Int J Clin Exp Med 2015;8(5):8185-8189
www.ijcem.com /ISSN:1940-5901/IJCEM0006038

Case Report

Ochronotic arthritis of bilateral knees: a case report

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Received January 16, 2015; Accepted March 30, 2015; Epub May 15, 2015; Published May 30, 2015

Abstract: Alkaptonuria ochronosis is a rare metabolic disease in which the body does not have enough enzyme called homogentisic acid oxidase. Due to the homogentisic acid oxidase deficiency, homogentisic acid accumulates in cartilage and connective tissues which leads to ochronotic arthritis. We reported a case of bilateral ochronotic arthritis verified by clinical presentation, imaging, arthroscopic and histological findings. The patient achieved a satisfying therapeutic outcome after arthroscopic debridement followed by intra-articular injection of sodium haluronate.

Keywords: Osteoarthritis, alkaptonuria, ochronotic arthritis, arthroscopy

Introduction

Alkaptonuria (AKU) is a rare hereditary metabolic disorder, with a prevalence of 1/250,000-1,000,000 [1, 2]. It was first described by Scribonius in 1584 who reported the case of a young boy whose urine turned black when exposed to the air. In 1866, Vircow described necropsy findings in a 67-year old man. In this case, the intervertebral discs, larynx, tracheal rings, menisci, articular cartilage, and arteriosclerotic plaques were heavily pigmented. He named the condition ochronosis because the pigment appeared yellow-brown in color microscopically. In 1902, Albrehent and Zdareck, interrelated the terms *alkaptonuria* and *ochronosis* [3].

Alkaptonuria is a metabolic disorder in which homogentisic acid oxidase is absent. Due to the homogentisic acid oxidase deficiency, homogentisic acid accumulates in cartilage, and connective tissues. This situation is called ochronosis. Ochronosis can affect hyaline cartilages, intervertebral discs, skin and sclera. The cardiovascular, genitourinary and respiratory systems can also be affected. Ochronotic arthritis results from the pigmented deposits in the joints.

We report a case of a patient with ochronotic arthritis in his both knees. The patient underwent arthroscopic debridement combined with intra-articular injection of sodium haluronate and achieved a satisfying therapeutic outcome after a long-term follow up.

Case report

A 52-year-old man was admitted to the joint department of our hospital in May 2007 complaining of right knee swelling and pain for more than 2 years. He reported no history of trauma. He suffered from right knee pain particularly during walking, stair climbing, and descending, especially in stair climbing. There was also crepitus in right knee during knee active movement. Occasionally, there was clicking and locking of the right knee. When asking the patient's history, he complained of a 40-year history of chronic, nonspecific low back pain and stiffness. In 1998, he was admitted to the spine department of our hospital for low back pain and diagnosed with Alkaptonuria (AKU). He had no family history of alkaptonuria. His parents denied of consanguineous marriage.

A physical examination revealed no brownish pigmentation on the ear auricle, the face, fingertip and any other part of the body. Range of motion of the right knee was 0 to 100 degrees. There was mild thoracic tenderness and percussion pain and limitation of lumbar spine motion. His International Knee Documentation

Figure 1. Anteroposterior X-radiograph of the both knees showed osteoproliferation, particularly in the right knee.

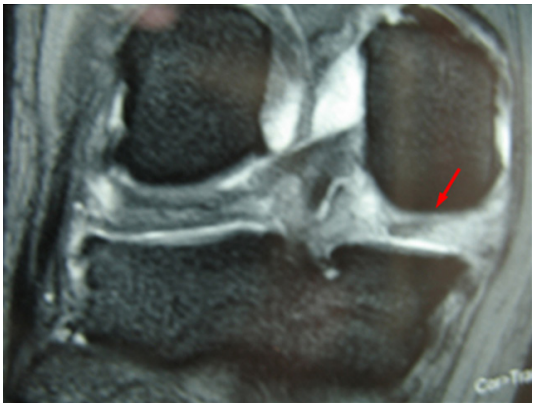

Figure 2. MRI of the right knee showed that obvious rupture of the medial meniscus.

Committee (IKDC) subjective score for the right knee joint was 54 points. Patella grinding test, straight-leg raising test (Lasegue sign) and McMurray sign were positive. Floating patella test and Patrick's test of the right knee was negative. There was tenderness at medial joint space of right knee. Crepitus was palpated during the knee motion.

The fresh urine was in a normal color (buff), when exposed to air for 3-5 h, the color gradually changed into black. There were no other abnormalities in the results of hematological and biochemical laboratory investigations nor did urinary ultrasonography or echocardiography investigations.

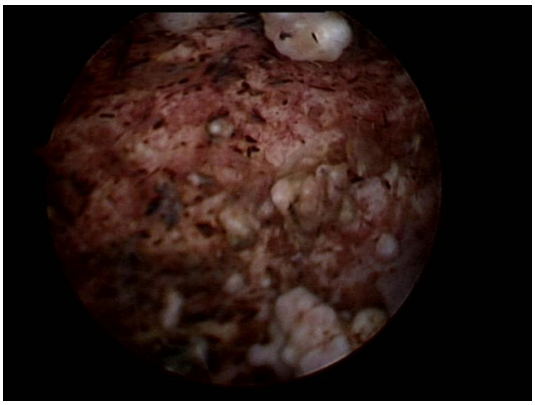

Figure 3. Arthroscopic examination of the right knee showed that hypertrophy of synovium accompanied with brown-yellow pigmentation.

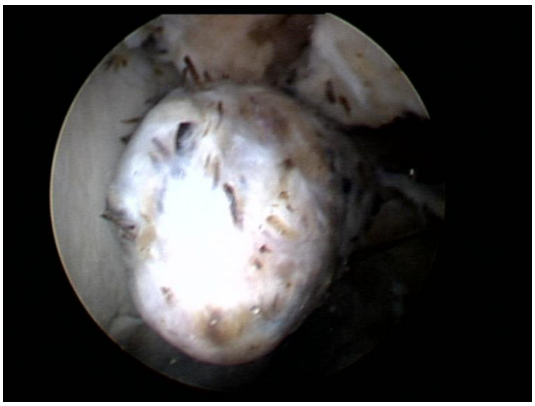

Figure 4. Arthroscopic examination of the right knee showed that synovial change neighboring the femoral trochlea.

Radiologic evaluation of the right knee revealed characteristic findings of osteoarthritis, including narrowing of joint spaces, subchondral sclerosis, irregularities of the joint surfaces, and peripheral new bone formation (**Figure 1**). The MRI of the right knee showed diffuse degenerative changes of cartilage and medial meniscus rupture and hydrops articuli (**Figure 2**).

The arthroscopic examination of right knee revealed hypertrophy of synovium, characteristic black pigmentation, complex rupture in the red-red zone of middle and posterior segments of medial meniscus and black pigment deposi-

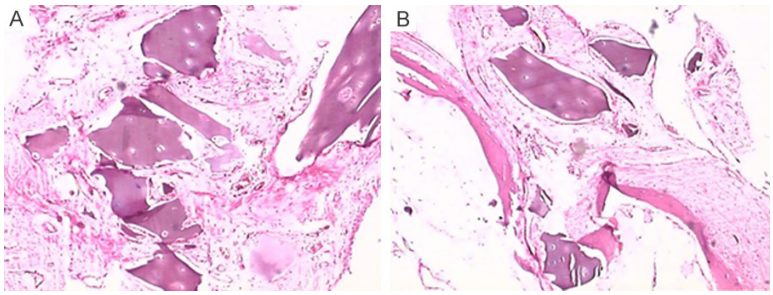

Figure 5. Histological appearance of left synovium (A) and right synovium (B).

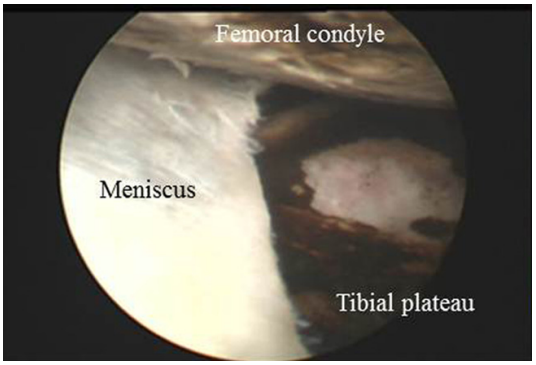

Figure 6. Arthroscopic examination of the left knee showed complete structure of anterior segment of medial meniscus.

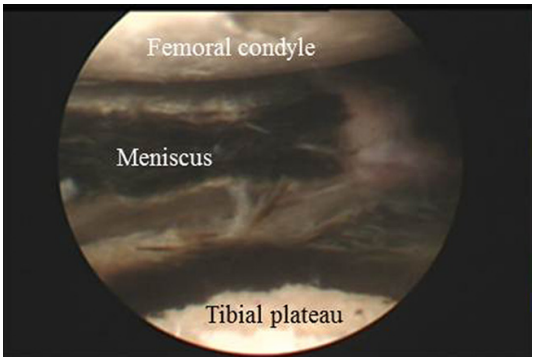

Figure 7. Arthroscopic examination of the left knee showed brown-yellow pigment in the remaining meniscus after resection of ruptured meniscus of the middle and posterior segments of the medial meniscus.

tions in the medial meniscus. Patellofemoral joint, medial and lateral femoral condyle, and articular cartilage of lateral tibial plateau showed extensive grade-2 degenerative changes.

Articular cartilage of medial tibial plateau showed extensive grade-2 degenerative changes accompanied with focal grade 3 degenerative changes. Arthroscopic synovectomy was performed to remove degenerative synovia. Samples of excised synovium were sent for analysis. Punch and shaver was used to remove ruptured meniscus (**Figures 3**, **4**). Radio-frequency (RF)-generated gas plasmas were used to clean and restore the degenerative aspect of the articular cartilage. The histological investigation of the resected material proved to be degenerated and pigmented (**Figure 5**). Intra-articular injection of sodium hyaluronate (25 mg) was begun on the second week and given once a week after surgery and continued for 5 times.

In January 2009, the patient was again admitted to our hospital complaining of left knee pain for half a year. He suffered from left knee pain particularly during walking, stair climbing, and descending, especially in stair climbing. There was also crepitus in left knee during knee active movement. Occasionally, there was clicking and locking of the left knee. His IKDC subjective score for the left knee joint was 56 points. During physical examination, floating patella test of the left knee was negative. Patella grinding test and McMurray sign of the left knee were positive. There was tenderness at medial joint space of left knee. Range of motion of the left knee was 0 to 105 degrees. Crepitus was palpated during the knee motion. Floating patella test McMurray sign of the right knee was negative. Patella grinding test of the right knee was positive. There was no tenderness at joint space of right knee. Range of motion of the right knee was 0 to 120 degrees. There was crepitus in right knee on active movement. X-ray examination of the left knee revealed characteristic findings of osteoarthritis. The MRI of the left knee showed diffuse degenerative changes of cartilage and medial meniscus rupture and hydrops articuli. The arthroscopic findings of left knee were similar to the right knees (**Figures 6**, **7**). Arthroscopic debridement of left knee was performed. Intra-articular injection of sodium hyaluronate (25 mg) was begun on the second week and given once a week after surgery and continued for 5 times.

The patient was followed up in February every year for 6 and 4 years for right knee and left knee respectively. During the follow-up period, the patient received several functional exercises such as straight-leg raising exercises. Intra-articular injection of sodium hyaluronate (25 mg) was given into each knee once a week for 5 times. However, there was still knee pain during stair climbing, descending, squat and rise. Patella grinding test for the both knees was still positive. There was also crepitus in both knees during knee active movement, which was similar to osteoarthritis. The IKDC subjective score of the right knee joint during the 6-year follow-up was 86, 82, 80, 79, 78, and 77 points. The IKDC subjective score of the left knee joint during the 4-year follow-up was 88, 85, 84, and 83 points.

Discussion

Alkaptonuric ochronosis, a rare metabolic disorder, is typically characterized by black discoloration of urine when exposed to air. It may affect various organs of body, such as deposits of brown-black pigment in face, ear and fingernail, calcifications in heart valves and intervertebral disc, narrowing of intervertebral space, and osteoarthritis [4, 5]. Aynaci et al. reported that the deposition of oxidized homogentisic acid within the connective tissues of peripheral joints turn to the brown colored pigments, which has high affinity to the surrounded articular cartilage and intervertebral disc [6]. Levin et al. found that deposits of brown pigments in cartilage can induce cartilage pigmentation, elastic loss, embrittlement, and loss of resistance to stress [7]. Knee joints as the primary load-bearing joints, are susceptible to be affected and leads to ochronotic arthritis, which has clinical feature that resembles those of osteoarthritis. In our study, the patient presented with pain particularly during walking, stair climbing, descending, squatting and rising especially after overstrain. Arthroscopic examination combined with histological investigation and detailed collection of case history as well as radiological examination of spine and other peripheral joint can make differential diagnosis [8].

Ochronotic arthropathy causes degenerative and destructive damage of the spine and the peripheral joints. Currently, there has been no specific treatment. However, for alkaptonuric arthritis, various therapeutic protocols can be opted according to patients' condition. The value and efficacy of sodium hyaluronate for the treatment of osteoarthritis has been widely accepted, especially for mild and moderate osteoarthritis. Alkaptonuric arthritis resembles those of osteoarthritis. Toussirot et al. [9] administered hyaluronic acid (purified sodium hyaluronate) into the knee with ochronotic arthropathy. They found an improvement in functional symptoms and pain and they concluded that it is possible to use hyaluronate injections in early ochronotic arthropathy to improve functional symptoms and patient quality of life. However, the long-term benefits are as yet unknown. In addition, due to the low morbidity, it is hard to perform a large scale clinical trial. In our study, the patient received intra-articular injection of sodium hyaluronate (25 mg) once a week and continued for 5 times after surgery. A long term follow up (6 years for right knees and 4 years for left knees) showed slowly degenerative changes of bilateral knee joints which suggests that sodium hyaluronate plays a positive therapeutic efficacy for the treatment of alkaptonuric arthritis.

Arthroscopic surgery has certain healing effect on the osteoarthritis. Ochronotic arthritis can also be treated with arthroscopic surgery, particularly when accompanied with meniscus tear, intra-articular loose bodies, or synovium was severely affected. Several previous studies using arthroscopic surgery reported positive effect on the on the complaints caused by ochronotic arthritis [10, 11]. Destruction of the joint architecture and severe functional impairment due to ochronotic arthritis necessitated total joint replacement [12, 13]. In our case, arthroscopic debridement was firstly performed on the right knee and a satisfying outcome was obtained after a 6-year follow up. 2 years later, the patient referred to our hospital due to the similar clinical symptoms on the left knee. The patient underwent secondary arthroscopic debridement for ochronotic arthritis of the left knee after the failure of conservative treatment.

Arthroscopic surgery can restore the meniscus tear, and articular cartilage degeneration and remove hyperplastic synovial membrane. Although there was still knee pain during stair climbing, descending, squat and rise, our therapeutic method-arthroscopic surgery combined

with postoperative function exercises and intra-articular injections of sodium hyaluronate-does have a therapeutic effect on the complaints of locked knees, flaccid leg. In addition, the patient IKDC was greatly improved compared to the preoperative values which suggest a slowly degenerative joint function.

Conclusions

There is no specific treatment for alkaptonuric ochronosis. However, for ochronotic arthritis resulting from alkaptonuric ochronosis, we consider that arthroscopic debridement combined with intra-articular injection of sodium hyaluronate may offer a satisfying therapeutic outcome.

Disclosure of conflict of interest

None.

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References

[1] Manoj Kumar RV and Rajasekaran S. Spontaneous tendon ruptures in alkaptonuria. J Bone Joint Surg Br 2003; 85: 883-886.

[2] Demir S. Alkaptonuric ochronosis: a case with multiple joint replacement arthroplasties. Clin Rheumatol 2003; 22: 437-439.

[3] Drakoulakis E, Varvitsiotis D, Psarea G and Feroussis J. Ochronotic arthropathy: diagnosis and management: a critical review. Am J Orthop (Belle Mead NJ) 2012; 41: 80-83.

[4] Collins E and Hand R. Alkaptonuric ochronosis: a case report. AANA J 2005; 73: 41-46.

[5] Nas K, Gur A, Akdeniz S, Cevik R, Harman M and Sarac AJ. Ochronosis: a case of severe ochronotic arthropathy. Clin Rheumatol 2002; 21: 170-172.

[6] Aynaci O, Onder C and Turhan AU. Bilateral hip arthroplasty for ochronotic arthropathy. Clin Rheumatol 2000; 19: 150-152.

[7] Levin CY and Maibach H. Exogenous ochronosis. An update on clinical features, causative agents and treatment options. Am J Clin Dermatol 2001; 2: 213-217.

[8] Zhao BH, Chen BC, Shao de C and Zhang Q. Osteoarthritis? Ochronotic arthritis! A case study and review of the literature. Knee Surg Sports Traumatol Arthrosc 2009; 17: 778-781.

[9] Toussirot E and Aquaron R. Short-term efficacy of hyaluronic acid joint injections in a case of ochronotic arthropathy. J Clin Rheumatol 2013; 19: 152-153.

[10] Kural C, Cetinus EM, Kural A, Ugras AA and Kaya I. [Knee ochronotic arthropathy and arthroscopic findings]. Acta Orthop Traumatol Turc 2009; 43: 67-71.

[11] Raaijmaakers M, Steenbrugge F and Dierickx C. Ochronosis, arthroscopy of a black knee: a case report and review of the literature. Knee Surg Sports Traumatol Arthrosc 2008; 16: 182-184.

[12] Kerimoglu S, Onder C, Aynaci O and Malkoc CH. Hip arthroplasty for ochronosis. Saudi Med J 2005; 26: 1812-1814.

[13] Aydogdu S, Cullu E, Ozsoy MH and Sur H. Cementless total knee arthroplasty in ochronotic arthropathy: a case report with a 4-year follow-up. J Arthroplasty 2000; 15: 539-543.