Case report

Alkaptonuria; a case report

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ABSTRACT

Introduction and importance: Alkaptonuria is an autosomal recessive disease due to lack of the enzyme homogentisic acid oxidase. Homogentisic Acid (HA) is in the metabolism pathway of phenylalanine. The musculoskeletal symptomatology begins generally in the fourth decade. We reported the case of a 50 year old man who had ochronotic arthropathy and degenerative changes in knee joint and who was treated with total knee arthroplasty.

Case presentation: A 50 year old man presented to our outpatient clinic with bilateral knee pain. Pain was exaggerated with effort and decreases with rest. The patient had no medical history. While performing the total knee arthroplasty for our patient, we discovered intraoperatively the black coloration of the articular cartilage of the knee. At 6 months follow up, the patient was satisfied with the result with no knee pain in the treated knee. Range of knee motion was 0° in total extension to 100° of flexion. Radiological control showed a stable prosthesis not affected by ochronose.

Clinical discussion: Alkaptonuria is caused by lack of the enzyme homogentisic acid oxidase, is a rare autosomal recessive disease leading accumulation of homogentisic acid in connective tissue. This leads to many manifestations such as urinary, cardiac, dermatologic, ophthalmologic or musculoskeletal symptoms. Deposit of Homogentisic acid in articular cartilage gives the characteristic black or dark brown pigmentation of the cartilage. Its clinical traduction is symptomatology of degenerative modifications in multiples joints such as knee, shoulder or hip beside the lumbar spine arthrosis.

Conclusion: Alkaptonuria is a very rare condition. Revealed by its orthopedic features is exceptionally. The patients, generally, need articulations replacement and the illness have no effect on its prognosis.

1. Introduction

Alkaptonuria is an autosomal recessive disease due to lack of the enzyme homogentisic acid oxidase. Homogentisic Acid (HA) is in the metabolism pathway of phenylalanine [1]. The lack of Homogentisic Acid Oxidase leads to accumulation of HA in connective tissue. This leads to increased vulnerability in articular cartilage [3] with degenerative change. The incidence of Alkaptonuria is 1/250000 to 1/1000000 [1,3,4] depending on studies and is more common in Slovenian and Dominican population [5]. Gender-ratio is equal to 1 [5]. Clinical manifestation can go from dark urine [6] to dark pigmentation of the skin or the sclera, urinary lithiasis, renal failure or hypertension [2]. The most commonly affected joints are knee and spine joints [5]. The musculoskeletal symptomatology begins generally in the fourth decade [5]. We reported a case of a 50 year-old man who had ochronotic arthropathy and degenerative changes in knee joint and who was treated with total knee arthroplasty. This case report has been reported in line with the SCARE Criteria [7].

2. Case report

A 50 year old man presented to our outpatient clinic with bilateral knee pain. Pain was exaggerated with effort and decreased with rest. The patient had no medical history nor allergies. He suffered also from occasional lumbar spine pain and had...
Fig. 1. Cervical spine radiograph.

Fig. 2. Lumbosacral spine radiograph.
Fig. 3. Standing anteroposterior radiograph of both knees.

Fig. 4. Lateral radiographs of both knees.
diminished walking distance without taking any medication so far.

Physical examination showed genu valgum, bilateral diffuse knee swelling and tenderness, right Baker's cyst. Palpation of both knees showed pain in the lateral tibiofemoral joint line. Examination also revealed a rigid lumbar spine.

Laboratory investigations showed that the patient had no renal failure with Urea = 6.9 mmol/l (normal between 2.8 and 7.2 mmol/l). Erythrocyte sedimentation rate was normal within first hour 5 mm (normal <15 mm). Bacteriological examination of urine showed a little cloudy aspect with presence of calcium oxalate crystals.

Cervical spine radiographs showed signs of cervical arthrosis (Fig. 1). Lumbosacral spine radiography showed important intervertebral disk narrowing and calcification with osteal bridges between adjacent vertebral bodies (Fig. 2).

Anteroposterior and lateral radiographs of both knees (Figs. 3, 4) showed narrowed joint space more significant in the lateral tibiofemoral joint with condensation in subchondral bone and osteophytosis.

Telemetric view of lower limbs (Fig. 5) showed a bilateral genu valgum.

The intervention was performed by a senior orthopedic surgeon in an orthopedic surgery department of a university hospital in Tunisia.

While performing the total knee arthroplasty for our patient, we discovered intraoperatively black coloration of the articular cartilage of the knee (Fig. 6).

The urine coloration of the patient was black.

The diagnosis of alkaptonuria was confirmed by the detection of a significant amount of in the Homogentisic Acid urine.

This way no adjuvant treatment was recommended.

At 6 months follow up, the patient is satisfied with the result with no knee pain in the treated knee. Range of knee movements was from 0° in total extension to 100° of flexion. Radiological control showed a stable prosthesis not affected by ochronose (Fig. 7).

The patient was able to walk and do all her usual activities with no pain nor discomfort.

The patient avoided physical stress to the spine and large joints (including heavy manual labor or high-impact sports) to try to reduce progression of severe arthritis.

As Alkaptonuria was an recessive autoosomal disease, we evaluated apparently asymptomatic older and younger siblings of the patient in order to identify as early as possible those who would benefit from preventive measures to help preserve overall joint mobility and function and no relative were affected. We did not perform a genetic test for the family of the patient.

3. Discussion

Although the term Alkaptonuria was first used in 1859 by Boedeker to describe urine discoloration, the earliest described case of ochronosis goes back to 1500 B.C in an Egyptian mummy [10]. Alkaptonuria is caused by lack of the enzyme homogentisic acid oxidase, is a rare autosomal recessive disease leading accumulation of homogentisic acid in connective tissue. This leads to many manifestation such as urinary, cardiac, dermatologic, ophthalmologic or musculoskeletal ones. Deposit of Homogentisic acid in articular cartilage gives the characteristic black or dark brown pigmentation of the cartilage. Its clinical traduction is symptomatology of degenerative modifications in multiples joints such as knee, shoulder or hip beside the lumbar spine arthrosis. Symptomatology usually appears in the fourth decade. This Delay may be explained by the efficiency of the renal tubular excretion until that age [10].

No specific treatment is known of ochronotic arthropathy. Symptoms can be managed through pain medication. Physical therapy can also be helpful but only temporarily [2]. Some authors use ascorbic acid (vitamin C) [8,11] for its antioxidant effect with no proven result [12]. Nitisone [13] can be also used due to its role in the phenylalanine and tyrosine metabolic path [2] but if used it should be in early ages before
Fig. 6. Clinical images before osteotomy, and after osteotomy
Black coloration of femoral and tibial cartilage and synovium.

Fig. 7. Postoperative knee radiography.
the beginning of the deposits in connective tissue [12]. Total arthroplasty seems to be the more effective treatment of ochronotic arthropathy after which the patient joins the population of people who had total arthroplasty since alkaptonuria has no effect on prosthesis [5,14].

4. Conclusion

Alkaptonuria is a very rare condition. Revealed by its orthopedic features is exceptionally. The patients generally needs articulations replacement and the illness have no effect on its prognosis.

Patient consent statement

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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CRediT authorship contribution statement

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Declaration of competing interest

None.

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