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Case Report

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Alkaptonuria and Ochronotic Arthropathy: The Path to Pain-Free Mobility

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ABSTRACT

This article discusses a case of ochronotic arthropathy, a manifestation of alkaptonuria. Alkaptonuria is characterized by the accumulation of homogentisic acid [HGA] in tissues, leading to a distinctive blue-black pigmentation and early joint degeneration. A 68-year-old female patient, with a history of alkaptonuria, presented with progressive hip pain and was eventually treated with an elective total hip replacement. Due to vertebral calcifications, the operation was performed under general anesthesia. Pre- and post-operative care was guided by the patient's comorbidities and potential complications related to alkaptonuria, including potential cardiac and respiratory issues. Following surgery, the patient exhibited significant improvements in hip joint functionality. The paper also discusses the challenges in diagnosing alkaptonuria, the absence of definitive treatment, and the potential of dietary restrictions and symptomatic treatments. Moreover, it addresses surgical considerations for ochronotic arthropathy and emphasizes the role of regular calcium and vitamin D intake in maintaining bone quality. The success of the hip replacement surgery in this case suggests a potential intervention for managing ochronotic arthropathy in alkaptonuria patients.

Introduction

Alkaptonuria, a defect in the metabolism of homogentisic acid [HGA], is caused by autosomal recessive mutations of the homogentisic acid oxidase gene [1]. Ochronosis is the connective tissue manifestation of alkaptonuria. HGA builds up, polymerizes, and eventually deposits as a blue-black pigment in the skin, cartilage, and collagenous tissues [2]. Ochronotic arthropathy is the result of this process, in which the discs degenerate more quickly than the shoulder, knee, and hip joints. The non-articular manifestation of alkaptonuria is pigmentation of the ear lobes, sclera, nose, axillae, and perineum. The color of the urine gradually changes as the first sign of alkaptonuria. Patients and their families might ignore darkening of the urine and discoloration of the external ear and sclerae [3, 4, 5].

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As a result, the diagnosis of alkaptonuria might not be made until ochronosis appears. Ochronotic arthritis typically affects weight-bearing joints. The most commonly impacted joints are the knees, but hip and shoulder joints can also be affected [6, 7]. Ochronotic arthritis symptoms can resemble those of ankylosing spondylitis and rheumatoid arthritis. Small joints are typically not spared in ochronotic arthritis. Osteophytic changes are present, but not as obviously as in osteoarthritis [3].

Case Report

A 68-year-old female patient, a known case of alkaptonuria (from 3 years ago), was referred to us with a history of progressive pain in her right hip joint for the last 3 years and low backache from the last 10 years. Her brother had died because of a cardiac problem due to alkaptonuria. She used calcium, vitamin D, vitamin C, and nitisinone as routine. Her Body Mass Index was 30.5. Upon examination, the patient had painful gross restriction of right hip movements with 5 cm shortening. The opposite hip had THA surgery 2 years ago in another institution, and knees were clinically normal. Spine movements were painful and restricted. The serial x-rays of the pelvis, which were taken earlier, showed progressive destruction of the femoral head (Figure 1). The x-ray of the lumbosacral spine showed intervertebral disk calcification with narrowing of the disk spaces and gross osteoporosis with degenerative changes (Figure 2). Patients with Ochronosis may have cardiac problems, such as coronary calcification, valvular stenosis, and conduction block. Moreover, these patients might have respiratory problems, such as airways involvement, dyspnea, and diminished vital capacity. Therefore, a consultation with a cardiologist and a pulmonologist was made before the surgery. The Charlson weighted Comorbidity Index [CCI] was 0, and the American Society of Anesthesiologists [ASA] score was 2.

The patient was planned for an elective total hip replacement under epidural anesthesia. However, the anesthesiologist could not gain access to the cerebrospinal fluid due to fusion and calcifications of the vertebrae. Therefore, the operation was performed under general anesthesia. The direct anterior approach was the preferred approach used by the senior author. During the exposure, the tissues around the joint were found to be dark in color with gross involvement of all the joint capsule and the synovium. The femoral head was completely black (Figure 3)]. We removed the joint capsule completely during hip joint replacement surgery to prevent local recurrence. The Corail Pinnacle poly on the metal implant with a head size of 32mm, a modular neck of +1.5, a stem size of 11, and an acetabulum cup

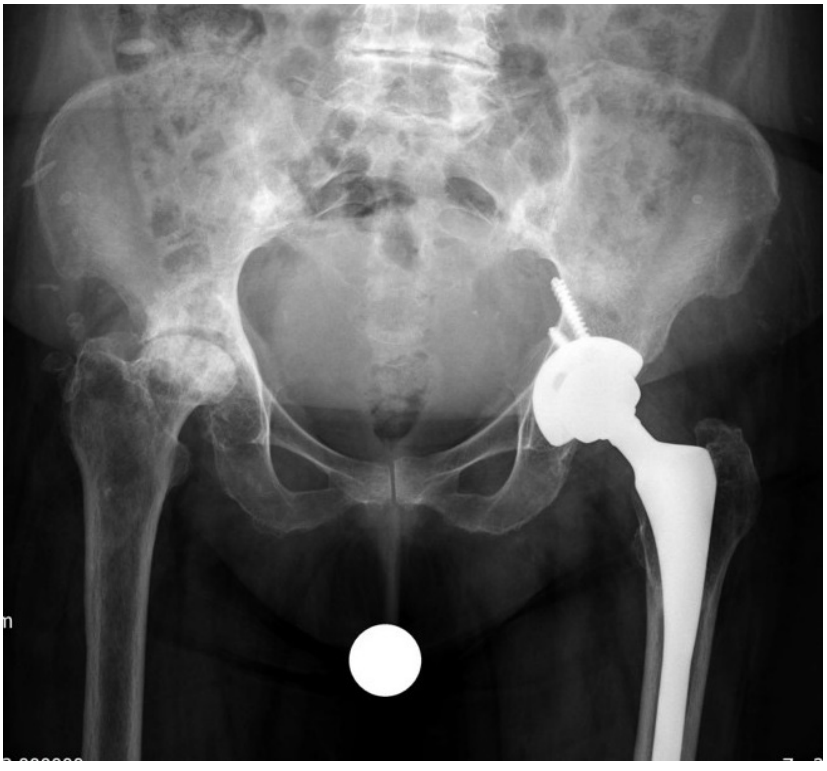

Fig. 1. Preoperative radiographic image of the pelvis, demonstrating progressive destruction of the femoral head associated with alkaptonuria.

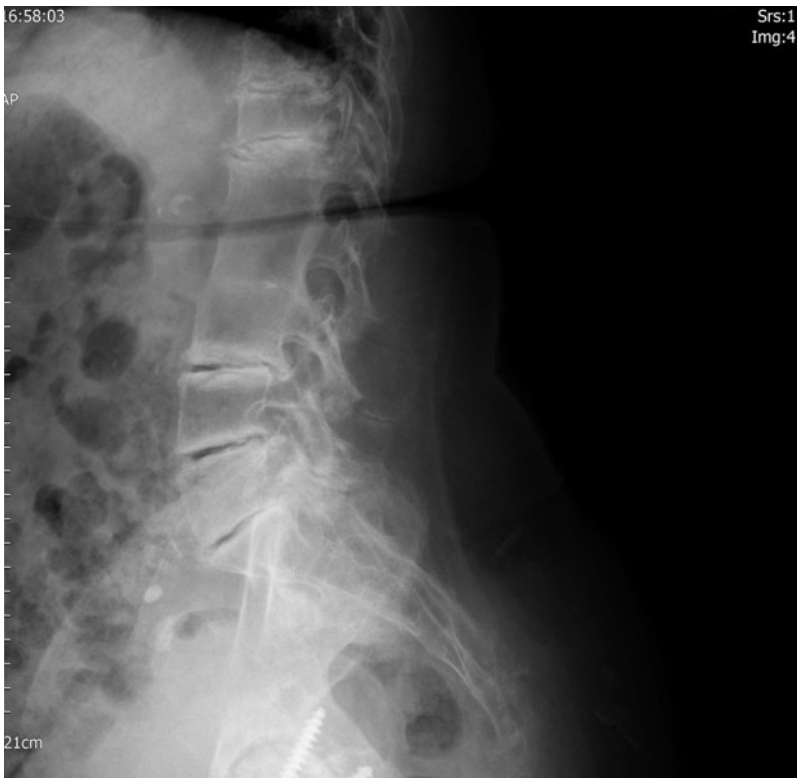

Fig. 2. Preoperative X-ray of the lumbosacral spine revealing intervertebral disk calcification, narrowing of disk spaces, and significant osteoporosis with degenerative changes.

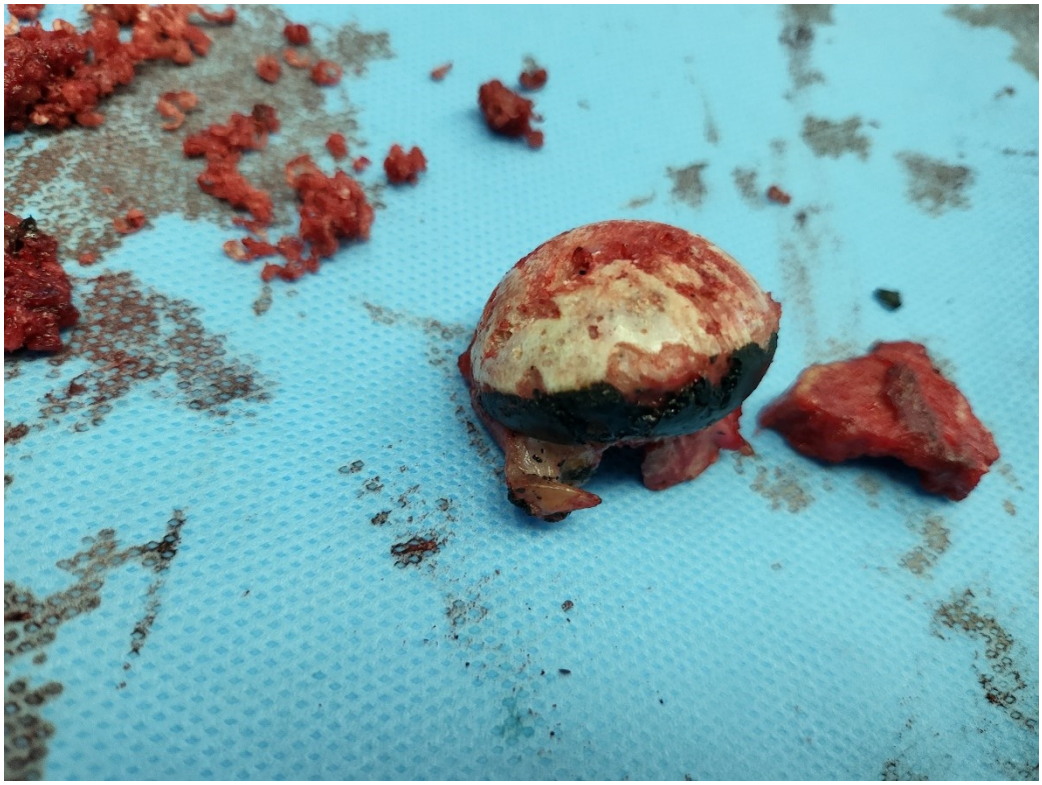

Fig. 3. Intraoperative image showing the gross involvement of joint capsule and synovium, along with the completely blackened femoral head, typical of ochronosis.

size of 50 was implanted for the right hip. During the operation, the acetabular bone was not found to be osteoporotic. The duration of the operation was 85 minutes, and the estimated blood loss was 530 cc. Our patient regained a functional range of movements by the end of 2 months. The patient was independently ambulant and pain-free with no complaints at the 6-month follow-up. At the 6-month follow-up, the mean HHS improved significantly, from 34 preoperatively to 92.

Discussion

Patients with alkaptonuria are typically asymptomatic, and arthropathy develops in the third or fourth decade with a rapid onset of pain that limits everyday activities [8]. The progressive age-related reduction in the renal ability to eliminate homogentisic acid results in a pathological relationship with signs and symptoms of homogentisic acid accumulation [9]. There is currently no definitive treatment for alkaptonuric ochronosis. The only treatment option for alkaptonuria consequences is symptomatic treatment, including pain management, physiotherapy, chiropractic care, and home exercise instruction. Primary repair is an effective treatment for tendon ruptures caused by ochronosis [10]. A high dose of vitamin C lowers urine benzoquinone acetic acid, but has no effect on HGA excretion; furthermore, no convincing trials have demonstrated the clinical efficacy of vitamin C treatment [11]. Nitisinone, a powerful inhibitor of 4-hydroxyphenylpyruvate dioxygenase, greatly lowers homogentisic acid synthesis and urinary excretion; nevertheless, its efficacy in treating ochronosis is uncertain [12]. The mainstay of ochronosis treatment is the restriction of phenylalanine and tyrosine in the diet. However, long-term adherence to the diet restriction is the negative aspect of this treatment plan [11]. Many of these patients may be undiagnosed at the time they are referred for orthopedic care. Therefore, Ochronosis should be suspected in individuals with multiple joint degenerative arthritis, particularly knee and hip joints and spinal column. Black pigmentations in the sclera and pinnae can be used as diagnostic indicators [13].

During surgery, we did not observe an increase in blood loss. However, Pachore et al. noticed an increase in blood loss, which they believed could be a result of en bloc synovectomy of the hypertrophied synovium [14]. In the literature, Cebesoy et al. advocated the removal of the joint capsule in its entirety [15]. However, Pachore et al. hypothesized that thorough capsular excision could enhance the rate of postoperative dislocation [14]. Therefore, the capsule was maintained. In their follow-up, no complications were discovered. The bone quality surrounding the hip joint impacts the prosthesis's stability. Regardless of the patient's age, Cebesoy et al. discovered poor bone quality in the acetabulum and proximal femur during reaming and broaching [15]. In our situation, we did not observe diminished bone quality. One probable explanation is that our patient regularly ingested calcium and vitamin D.

Some studies reported cases of successful staged bilateral total hip arthroplasty in individuals with ochronotic arthropathy. In all investigations, however, the time between procedures was shorter than one year [3, 16-18]. In patients with ochronotic arthropathy, there is no evidence that staged bilateral THA is superior to THA performed bilaterally in a single sitting.

Initially, cautious treatment was administered to our patient. After 3 years of extremely limited success with conservative treatment, a bilateral hip replacement with a 2-year gap was scheduled and performed on our patient. After bilateral hip replacement, our patient was symptom-free, had no activity restrictions, and was independently mobile.

No case of prosthesis failure following arthroplasty in patients with ochronosis has ever been recorded[3, 13-22]. On radiographs, we did not find instability, early loosening, subsidence, or protrusion issues in the present investigation. On the acetabular socket, no radiolucent lines, migration, or change in alignment were noted. These indicators point to a stable implant with bone ingrowth.

Ethical Considerations

Compliance with ethical guidelines

There were no ethical considerations to be considered in this article.

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The patient provided written informed consent for the use of her data in this case report, ensuring adherence to ethical standards and patient confidentiality.

Conflict of Interests

The authors declare that they have no conflict of interest.

Acknowledgement

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References

[1] Keller JM, Macaulay W, Nercessian OA, Jaffe IA. New developments in ochronosis: review of the literature. Rheumatol Int. 2005;25(2):81-5. https://doi.org/10.1007/s00296-004-0498-1

[2] Spencer JM, Gibbons CL, Sharp RJ, Carr AJ, Athanasou NA. Arthroplasty for ochronotic arthritis: no failure of 11 replacements in 3 patients followed 6-12 years. Acta Orthop Scand. 2004;75(3):355-8. https://doi.org/10.1080/00016470410001321

[3] Acar MA, Erkocak OF, Aydin BK, Altan E, Senaran H, Elmadağ NM. Patients with black hip and black knee due to ochronotic arthropathy: case report and review of literature. Oman Med J. 2013;28(6):448-9. https://doi.org/10.5001/omj.2013.124

[4] Phornphutkul C, Introne WJ, Perry MB, Bernardini I, Murphey MD, Fitzpatrick DL, et al. Natural history of alkaptonuria. N Engl J Med. 2002;347(26):2111-21. https://doi.org/10.1056/NEJMoa021736

[5] Mistry JB, Bukhari M, Taylor AM. Alkaptonuria. Rare Dis. 2013;1(1):e27475. https://doi.org/10.4161/rdis.27475

[6] Ranganath LR, Jarvis JC, Gallagher JA. Recent advances in management of alkaptonuria (invited review; best practice article). J Clin Pathol. 2013;66(5):367-73. https://doi.org/10.1136/jclinpath-2012-200877

[7] Perry MB, Suwannarat P, Furst GP, Gahl WA, Gerber LH. Musculoskeletal findings and disability in alkaptonuria. J Rheumatol. 2006;33(11):2280-5.

[8] Ranganath LR, Cox TF. Natural history of alkaptonuria revisited: analyses based on scoring systems. J Inherit Metab Dis. 2011;34(6):1141-51. https://doi.org/10.1007/s10545-011-9374-9

[9] Fernández-Cañón JM, Granadino B, De Bernabé DBV, Renedo M, Fernández-Ruiz E, Peñalva MA, et al. The molecular basis of alkaptonuria. Nat Genet. 1996;14(1):19-24. https://doi.org/10.1038/ng0996-19

[10] Manoj Kumar RV, Rajasekaran S. Spontaneous tendon ruptures in alkaptonuria. J Bone Joint Surg Br. 2003;85(6):883-6. https://doi.org/10.1302/0301-620X.85B6.13662

[11] Morava E, Kosztolányi G, Engelke UFH, Wevers RA. Reversal of clinical symptoms and radiographic abnormalities with protein restriction and ascorbic acid in alkaptonuria. Ann Clin Biochem. 2003;40(1):108-11.https://doi.org/10.1258/000456303321016268

[12] Suwannarat P, O'Brien K, Perry MB, Sebring N, Bernardini I, Kaiser-Kupfer MI, et al. Use of nitisinone in patients with alkaptonuria. Metab Clin Exp. 2005;54(6):719-28. https://doi.org/10.1016/j.metabol.2004.12.017

[13] Mazoochy H, Razi M. Knee and Hip Joint Replacement Surgery in a Patient with Ochronotic Arthropathy: Surgical Tips. Arch Bone Jt Surg. 2018;6(6):577-81.

[14] Pachore JA, Shah VI, Upadhyay S, Shah K, Sheth A, Kshatriya A. Primary hip arthroplasty for the treatment of alkaptonuric hip arthritis: 3- to 24-year follow-ups. Arthroplasty Today. 2019;1(1):8. https://doi.org/10.1186/s42836-019-0010-8

[15] Cebesoy O, Isik M, Subasi M, Kaya A, Bilgin F, Kaya O. Total hip replacement for an ochronotic patient: A technical trick. Am J Case Rep. 2014;15:27-30. https://doi.org/10.12659/AJCR.890008

[16] Araki K, Sudo A, Hasegawa M, Uchida A. Devastating ochronotic arthropathy with successful bilateral hip and knee arthroplasties. J Clin Rheumatol. 2009;15(3):138-40. https://doi.org/10.1097/RHU.0b013e31819e6b41

[17] Siavashi B, Zehtab MJ, Pendar E. Ochronosis of hip joint; a case report. Cases J. 2009;2:9337. https://doi.org/10.1186/1757-1626-2-9337

[18] Fernando OSF, Supreeth N, David GD, Borja L, Ricardo L. An Unusual Case of Bilateral Ochronotic Arthropathy of the Hip Successfully Managed by a Staged Bilateral Total Hip Replacement- An Insight with a Surgical Note. J Orthop Case Rep. 2018;8(4):11-4.

[19] Kitahara Y, Kaku N, Tagomori H, Tsumura H. Alkaptonuria with rapidly destructive arthropathy of the hip: A case report and literature review. Acta Orthop Traumatol Turc. 2021;55(6):563-8. https://doi.org/10.5152/j.aott.2021.21205

[20] Meschini C, Cauteruccio M, Oliva MS, Sircana G, Vitiello R, Rovere G, et al. Hip and knee replacement in patients with ochronosis: Clinical experience and literature review. Orthop Rev (Pavia). 2020;12(Suppl 1):8687. https://doi.org/10.4081/or.2020.8687

[21] Al-Ajlouni JM, Alisi MS, Yasin MS, Khanfar A, Hamdan M, Halaweh AA, et al. Long-Term Outcomes of the Knee and Hip Arthroplasties in Patients with Alkaptonuria. Arthroplast Today. 2020;6(4):689-93. https://doi.org/10.1016/j.artd.2020.07.037

[22] Gowda N, Kumar MJ, Kumar AK. Black hip: a rare case treated by total hip replacement. Ann Saudi Med. 2013;33(4):368-71. https://doi.org/10.5144/0256-4947.2013.368