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Knee ochronotic arthropathy and arthroscopic findings

Diz okronotik artropatisi ve artroskopik bulguları

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Okronotik artropati, alkaptonürili olgularda nadir görülen bir patolojidir. Alkaptonuri, homogentisik asit oksidaz enzim eksikliğine bağlı olarak homogentisik asit pigmentinin kıkırdak, menisküs, ligamanlar ve değişik dokularda birikmesiyle bulguların ortaya çıktığı, herediter metabolik bir hastalıktır. Bu pigmenter değişiklikler okronozis olarak adlandırılır. Bu yazıda, diz yakınmaları sonucu yapılan diz artroskopisi sırasında menisküs ve kıkırdaklarda kahverengi-siyah renk değişimi saptanan ve ileri araştırmalarla alkaptonüri tanısı konan 50 yaşında bir kadın hasta sunuldu.

Anahtar sözcükler: Alkaptonüri/tanı; artrit; artroskopi; diz eklemi/patoloji; okronozis/etyoloji.

Ochronotic arthropathy is a rare condition found in patients with alkaptonuria which is a hereditary metabolic disease associated with deposition of homogentisic acid derivatives in the articular cartilage, menisci, ligaments, and connective tissues due to homogentisic acid oxidase deficiency. These pigmentary changes are termed ochronosis. We presented a 50-year-old woman in whom arthroscopic examination of the right knee revealed brown-black discoloration of the articular cartilage and menisci leading to the diagnosis of alkaptonuria by further laboratory examinations.

Key words: Alkaptonuria/diagnosis; arthritis; arthroscopy; knee joint/pathology; ochronosis/etiology.

Alkaptonuria (AKU) is a rare autosomal recessive disease, resulting from a deficiency of the enzyme homogentistic acid oxidase (HGAO), which is involved in the metabolism of phenylalanine and thyrosine aminoacids. The insidence of alkaptonuria is 1:250000 births.[1,2,3]

Dark urine in AKU was first described by Scribonius in 1584 in the case of a school-boy who excreted urine as black as ink (1). Due to the partial or total deficiency of HGAO in the liver and kidneys, homogentisic acid accumulates in the blood, part being excreted in the urine.[4] On exposure to the athmosphere urine containing homogentisic acid gradually darkened to a black blue colour. Homogentisic acid and oxydation products accumulate expecially in the hyaline cartilage, tendons and cartilage. Homogentisic acid is also reported to be deposited in the skin, tympanic membrane, heart valves, sclera, the cartilages of the nose and ears, kidneys, pancreas and large vessels.[5,6] Due to accumulation of homogentisic acid, cartilages get a dark discoloration and become brittle and more vulnerable to mechanical stress. The diminished quality of the cartilage causes arthropathy of large joints and the spine. Development of degenerative arthritis with accompanying blue-black pigmentation of the tissues and dark discoloration of the urine is called "ochronosis". Ochronosis was first described by Wirchow in 1866 during the course of a necropsy, he found pigmentation of the tissues, caused by the deposition of ochre-coloured granules. Gross and Allard (1907) noted the striking incidence of arthritic changes in some patients with alcaptonuria, and the pigmentation of joint cartilage was described independently by Clemens (1907). Radiological changes in the vertebrae and intervertebral discs were demonstrated by Soderberg in 1915, for these he coined the term "osteitis

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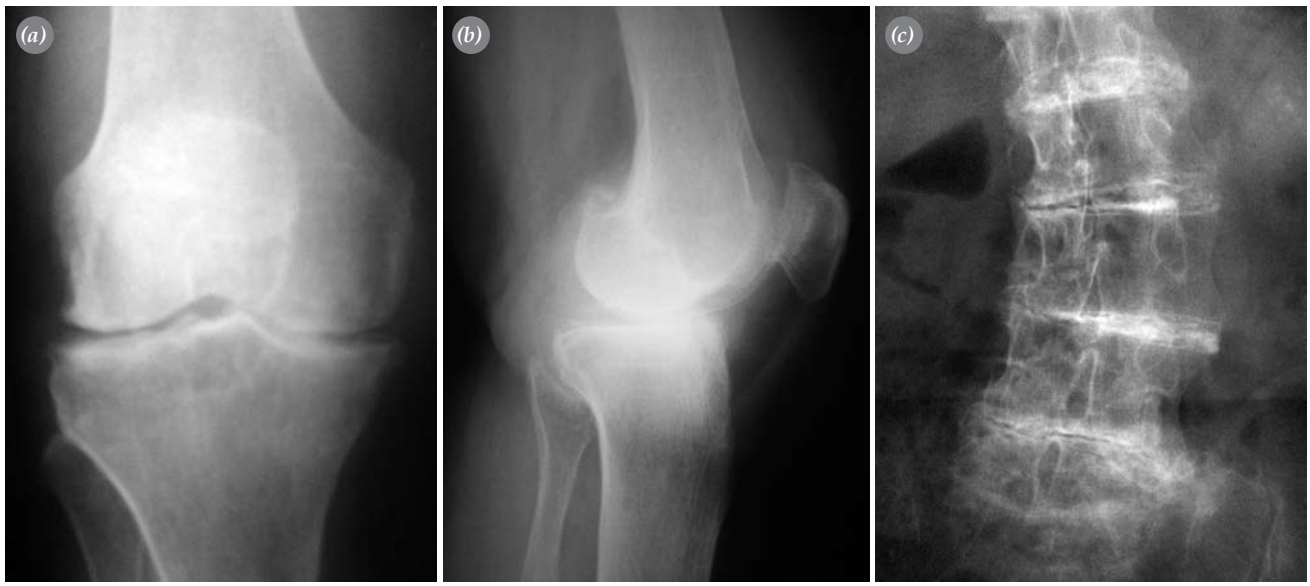

Figure 1. (a) AP radiography of the right knee. **(b)** Lateral radiography of the right knee. **(c)** Radiography of the lumbosacral spine ; degenerative changes in intervertebral spaces.

deformans alcaptonurica".[7] In 1996 during clooning studies, alcaptonuria gene was shown to be mapped on the 3q 21-23 locus.[8]

The clinical symptoms of ochronotic arthropathy begin after the 4 th decade of life. Clinical diagnosis is made observing skeletal manifestations including low back pain, stiffnes and degenerative arthropathy of the large joints, ochronotic pigmentation of the tissues and blue, black discoloration of the urine. The definitive diagnosis of the alkaptonuria may be confirmed with several biochemical tests for the quantitative presence of homogentisic acid in urine. Since there is no effective medical treatment for alkaptonuria, treatment at present is symptomatic by local heat, physioteraphy, analgesics and external support and with surgical treatment in the form of synoviectomy, arthroscopic debridement, fusion or arthroplasty as indicated regarding the effected joint.[3,7,9]

In this article our purpose is to present a patient who was diagnosed to have alkaptonuria with biochemical tests after observing ochronotic blue black pigmentation of the menisci and tibial cartilage during arthroscopy of the knee. Bu yazıda, diz ağrısı yakınması nedeniyle diz artroskopisi yapılan ve artroskopi sırasında menisküslerde ve tibial platoda okronotik mavi-siyah pigmentasyonun gözlenmesi nedeniyle ileri tetkikler yapılarak alkaptonüri tanısı konan bir olgu sunuldu.

Case report

50 years old woman presented with complaints of long lasting chronic low back pain which was worsened for the last 4 years and pain in both knees for 1 year. Her symptoms necessitated the use of nonsteroid anti-inflammatory drugs (NSAID), but especially her right knee pain gradually worsened restricting her daily activities. Because of those complaints she was decided to have diagnostic arhroscopy. Her physical examination revealed crepitation and mild effusion of the right knee. We noted that extension was painless and knee flexion was terminally painfull at last 30 degrees. There was medial joint line tenderness, Steinman test was negative and ligaments appeared normal. There was tenderness with palpation over the vertebrel colon and marked pain with rotation. Neurologic examination denoted normal findings. Ordinary X ray images of the knees (fig 1a, b), and servical, thorasic-lumbar spine (fig 1c) demonstrated osteoartritis. Magnetic resonance imaging (MRG) of the right knee (fig 2a) revealed minimal effusion in the suprapatellary space and the joint, medullary edema at both femoral condyles and proximal tibia and minimal osteophytes at the medial joint space. The patient underwent diagnostic arthroscopy and findings were illuminating. There was mild synovial hypertrophy with normal colour and small black particles in the suprapatellary pouche. In the medial joint space there was large grade 4 degeneration at the tibial plateau and there was

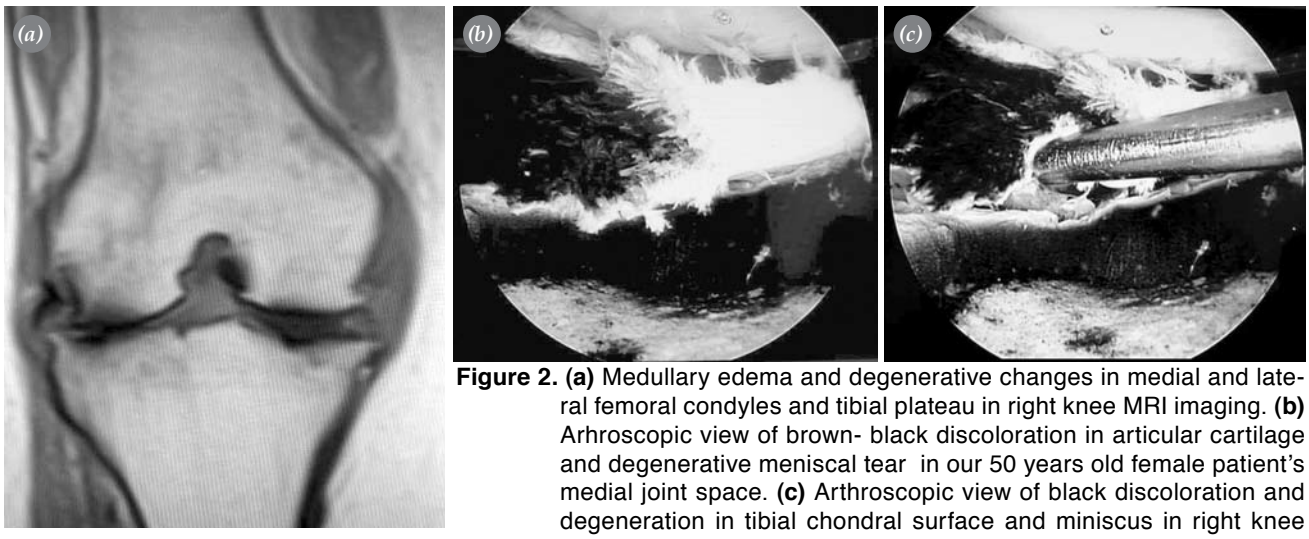

Figure 2. (a) Medullary edema and degenerative changes in medial and lateral femoral condyles and tibial plateau in right knee MRI imaging. **(b)** Arhroscopic view of brown- black discoloration in articular cartilage and degenerative meniscal tear in our 50 years old female patient's medial joint space. **(c)** Arthroscopic view of black discoloration and degeneration in tibial chondral surface and miniscus in right knee lateral joint space.

black discoloration at the cartilage. A degenerative tear was found in the corpus of the medial meniscus which appeared to be black as well (fig 2b). Anterior cruciate ligament was intact. Lateral tibial plateau and meniscus also showed black discoloration with partial grade 4 degeneration with the meniscus being intact. Femoral and patellar joint surfaces showed grade 2-3 degeneration. Specimens of articular cartilage and synovium were removed for histological examination. Lesions were shaved and debrided and partial meniscectomy was performed for the torn medial meniscus following the joint lavage. Further researh was planned for the diagnosis of ochronosis considering the black discoloration of the joint cartilage and menisci. The patients freshly passed urine turned brown after addition of sodium hydroxide to the sample to facilitate oxydation. The diagnosis is confirmed with establishing the excess amounth of homogentisic acid with organic acid research in the urine (gas chromatography and mass spectrometry). No pathological findings were detected with the detailed examination of the ear, sclera, skin and cardiovascular system. After the diagnosis through detailed questioning her mother remembered that the colour of her nappies were black. Treatment was initiated by administering vitamin C and NSAID and she was discharged consequently. She reported at 6 months follow up that her complaints had diminished respectively.

Discussion

Few reports of arthroscopic diagnosis and treatment of ochronosis have been found in the literature. [4,9,10,11,12] Our patient is the fourth case who was diagnosed arthroscopically.[4,9,10] Chen et al. reported the arthroscopic findings of a 50 years old male patient who was complaining of pain in both knees. Thacker et al. reported the arthroscopic findings of a 40 years old man who had arthroscopy of the knee and shoulder, [4] and Raaijmaakers et al. reported a 49 years old patient's knee arthroscopy findings. Our arthroscopic findings were consistent with those of other cases in the literature. Generalized synovial hypertrophy accompanying brown-black discoloration of articular cartilage and menisci and generalized cartilage degeneration were our common arthroscopic findings with other cases in the literature. In our case there was an additional meniscus tear unlike in that of Thacker's case [4] and similar with Chen's[10] and Raaijmaaker's cases.[9] Partial meniscectomy was performed for the torn meniscus.

Thacker et al.[4] had diagnosed ochronosis before performing arthroscopy [4] , where as in our case, similar to Raaijmaaker's case [9] arthroscopy was a diagnostic and treatment tool to remind us of ochronosis and lead us for further research. During arthroscopy, brown-black discoloration of the articular cartilage and menisci and generalized articular destruction warned us to have advanced research for ochronosis. Macroscopic examination of the urine following alkalization and establishing the excess amount of homogentisic acid in the urine with gas chromatography and mass spectrometry confirmed the diagnosis.

Lumbosacral and servical X rays revealed calsification of the intervertebral discus and generalized

osteophytes. Also narrowing of the intervertebral disc space with vacuum phenomena is suggestive of ochronotic arthropathy.[13] Approximately 50% of the alkaptonuric patients manifest one clinical form of ochronosis after the fourth decade. First signs are skin and soft tissue pigmentation. Diagnosis can be made during childhood by observing dark colouration of diapers or urine when left standing.[3] Our patient's mother had remarked the dark colour of her urine in early childhood. Ochronotic discolorating of the cartilage of the ears and nose may be observed at the age of 30. Other less common extraarticular manifestations are ochronosis of the heart with valve stenosis and urinary tract obstruction by ochronotic calculy.[3,13] No extraarticular manifestation is observed in our patient.

Initial spinal symptoms are low back pain and sciatalgia .[14] Vertebral micro fractures and joint degeneration is thought to be responsible for the pain.[1,15] Radiological findings of peripheral joint involvement are ankilozing spondylitis,haemochromatosis, idiopatic chondrocalcinohoid, acromegali, reumathoid arthritis and calcium pyrophosphate dihyrade disease should be considered in differential diagnosis since spinal radiographic findings are similar.[15,16,17] In our case radiography revealed medial joint space narrowing and subchondral sclerosis in both knees as well as degenerative spinal findings and minimal ostophytes. Our X ray findings corresponds with the other cases in the literature.

No curative treatment for this disease exists. Some treatment modalities are under proof phase. Treatment with high dose of acsorbic acid proved to lower the levels of HGA in excreted urine [2,3,9], but does not prevent the occurence of arthropathy.Nitisinone is shown to have significantly altered the excretion of HGA with urine in both human and rat studies. Nitisinone is suggested to be used for treatment of tirosinemia type 1 but it's use in ochronotic patient's has yet to be proved.[3] Since there is no effective treatment to replace the defficient enzym, symptomatic treatment is initiated with NSAID, intraarticular steroid injection and ascorbic acid. Arthroscopic debridement, synoviectomy, partial ot total joint arthroplasties and fusion are the surgical treatment options. [3,16,17,18] Spencer et all performed arthroplasthy for 3 patient's 11 joints who had lower and upper extremity ochronotic degenerative joint disease and reported good results at 12 years follow up.Arthroplasty seems to be the best choice for patients whose symptoms resist despite conservative treatment.[19,20] Raaijmaakers et al [9] reported to provide symptomatic relief with administering 400 mg/day chondroitin sulphate and 1500 mg/day glucosamine for 4 months.

Finally, ochronosis is a rare methabolic disorder affecting peripheral joints as well as spine and the soft tissues. We believe that arthroscopy has great importance in suspecting and diagnosing ochronosis.

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