Case Report

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A shocking intraoperatively diagnosis of ochronotic knee arthropathy: a case report

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Introduction: Alkaptonuria is an autosomal extremely rare recessive metabolic disorder with incidence reported to occur as 1:100 000–1:250 000 live births worldwide. This rare metabolic disorder is characterized by the accumulation of homogentisic acid due to a deficiency in homogentisic acid 1,2 dioxygenase. Homogentisic acid subsequently oxidizes and accumulates in the connective tissue. The knee is the most significant peripheral joint to be affected by the disorder. The authors present the first case of ochronotic arthropathy in Syria.

Case presentation: A 46-year-old male presented with bilateral pain in the knees. the pain was affecting his day-to-day activities, and not responding to conservative management. Anteroposterior standing radiographs demonstrated extensive degenerative disease. Intraoperatively, the diagnosis was done after noticing that the quadriceps tendon and the articular cartilage of the femur, tibia, and patella were blackened during cemented total knee replacement of the knee.

Conclusion: Ochronotic arthropathy should be kept in mind in middle age patients with severe osteoarthritis to not be surprised by the rare alkaptonuria diagnosis if arthroplasty was indicated.

Keywords: Alkaptonuria, arthropathy, knee, ochronosis, osteoarthritis

Introduction

Alkaptonuria is an autosomal recessive metabolic disorder with incidence reported to occur as 1:100 000–1:250 000 live births worldwide[1]. In 1902 Archibald Garrod was the first to describe the autosomal recessive Mendelian inheritance for the disorder which also was the first disorder recognized to follow this type of inheritance in the medical literature[1]. The disorder has a higher incidence in Slovakia and the Dominican Republic[2,3]. This rare metabolic disorder is characterized by the accumulation of homogentisic acid (HA) due to a deficiency in (HA) 1,2 dioxygenase. HA subsequently oxidizes and accumulates in the connective tissue especially with the rich collagen after being converted to melanin-like pigments and affects tendons, ligaments, and joints by leading to degenerative disorder[4].

HIGHLIGHTS

- There is no satisfactory treatment or prophylactic treatment for alkaptonuria.
- Arthroplasty is the definitive treatment for ochronotic arthropathy.
- Difficulty in spinal anaesthesia must be kept into consideration also.

The knee is the most significant peripheral joint to be affected by the disorder followed by the hip, shoulder, and sacroiliac joint[5]. The patients often have no clinical manifestations until the 4th–5th decade when they complain of joint pain or chronic back pain.

The diagnosis of alkaptonuria is performed by a histopathologic examination of affected tissues in addition to the evaluation of the homogentisic acid amount in the urine[6]. Whereas surgical treatment may be indicated in important degenerative arthritis, the treatment of ochronotic arthropathy (OA) is only symptomatic[2,7]. We present in this rare case report a shocking diagnosis of alkaptonuria after seeing a knee OA during knee replacement surgery. the work has been reported in line with the SCARE 2023 criteria[8].

Case presentation

A 46-year-old male presented with bilateral pain in the knees which was more severe in the left knee. The pain started 2 years ago and gradually progressed over the years and was also aggravated by exertion and relieved by rest and analgesics during the initial years. At the time of the presentation, the pain was affecting his day-to-day activities, and not responding to conservative management. Moreover, no cutaneous signs of ochronosis were noticed. On physical examination, there was a neutral

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alignment of both knees. There was no swelling or effusion but on deep palpation, there was medial joint line tenderness. The range of motion of the right knee was 0°–100° and the left knee was 0°–90°. Anteroposterior standing radiographs [Figure 1] were taken which demonstrate extensive degenerative disease in the left knee with medial joint space narrowing, subchondral sclerosis, small marginal osteophytes, and altered shape of the femoral condyles and tibial plateau. in the right knee, there is a mild degenerative disease with joint space narrowing and subchondral sclerosis. Cemented total knee replacement of the left knee and total synovectomy were done, followed by the right knee after 2 years [Figure 2]. Intraoperatively, an anterior midline incision with a medial para-patellar approach was performed [Figure 3]. There was marked blackened synovial hypertrophy. The joint capsule was contracted with a hard consistency. The strength of ligaments and tendons seemed to be normally excluded the patellar tendon and ACL ligament were fragile but not ruptured. The quadriceps tendon and the articular cartilage of the femur, tibia, and patella were blackened. Both of the meniscus were also blackened and stiffed. While taking bone cuts, a black discoloration was marked on the thickened cartilage, while the subchondral bone was fragile and had a normal colour. The standard cementing technique was performed without difficulty. The case was discussed intraoperatively with the Senior Surgeon and the OA diagnosis was the most probable diagnosis. No excessive bleeding was noted and the drain was removed on the 2nd postoperative day when the patient start to move out from the bed. The brother had a history of spontaneous rupture of the Achilles tendon which was revealed by the patient only after surgery when asked again. The diagnosis of ochronosis was confirmed retrospectively in the postoperative period. A careful physical examination revealed black ochronotic pigmentation in the sclera and ear cartilage. Biopsy of the resected specimen was proved to be ochronosis [Figure 4]. Physical therapy was given postoperatively. The knee society score (KSS) was 88 and 92 on the right and left sides, respectively, and the knee function score was recorded to be 90 and 95 on the right and left sides, respectively. The follow-up radiographs showed neutral mechanical alignment and the absence of radiolucent lines, osteolysis, wear or loosening around the components.

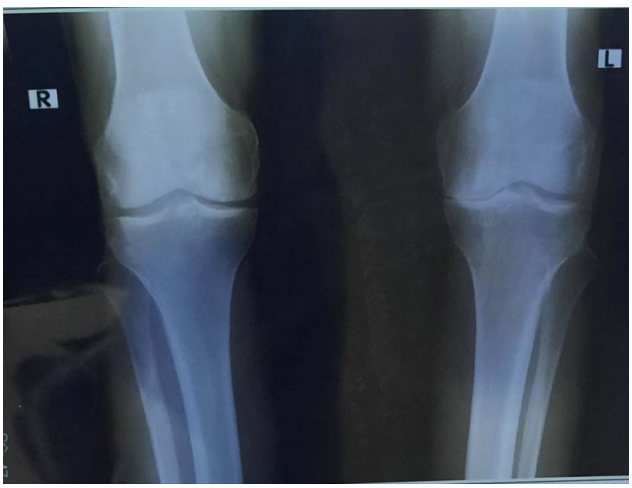

Figure 1. Anteroposterior standing radiographs which demonstrate extensive degenerative disease in the left knee and mild degenerative disease in the right knee.

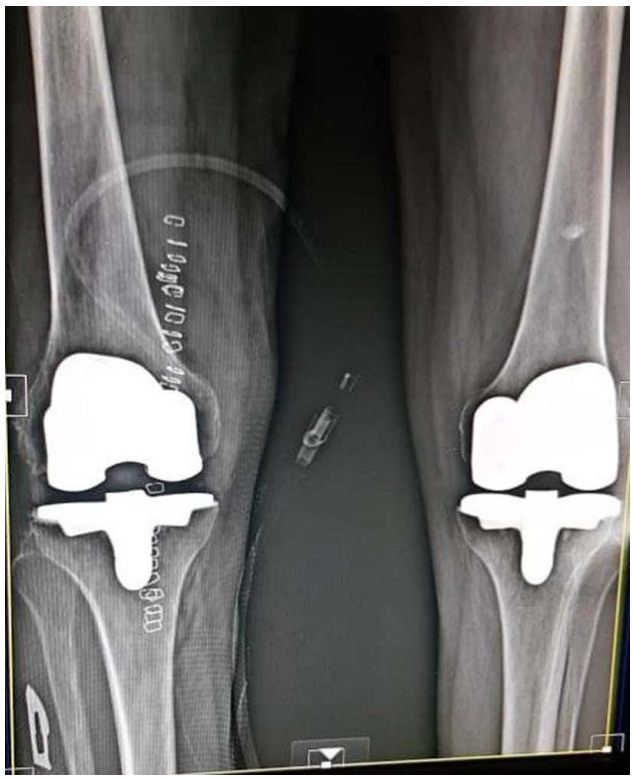

Figure 2. Anteroposterior standing radiographs after cemented total knee replacement.

Discussion

Alkaptonuria is a rare metabolic disease characterized by the accumulation of HA in cartilages causing OA and eventually osteoarthritis. The knee and hip are the most affected sites and the majority of patients remain asymptomatic until the 4-5th decade of life[3]. In 50% of patients, early involvement of the inter-

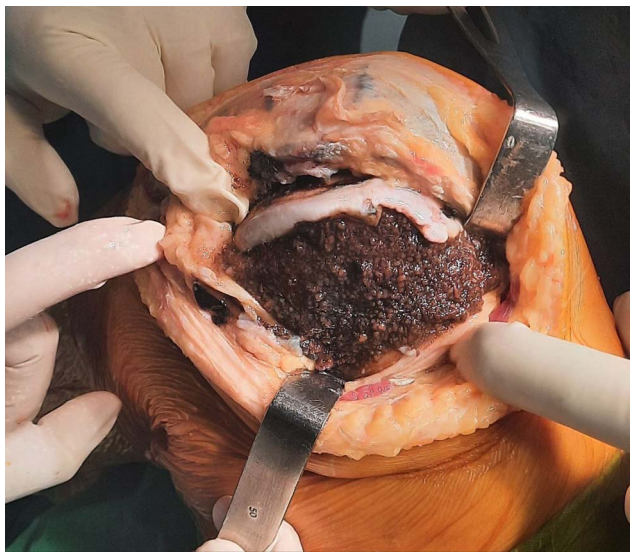

Figure 3. Intraoperatively gross feature of knee shows the blackened suprapatellar bursa.

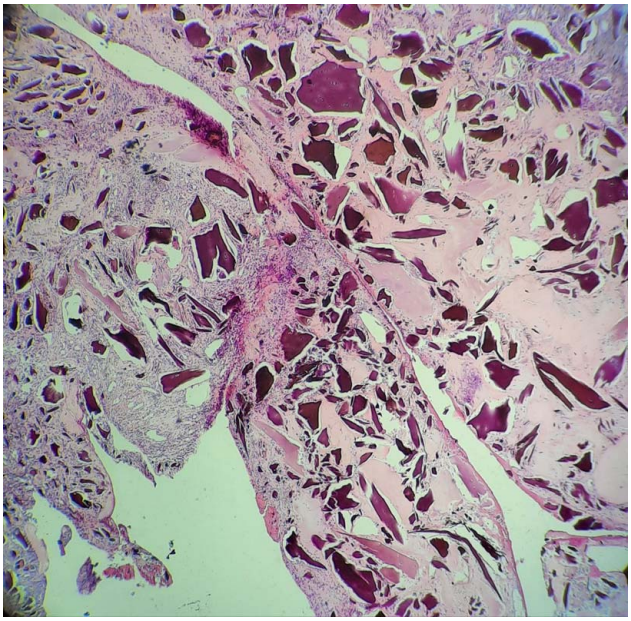

Figure 4. Histological feature of ochronosis.

vertebral discs at the thoracic and lumbar areas is common. Even though noticing dark spots in the diapers in children during their first months of life can be a hallmark of alkaptonuria[1,6,7] The clinical manifestations are more likely to occur in males than females[4]. The dark urine is a consequence of HA oxidization to benzoquinone acetate (BQA) after exposure to air[4]. Additional clinical signs include pigmentation of the sclera and corneal limbus of the eye, the cartilage of the ear[5], and laryngeal cartilage leading to hoarseness of voice. The ochronotic pigment accumulation in tendons makes them thicker and more vulnerable to being ruptured, in addition to muscle tearing due to their severe fragility after any trauma[1,9]. The most apparent locations to see the pigmentation clearly in the skin are the thick areas such as the thenar and hypothenar eminences and the sides of the fingers. However, joints and tympanic membranes have thick connective tissue. Thus, they are also good sites to see pigmentation. Alkaptonuria diagnosis is performed with histopathologic examination of tissue biopsies and measurement of homogentisic acid in the urine but the diagnosis in our case was not proven preoperative and it surprised us during the surgery. There is no satisfactory treatment or prophylactic treatment for alkaptonuria. Despite the treatment being only symptomatic and focused on the effects of OA[1,2], trying to minimize types of foods containing tyrosine and phenylalanine has been revealed to be effective in limiting symptoms of ochronotic arthritis. Due to the mild antioxidant nature of ascorbic acid which helps to retard the process of conversion of HA to the polymeric material that is accumulated, Supplementation with vitamin C is recommended[7,10]. Nitisinone which is an inhibitor of 4-hydroxyphenyl pyruvate dioxygenase could reduce urinary excretion of homogentisic acid. The effectiveness of Nitisinone in treating OA is unknown[11]. Early stages of OA are managed conservatively, but for severely affected hip and knee joints, only replacement can improve the quality of life[12]. After the surgery physical therapy is indicated to conserve muscle flexibility and strength. The osteoporosis mechanism in Alkaptonuria is well explained by a decline in osteoprotegerin and the activation of osteoclasts along with an increase in receptor activator of nuclear factor-kappa B ligand[13]. So, increasing mechanical stress to the subchondral bone with the decreased cartilage elasticity will increase the risk of subchondral fracture as a result of osteoporosis. In contrast to the high morbidity, life expectancy is near normal[8]. Several studies reported good functional results for joint arthroplasty in OA, similar to osteoarthritis patients without ochronosis. Spencer *et al.*[14] in 2009 published a 6–12 year follow-up of 11 replacements in three ochronotic arthritis patients and found no prosthetic failures in 12 year follow-up period. A case report by Patel reported the osteopenic nature of the subchondral bone and the fragile tendency of the patellar tendon during total knee arthroplasty (TKA) for OA of the knee[11]. Further, In our case, we did not notice an increase in blood loss but Patel noticed increased blood loss because of the extensive synovectomy which caused delayed drain removal but without needing to blood transfusion[11].

Conclusion

OA should be kept in mind in middle age patients with severe osteoarthritis to not be surprised by the rare alkaptonuria diagnosis if arthroplasty was indicated. Moreover, investigate other symptoms such as black urine which often be absent which explains the delayed diagnosis. Arthroplasty is the definitive treatment for OA while other symptoms must be treated symptomatically. Difficulty in spinal anaesthesia must be kept into consideration also.

Ethical approval

Not required for case reports at our hospital. Single case reports are exempt from ethical approval in our institution.

Consent

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

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Author contribution

M.N.S.: contributed to project administration and was the corresponding author. M.S.A.: analyzed and interpreted the patient data, wrote the manuscript. A.A., Y.A. and S.A.K.: data collection, revision. M.M.A.: supervisor, orthopaedic surgeon, supervised and managed the patient. V.R.: supervisor, pathologist, performed the histological examination. All authors read and approved the final manuscript.

Conflicts of interest disclosure

The authors declare that they have no conflicts of interest.

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None.

Guarantor

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