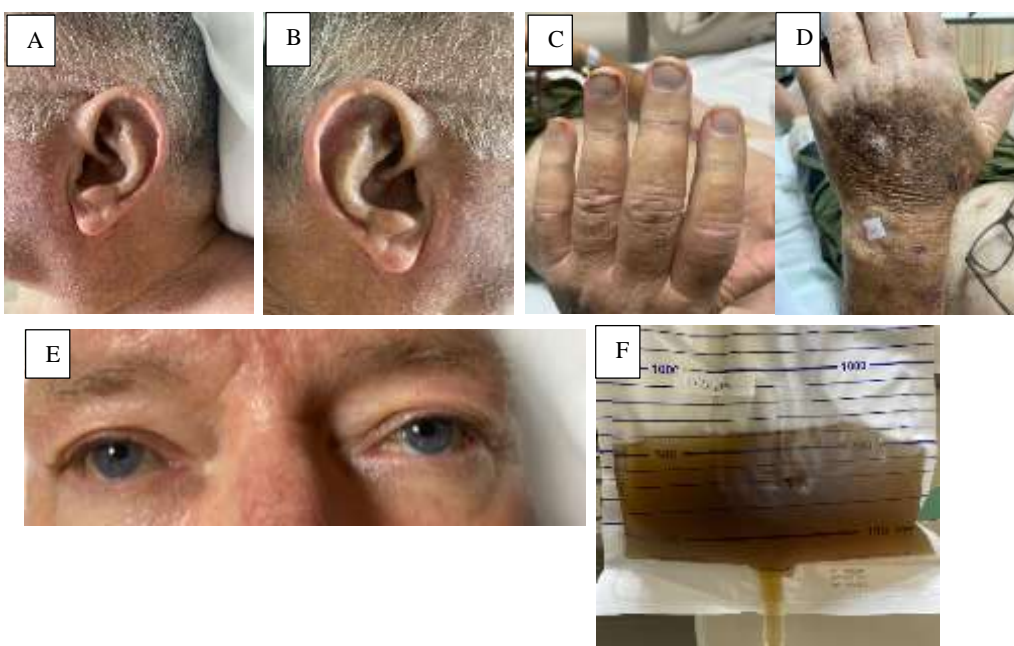


Figure 1. Hyperpigmentation of patient
(a) Left ear, (b) Right ear, (c) Nails, (d) Back of left hand, (e) Sclera, (f) Urine

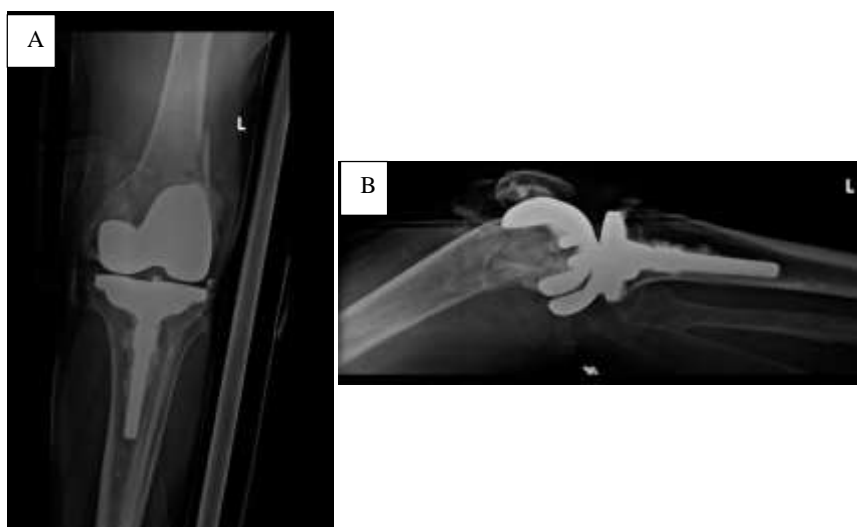


Figure 2. Left knee preoperative radiograph
(a) Anteroposterior view, (b) Lateral view



Figure 3. Left knee postoperative radiograph
(a) Anteroposterior view, (b) Lateral view



Figure 4. Left knee 4 weeks postoperative radiograph
(a) Anteroposterior view, (b) Lateral view



Figure 5. Left knee 6 weeks postoperative radiograph
(a) Anteroposterior view, (b) Lateral view

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We decided to get the patient an internal fixation on the left femur by using a locking plate through the lateral cortex with bone grafts using minimally invasive plate osteosynthesis (MIPO) technique. Intraoperatively, we found the bone was extremely brittle, and a slight black discoloration was seen on the patient's femur. Patient was discharged 3 days after the surgery. Six weeks postoperatively, the patient could engage in full-weight bearing mobilization.

DISCUSSION

AKU incidence is uncommon in Indonesia. Although AKU has been documented in people of all races and ethnicities, its incidence and prevalence may vary by community. The incidence of AKU is rare, and Slovakia had a significantly higher AKU incidence in 1978 than the rest of the world, approximately 1 in 19,000 individuals.⁽⁸⁾ AKU also found more prevalent in Dominican Republic and Jordan.⁽⁹⁾

Caucasians are more likely than Asians to have AKU, likely caused by HGD gene mutations and the founder effect. Individuals of European ancestry are more likely to carry a defective HGD mutation (p.G152fs) than those of African or Asian descent.⁽¹⁰⁾ And the majority of Europeans belong to the Caucasian ethnicity.⁽¹⁰⁾ This mutation causes a gene defect that prevents the formation of homogentisate 1,2-dioxygenase, an enzyme associated with an accumulation of HGA that causes AKU.⁽¹⁰⁾

AKU is an autosomal recessive disorder, meaning that two copies of the defective gene must be passed down to the child from each parent for the condition to manifest.⁽²⁾ Thus, the founder effect, which establishes a new smaller population, is likely to have less genetic diversity than the original population because the new population carries only a subset of the genetic variation found in the original population.⁽¹¹⁾ AKU may become more prevalent in the new community due to the decreased genetic diversity.

Our patient has experienced AKU symptoms from an early age, but was not diagnosed until he was 20 years old. HGA is excreted through the urine and can accumulate in cartilage, connective tissue, and bones, causing tissue damage and degeneration, known as ochronosis.⁽¹²⁾ In accordance with some theories, our patient's symptoms manifest in the third decade as a result of HGA accumulation.⁽¹³⁾ HGA is excreted through the urine and can accumulate in cartilage, connective tissue, and bones, causing tissue damage and degeneration, known as ochronosis.⁽¹²⁾ HGA deposits in connective tissue, such as the sclera, skin, and cartilage.⁽¹²⁾ This condition matches the symptoms shown in the patient. We found some brown-blue pigmentation on the back of his hands, both the sclera and auricle. The patient's urine also showed some brownish pigmentation. The patient also underwent heart valve replacement in 2019 due to some findings on cardiovascular ochronosis, as HGA also may deposit in heart valve and causing a thickening and stiffening of the valve.⁽¹⁴⁾ Then, we confirmed the diagnosis of AKU

that manifested in the bone in the patient by seeing the black discoloration of the patient's left femoral cartilage during surgery.

Ochronotic arthropathy, a musculoskeletal manifestation of AKU, predominantly affects weight-bearing joints, leading to joint pain, stiffness, and restricted range of motion. This condition matches with patient's condition as when he reached his 30s, the patient began to experience severe arthritis symptoms. Patient complained about joint pain and limited range of motion predominantly in his large joints (hip and knee) and spine that causing him to stop his dream as professional athlete. Failure to recognize the signs and symptoms of ochronotic arthropathy can result in irreversible joint damage and early joint replacement surgery, despite approximately half of AKU patients undergoing joint surgery before age 55. Treatment options for ochronotic arthropathy include NSAIDs, physical therapy, and joint replacement surgery. During the years of diagnosis, he only consumed analgesics to reduce joint pain, which were taken occasionally. Monitoring joint function and symptoms is crucial to prevent irreversible joint damage and enhance the quality of life for patients with AKU. The patient has had a good run of the current treatment options for ochronotic arthropathy; he is also having regular check-ups regarding his condition. Because of this, the patient underwent joint replacement surgeries in his 60s, above the average age for joint replacement surgeries. Deterioration of the patient's condition can be exacerbated by not consuming anti-inflammatory nutrients such as vitamin C, selenium, and zinc.⁽¹³⁾ Consumption of high-dose of Vitamin C (1 gram/day) can reduce the AKU severity score index (AKUSI) because Vitamin C prevents the accumulation and deposition of HGA.⁽¹³⁾ Even though most AKU patients have an average life expectancy⁽⁵⁾, most elderly with AKU will experience a lower quality of life due to their inability to engage in certain activities.

Alkaptonuria is linked to a reduction in bone mineral density (BMD), which raises the chance of fragility fractures.⁽¹⁵⁾ In this case, the patient dove into the 1-meter-deep pool and fell on his left foot. Even with mild trauma, age and HGA deposition affected the bone's density, which made the bone brittle and caused the periprosthetic distal femur fracture. The mineralization process may be hampered during the formation of the new and uncalcified osteoid matrix that is exposed to the ochronotic pigment.⁽¹⁵⁾

Aliberti et al. published a paper in 2003 where they outlined the biochemical markers of bone and presented evidence that the deposition of HGA in the bone matrix leads to increased bone resorption. This, combined with regular bone formation, results in an overall increase in bone loss.⁽¹⁶⁾ Also, HGA deposits may cause collagen crosslink impairment and matrix microdamage, which could weaken the bone even more.⁽¹⁶⁾ Patient also had multiple history of

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bone fracture due to minimal trauma. During surgery, we were also found that the bone was very brittle.

Patient underwent internal fixation using locking plate and screws, and using minimally invasive plate osteosynthesis procedure (MIPO) with bone grafts, enabling the patient for early mobilization. Rorabeck type II is the most common type of periprosthetic distal femur fracture after TKA.⁽⁷⁾ Locked plating and intramedullary nailing are the most popular procedures for treating these kinds of fractures, and their respective healing rates are 87 and 84%. The rate of complications with locked plating, however, was lower than with intramedullary nailing.⁽⁷⁾ In the article written by Hassan et al.⁽¹⁷⁾, there are 96% of union rate out of 26 patients with periprosthetic fractures after total knee arthroplasty who were treated using locking plates. MIPO was used to minimize trauma and reduce recovery time. Hoffmann et al.⁽¹⁸⁾ reviewed that out of 111 periprosthetic fractures that occurred around the knee, 91% of them were fully healed. The results indicate that the minimally invasive approach resulted in fewer cases of non-union compared to the open technique, which is highly significant.

Patient was discharged from the hospital 3 days after the surgery. We did intensive non weight bearing physiotherapy for the first 2 weeks, then continue with partial weight bearing mobilization until 4 weeks after the surgery. Then, 6 weeks after surgery, patient was able to fully recover by mobilizing and bearing his full weight using both legs.

CONCLUSION

Our case report presents the management of a 74-year-old male patient with AKU who experienced a periprosthetic distal femur fracture and underwent surgery using MIPO technique and a locking plate with bone grafts for internal fixation. The MIPO technique was chosen due to its potential to reduce trauma and reduce recovery time, which is crucial in AKU patients. AKU is a rare autosomal recessive disorder characterized by the accumulation of HGA, leading to the formation of ochronotic pigment that deposits in connective tissues and joints. People with AKU are at an increased risk of developing osteoarthritis, which necessitates joint replacement surgeries. The patient's fracture was classified as a Rorabeck type 2 fracture, and locked plating is typically the preferred treatment option, with lower complication rates. The patient was discharged three days after surgery and was able to engage in full-weight bearing mobilization six weeks postoperatively. Early diagnosis and regular monitoring of AKU patients are critical in reducing the risk of osteoarthritis and fractures, especially in those who have undergone joint replacement surgeries. Despite its rarity, recognizing the clinical features and treatment options for AKU is critical in avoiding further complications.

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CONFLICT OF INTEREST

There is no conflict of interest.

STATEMENT OF INFORMED CONSENT

The patient included in the study has given informed consent.

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