A Hidden Pigment, A Damaged Joint: The Ochronotic Knee - A Case Report

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Abstract

Summary: Ochronotic arthropathy (alkaptonuria) is a rare hereditary disorder that poses a diagnostic dilemma. It is usually diagnosed perioperatively or by conducting investigations based on perioperative findings in the postoperative period, followed by retrospective analysis. This report discusses a case of a 37-year-old male who presented with bilateral knee pain. Radiological studies were indicative of grade III osteoarthritis but perioperatively black pigmentation was noted. Backtracking revealed it to be a case of alkaptonuria. This typically presents as early-onset osteoarthritis involving major joints like the knee, hip, shoulder, and spine. Orthopedic surgeons should have an inquisitive mind and keep this as their differential diagnosis while dealing with young patients with similar symptoms to avoid surprises during surgery. Our study aims to increase understanding of this condition for effective management and improving functional outcomes.

Keywords: Alkaptonuria, Ochronosis, Osteoarthritis, Rare Disease.

Introduction

Ochronotic arthropathy is a rare condition that occurs in patients of alkaptonuria with a reported incidence of 1:100 000–1:250 000 live births worldwide. It follows an autosomal recessive mode of inheritance.[1] This disorder has a higher prevalence in regions of Slovakia and the Dominican Republic.[2,3] Pathophysiology of this rare metabolic disorder lies in the accumulation of homogentisic acid (HA) due to deficiency of the enzyme homogentisic oxidase[1,2]. HA oxidizes, converts to melanin-like pigments, and then deposits in connective tissue rich in collagen, like ligaments, tendons, and joints, inducing early degenerative changes.[4]
The knee joint is the most commonly affected large joint, whereas the hip and sacroiliac joints are the next most affected joints. Usually, stiffness and pain of the knees and hip become evident in the 3rd–4th decade of life. Other manifestations occur due to HA accumulation in the sclera, skin, heart valves, nose and ears cartilage, renal tubule epithelial cells, pancreas, central nervous system, endocrine organs, respiratory organs, and arteries.[6] Currently, nitisinone is the only approved medical treatment available to reduce HA levels, and symptomatic treatment can be done with local heat, physiotherapy, and analgesics. Some possible surgical options for the affected joint are synovectomy, arthroscopic debridement, fusion, or arthroplasty.[7-9] This report describes a case of ochronotic knee that presented with OA at a young age.

Case Presentation

A 37-year-old male patient who was a driver by profession presented to our outpatient department. He had bilateral knee pain, which started 1.5 years back and gradually progressed over time. Pain was more on the left side and was recurrent in nature, as it only temporarily responded to oral analgesics and anti-inflammatory drugs, which he took from various small clinics he visited previously. He had multiple joint fluid routine examinations performed as well, which were normal. His uric acid levels used to fluctuate between 6.8-7.5 mg/dl, and he was put on anti-hyperuricemia agents (febuxostat, allopurinol) by some practitioners, which used to decrease his uric acid levels, but pain did not improve. There was no positive family history. On examining the patient, there were no cutaneous signs of ochronosis (**Error! Reference source not found.**). Although both knees were neutral aligned, mild effusion on the left side was noted (for which R/E was performed by some clinicians). Upon deep palpation, he experienced tenderness along the medial joint line of the left side. The range of motion on the right side was 0-100°, and on the left was 0-90°. Standing radiographs were taken with orthogonal views. These showed advanced degenerative disease, especially on the left. We see joint space narrowing, loose bodies, and marginal osteophytes. (**Error! Reference source not found.**). Since the patient was non-affording, there was a delay in intervention as multiple previous consultations advised him to undergo arthroscopic evaluation, but he refused due to financial limitations. We decided to proceed with total knee replacement after pre-anesthesia assessment, but as he could not afford it considering the needs of the patient, we planned to do open arthrotomy with synovial biopsy, thorough joint lavage, and removal of loose bodies, and proceed according to intraoperative findings. We proceeded by anterior midline incision with a medial para-patellar approach. We noticed multiple black patches over the articular surface of the joint along with arthritic changes. There were 3-4 loose bodies in the joint as well (Figure 3). Peri-operatively, it was discussed as well to proceed with knee arthroplasty, but due to financial concerns of the patient, we were limited to taking a synovial biopsy, removal of loose bodies, and joint lavage. Keeping in mind the operative findings patient was investigated again, starting from history. His mother revealed that his diaper used to get dark stains, which were very difficult to remove. Similarly, one of his sisters had chronic back pain. Careful clinical examination showed one of his ears to have a slight blackish tinge. Urine stored for 6-8 hours changed its color to black (Figure 4). Urinary HA levels were done, biopsy sample sent came negative for malignancy and synovial chondromatosis. Retrospective diagnosis of ochronotic arthropathy was established. The biopsy sample sent came back negative for malignancy and synovial chondromatosis. Post-operatively, knee physiotherapy was started immediately on the second postoperative day. His pain improved

Contributions:
SR OI - Conception, Design
OI - Acquisition, Analysis, Interpretation
OI TF - Drafting
SR - Critical Review

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postoperatively. On his first visit, 2 weeks after surgery, he was satisfied with the results as his pain improved, and he was able to carry out his daily activities with ease. He was advised regarding the probable need for arthroplasty in the future. At his last follow-up, six months post-surgery, the patient remained pain-free and had resumed his occupation comfortably; however, he was subsequently lost to follow-up.

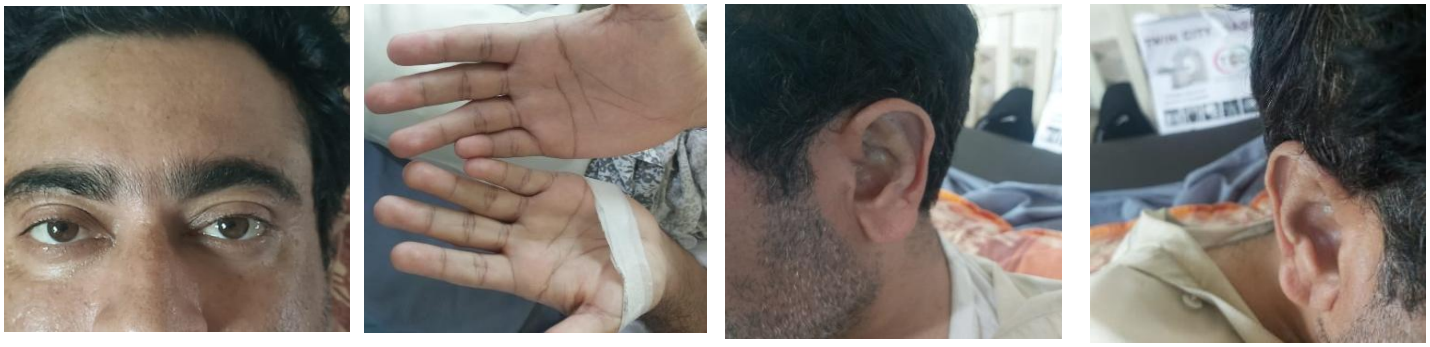

Figure 1: **Cutaneous Findings**

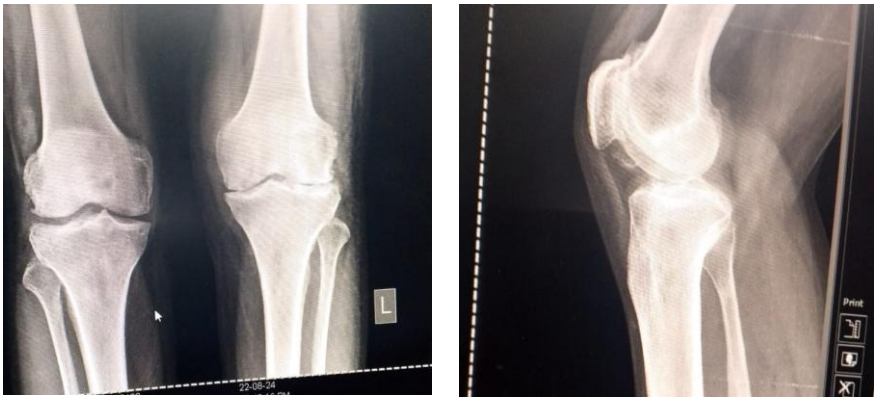

Figure 2: **Knee Radiographs showing advanced osteoarthritis**

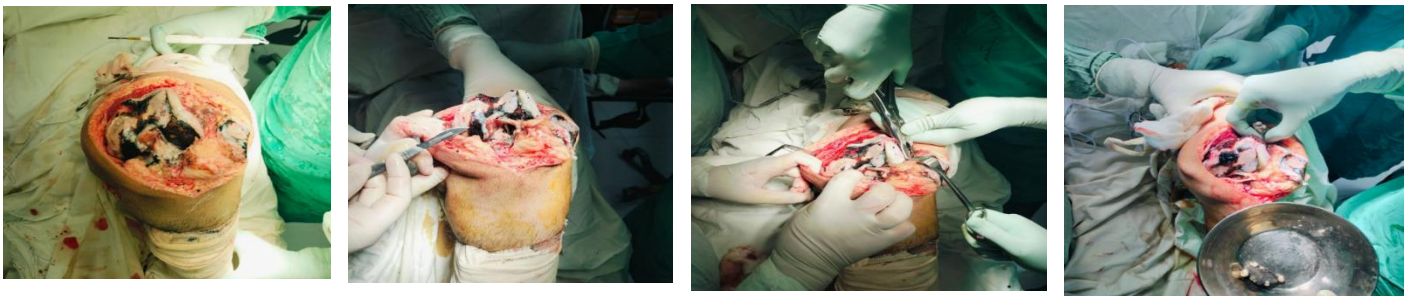

Figure 3: **Perioperative findings showing multiple black pigment patches over the articular surface and loose bodies in the joint**

Discussion

Alkaptonuria is a rare disease that occurs due to the accumulation of homogentisic acid in the cartilages and joints. In the fourth to fifth decade of life, joint pain was reported mostly in the hips and knees.[4] In about half the cases, the involvement of intervertebral discs at the thoracolumbar region is early on. Noticing dark spots in the diapers of babies during the first months of life can be a sign of alkaptonuria.[10,11] Clinical manifestations occur mostly in males. Exposure to the air of the HA causes its oxidation to benzoquinone acetate (BQA), which darkens the urine. Additional clinical symptoms are found, including discoloration of the sclera and cornea[5]. You can easily see skin pigmentation on the ulnar or radial surface of your hand. The ulnar side of your fingers also show additonal skin pigmentation. Nitisinone is the first FDA-approved treatment for alkaptonuria. It works by blocking the enzyme 4-hydroxyphenylpyruvate dioxygenase and can lower urinary homogentisic acid levels by up to 97%.[12,13] Recent studies have shown that patients treated with nitisinone experience significant improvements in pain, energy levels, and physical functioning.[14,15] In the early stages of osteoarthritis (OA), conservative therapy is effective. Another study reveals that health workers find it effective if started early with the use of individual follow-up to prevent side effects.[3] However, in severe cases affecting the hip or knee joints, arthroplasty is the only treatment that can improve quality of life.[16] Multiple studies have indicated that arthroplasty is a suitable option for this condition. It reduces pain and enhances patient mobility. A literature review by Singh, Liu, Awad, and Couto confirms that this treatment is both safe and effective for cases of ochronotic arthropathy.[17-19] However, a study by Narvekar et al.,[20] suggests that arthroscopic intervention can be useful for diagnosis and to avoid unexpected findings during surgery.

So, orthopaedic surgeons should be vigilant for unusual signs in early-onset osteoarthritis to avoid surprises during surgery related to darkened cartilage.

Figure 4: **Change in urine color**

Conclusion

Ochronotic arthropathy, although it is a rare condition, should always be considered in patients with early-onset osteoarthritis, particularly in younger patients. Awareness about this disorder helps to prevent perioperative surprises and helps in early diagnosis and proper management. Arthroscopy could be a useful diagnostic tool in doubtful cases, while arthroplasty remains an effective treatment option for this condition. Combining a high index of suspicion with thorough clinical history and careful observation of cutaneous findings could aid in early diagnosis. Early recognition of this uncommon entity and vigilance could improve functional outcomes.

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