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Arthroplasty for the treatment of joint degeneration caused by ochronosis in two cases

İki olguda okronozise bağlı eklem dejenerasyonunda artroplasti uygulamaları

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Okronozis homogentisik asit oksidaz enziminin eksikliğine bağlı oluşan ve nadir görülen bir metabolik hastalıktır. Yaşın ilerlemesiyle, eklem kıkırdağında meydana gelen pigmente homogentisik asit birikimi okronotik osteoartritle sonuçlanır. Bu yazıda, birinde iki taraflı kalça, diğerinde iki taraflı diz eklemlerini tutan okronozis nedeniyle total kalça ve diz artroplastisi uygulanan 55 ve 60 yaşlarında iki kadın hasta sunuldu. Artroplasti her bir hastada iki seanslı olarak çimentosuz (kalça) ve çimentolu (diz) uygulandı. Hastaların son ameliyattan sonra 12. aydaki (kalça) ve 10. aydaki (diz) kontrollerinde önemli yakınmaları yoktu. Düz grafilerde protez komponentlerinde anormal görünüm izlenmedi. Ameliyatta çıkarılan örneklerin histopatolojik incelemesinde, özellikle kıkırdak dokusunda olmak üzere, bağ dokusunda kahverengi-siyah renkte pigment birikimi izlendi.

Anahtar sözcükler: Alkaptonüri/komplikasyon; artroplasti, replasman, kalça; artroplasti, replasman, diz; okronozis/komplikasyon; osteoartrit/etyoloji.

Ochronosis is a rare metabolic disease caused by the deficiency of the homogentisic acid oxidase enzyme. With increasing age, accumulation of pigment deposits of homogentisic acid in the joint cartilage results in ochronotic osteoarthritis. We presented two female patients, with ages 55 and 60 years, who underwent staged bilateral uncemented total hip and bilateral cemented total knee arthroplasty, respectively, for osteoarthritis caused by ochronosis. Both patients had no significant complaints at final follow-up examinations made 12 months and 10 months after the second operation in the hip and knee, respectively. Plain radiographs did not show any abnormality in the components of the prostheses. Histopathologic examination of surgical specimens showed brown-black pigment deposits in the connective tissue and cartilage tissue.

Key words: Alkaptonuria/complications; arthroplasty, replacement, hip; arthroplasty, replacement, knee; ochronosis/complications; osteoarthritis/etiology.

Alcaptonuria is a rare autosomal-recessive metabolic disease that is caused by lack of enzyme homogentisic oxidase. Its incidence is less than 1/million.[1,2] Lack of homogentisic oxidase enzyme leads to accumulation of homogentisic acid which usually acts as an intermediary in phenylalanine and tyrosine and its disposal through urinary system. Pigment deposits of homogentisic acid accumulates at the walls of joint cartilage, tendons, ligament, skin, sclera, renal tubule epithelial cells, pancreas islet and some arteries.[3,4]

Excessive accumulation of homogentisic acid and oxidation products cause progressive tissue damage in the joint cartilage and other tissues involved. Change of color into blue-dark in the tissue and urine and the concurrent degenerative arthritis is called ochronosis. [1]

There is not a known medical treatment of alcaptonuria. There is limited number of publications and case reports in respect to the surgical treatment of the involved joints.[4-9] It is obvious that metabolic bone diseases affect the mechanical features of the skeleton system. The literature offering information on what kind of mechanical differences may occur on the bones and soft tissue of the patients who underwent joint arthroplasty due to joint degeneration and the types of prob-

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lems that can be encountered during the surgery and the follow-up process is not sufficient. Spencer et al. [8] reported that they performed arthroplasty on 11 joints of three cases with ochronosis and that the outcomes were comparable with those of the patients with primary osteoarthritis. Spine is the bone which becomes stiff first and more frequently than the other bones and the main complaint of the patients is the low back pain. Involvement of large peripheral joints is generally observed few years later than the involvement of the spine involvement.[10]

This case report presents two osteoarthritis patients, one with hip involvement and one with knee joint involvement, without the presence of spinal degeneration unlike the previously reported cases.

Case presentation

Case 1– 50-year-old women was admitted to Orthopedics and Traumatology Polyclinic when the severity of her pains and her inability of movement worsened in recent months following the failure of medical treatment and physiotherapy applied due to a hip pain lasting for the last two years. Physical examination revealed joint extension by 0°, flexion by 90°, internal rotation by 0o, external rotation by 50° on both hips. Fabere test was positive. Highly progressed narrowing was observed at the joint space, acetabular protrusion on femur head, subcondral cysts and sclerosis with the plain graph (Figure 1). Firstly, a total hip arthroplasty was planned on the right hip. During the surgery, it was thought that it might be difficult to move femur head due to the acetabular protrusion and such an attempt could lead to a fracture in the femur. Following a wide capsule resection, the head was moved carefully. It was seen that the joint capsule, femur head and the acetabular cartilage was strikingly brown- black (Figure 2). There was also synovial reaction, though not at a high extent. The bone quality at the acetabular and femur proximal was in line with the age of the patient. Spongios grafts prepared from the femur head was placed on acetabula which was deepened due to protrusion. A cementless total hip arthroplasty was performed by using standard method, without experiencing any additional problem. The samples taken during the surgery was sent to the pathological analysis unit as the appearance of the joint capsule, femur head and acetabula pointed out the possibility of alcaptonuria. Histopathological examination performed after hematoxylin-eosin staining revealed huge histiocytic cell reaction

Figure 1. Highly progressed narrowing and protrusion on the joint space of both hips on the front-back pelvis graph.

around the pigmented cartilage particles on the surface of the joint which was degenerated with the development of irregular fibrotic tissue (Figure 3). In the physical examination of the case which was thought to have ochronosis on the base of the clinical and pathological findings, it was thought that the grey blue pigmentation extended around the eye on the nose dorsum and dark color change on the earlap were attributable to ochronosis (Figure 4). Such findings were not present in the family history. The patient was diagnosed with ochronosis on the base of the findings of the physical, radiographic and histopathological examinations. Postoperative process was arranged as it is in the patients who underwent total hip arthroplasty due to the primary osteoarthritis and no problem was encountered. Three months later, cementless total hip arthroplasty was performed on the left hip upon the complaint of pains on the left hip by the patient. The findings during

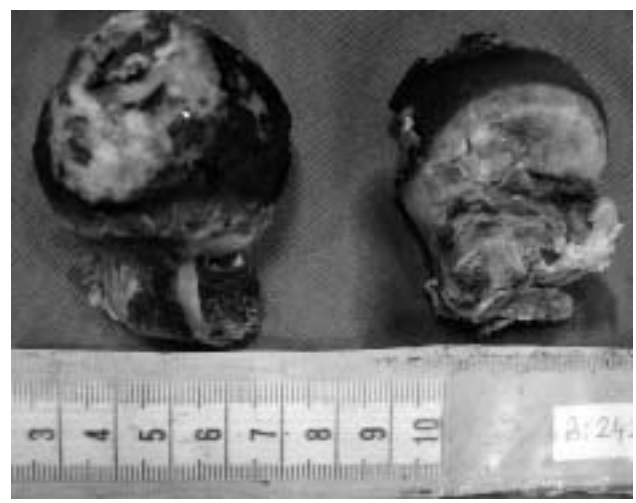

Figure 2. Black color on the head of the femur.

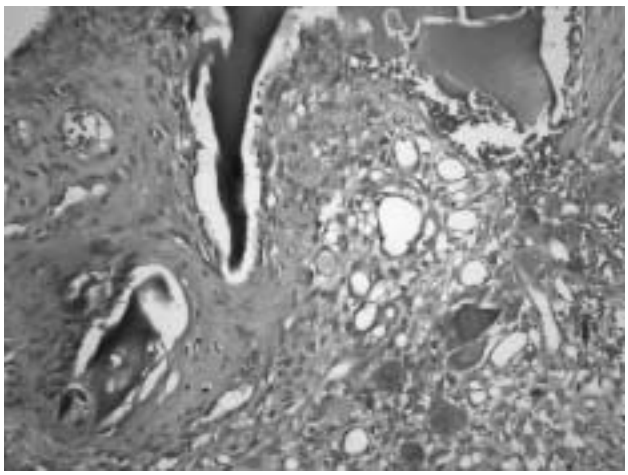

Figure 3. Pigmentation of the cartilage particles and histiocytic giant cell reaction around it (H&E x 200).

and following the operation were the same with those of the first operation. In the physical examination of the patient in the 12th month following the operation, extension was 0°, flexion was 100°, internal rotation was 20° and external rotation was 90° for both hips. There was not any significant complaint. No abnormality was detected on the components of the prostheses applied on the joints of both hips by plain graph (Figure 5). There was joint degeneration, tough not at an advanced stage, on the joints of the both hips of the patient and it was decided that the patient should be followed up with conservative methods.

Case 2– A 60-year-old women applied to Orthopedics and Traumatology Polyclinic with the complaint of pain on her knee for seven years. Physical examination revealed extension by 0°, flexion of 100° on both knees. Degenerative osteophytic changes and osteophytes formations on all compartments of both knees and narrowing and sclerosis on the medial joint space was observed by the plain graph. Right knee total arthroplasty was performed on the patient who was diagnosed with gonarthrosis in both knees, taking his desire into consideration. After the skin and sub-cutaneous was penetrated and patella lateral was overthrown with medial parapatellar incision, it was observed that some parts of the patella, femur condilles, tibia condilles, meniscus and joint capsules were brown-black (Figure 6). The patient was diagnosed with ochronosis. This diagnosis was also affected by the experienced obtained with Case 1. Structure of the bones was in harmony with her age. The patient underwent bilateral cemented total knee arthroplasty. Although the joint surface of the patella was not eroded enough to require patellar

Figure 4. Black-blue pigmentation on the earlap.

component application, it was replaced as the cartilage seemed brown-black due to the ochronosis. The wound was closed with traditional methods, by placing hemovac dren. The post-operative program which is used for the patients who underwent knee arthroplasty was administered to the patient. The patient encountered no problem. Moreover, the patient who complained about severe pains before the operation reported full satisfaction with the operation she underwent at an earlier date in comparison to the other patients who underwent knee arthroplasty. The histopathological examination conducted after staining the soft tissue and the joint cartilage with hematoxylin-eosin revealed the accumulation of brown-black pigment on the connective tissue, but especially on the cartilage tissue (Figure 7). The patient whose complaints about her left knee increased

Figure 5. Normal appearance of the prosthesis components on the joints of the both hips on front-back pelvis graph, 12 months after the operation.

Figure 6. Black pigmentation on the cartilage of the joint of the right knee.

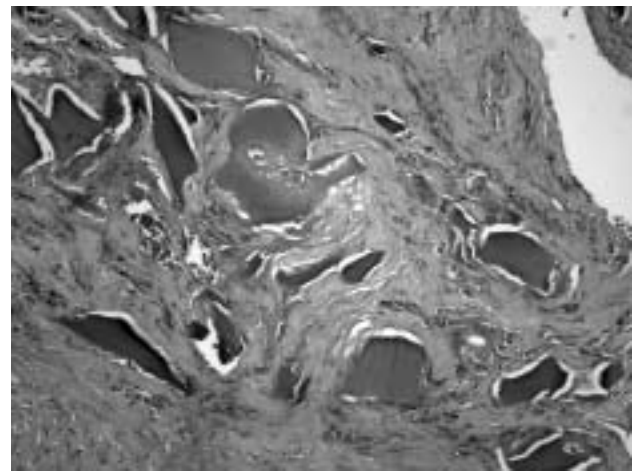

Figure 7. Pigmented cartilage particles within the fibrosis tissue taken from the right knee (H&E x 200).

applied to the Polyclinic approximately 12 months later. The physical examination pointed out paint after 40 degrees in the flexion movements of the left knee and sensitivity in the total extension although extension was full. There was crepitation during knee movements. Radiographic findings revealed degenerative osteophytic changes, osteophytes formations in all compartments of the knee and narrowing and sclerosis at the medial joint space (Figure 8a,b). The patient underwent cemented left total knee arthroplasty. During the operation, findings which were very similar to those of the right knee. Patellar joint surface was replaced although there was not advanced level of degeneration. The operation and the post-operative processes were conducted in the same with the right knee. The patient had no family history. The diagnosis of ochronosis became final on the base of the color change observed on the tissues during the operation and the histopathological findings. In the physical examination performed 10 months after the last operation, it was seen that extention was 0o, flexion was 100° on both knees and the patient did not have a significant complaint. No abnormality was observed on the femoral, tibial and patellar components in the plain graphy (Figure 9a,b). There was no complaint or physical examination finding which could be attributable to the involvement of another joint.

Discussion

Alcaptonuria is a rare disorder which was defined on the children with black urine in 1584 for the first time. The disorder was named as ochronosis as

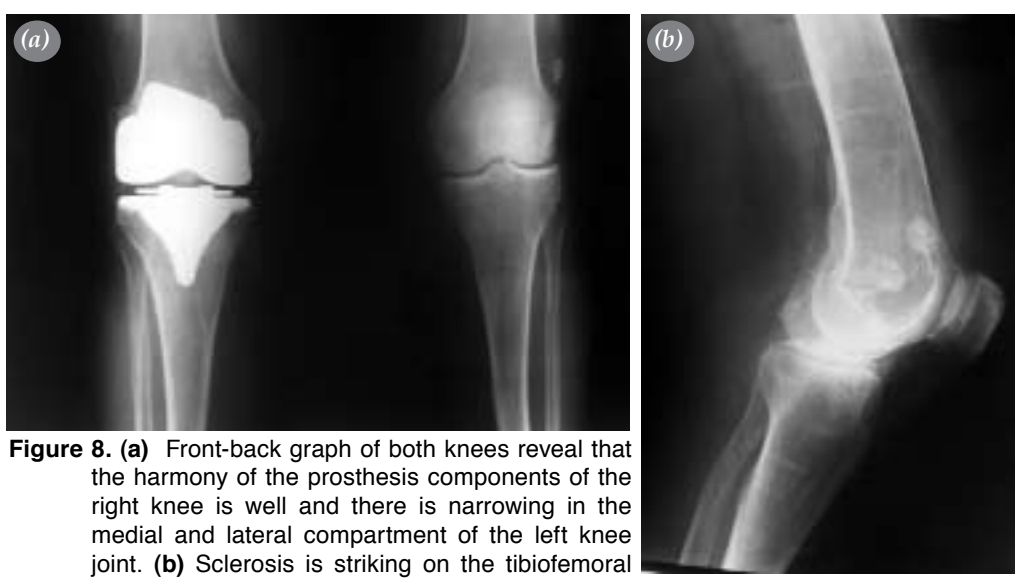

Figure 8. (a) Front-back graph of both knees reveal that the harmony of the prosthesis components of the right knee is well and there is narrowing in the medial and lateral compartment of the left knee joint. **(b)** Sclerosis is striking on the tibiofemoral joint surface of on the side-graph of the left knee.

Figure 9. In the 10th month following the operation, the harmony between the prosthesis components was evaluated as good **(a)** in the front-back and **(b)** lateral graphs.

yellow-brown pigments were found microscopically in the autopsy findings of a 67-year-old women who died due to the congestive cardiac deficiency in 1986. [11] The relation between the disorder and the alcaptonuria was found in 1902.[6,11] Sonderbergh, who studied the relation between the spinal arthritis and ochronosis, named the disorder as "osteitis deformation alcaptonuria" in 1915. It was found that the gene of alcaptonuria was present in the 3q21-23 locus at the end of 1990s.[12]

Ochronosis is generally seen in adults. Ochronotic pigment may accumulate in all connective tissues, primarily cartilage. Ochronotic arthropathy is mostly seen in people aged 40s.[7] The first complaint of the patients in respect to the joints is limited mobility of the waist and pain on the waist lasting long. In our two cases, low back pain was not on the foreground. The knees were the second most involving part after the spine. Other parts are hips, spine, sacroiliac joint and symphysis pubis. In ochronotic patients, large joints are involved as they are frequently subject to weight. Small joints of the hands and feet are not involved. [3] In none of our cases, small joints were not involved. The disorder can be seen in family members as well although it is seen rarely.[13] There was no family history in any of our patients. Similar to the patients with primary osteoarthritis, narrowing and sclerosis was observed on the joint space of the joint involved in the ochronotic patients.[14] Osseous particles seen in the soft tissues which make up the joints and the tendinous calcifications distinguish between typical degenerative changes in the patients. In our patient with gonarthrosis, there were tiny particles which resemble coal particles in the meniscuses which were totally got harder. In both cases, but especially in the case with gonarthrosis, pain complaint was significant. Moreover, clinical complaints were more on the foreground than the radiographic appearance. It was also very striking that the pains were over right after the operation. The color brown-black observed in the tissues that make up the joint during the operation was very typical. The color was engraved in the tissue and it was not bubbling over. This color is totally different than the black color changes that can be seen in the patients who underwent revision arthroplasty as a result of titanium compounds. The particles that fall from titanium strain the tissue form a dirty gray-black view on the area under its influence and bubble over the joint space.

The first finding in the patients with alcaptonuria is the color change in the urine.[3] The thickening in the urine color and the color change in the sclera and ears may be overlooked by the patient and his relatives. This was something which we also overlooked. This is why there may be delay in the diagnosis until the development of ochronosis. The number of cases with ochronotic arthropathy without the signs of ocular and cutaneous indicators is very low in the literature. In the case reported by Kusakabe et al. [15], osteoarthritis was seen on the cervical spine without ocular and dermatological findings. In both cases, ochronosis diagnosis was made on the base of the clinical, radiographic and histopathological findings, without the spinal findings. While no striking finding was found in the examination following diagnosis in the second case, color changes were detected on the face and ears following the diagnosis of ochronosis in the first case.

Spencer et al.[8] reported that they met no complication following arthroplasty on 11 joints of 3 patients diagnosed with osteoarthritis attributable to ochronosis. They reported no implant deficiency including total hip arthroplasty or any problem in 12-year follow up period. In their study, they stated that they had difficulty in dislocating patella as the quad-

riceps and the patellar tendon were hard one patient who underwent knee arthroplasty. In our case, we did not encounter any problem with median parapatellar entrance. Çetinus et al. [7] applied total cementless and cemented knee arthroplasty due to ochronosis on two cases and observed no problem in the last 2.5 and 3 year follow-up process. Aydo_du et al. [4] reported no problem in the last four year follow up period of a 48-year-old case who underwent cementless total knee arthroplasty due to ochronosis. The findings reported in the arthroplasty practices following the diagnosis of osteoarthritis related to ochronosis showed that no difficulty or problem was encountered during the operation and in the follow up period.[2,5,6,9,16-18] The experience we obtained from our arthroplasty practices on the four joints of two cases confirms it.

Consequently, total joint arthroplasty is an effective treatment method in the treatment of advanced stage osteoarthritis attributable to ochronosis on hip and knee. The findings are similar to the findings of the arthroplasty practices associated with osteoarthritis with different etiology. Pain complaints may be more dominant than the radiographic appearance. We think that there are not obvious differences between patients who underwent arthroplasty due to osteoarthritis associated with ochronosis or other causes, in terms of surgical indications and implementation process.

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