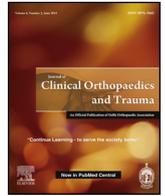




Contents lists available at ScienceDirect

Journal of Clinical Orthopaedics and Trauma

journal homepage: www.elsevier.com/locate/jcot



Case report

Arthroscopic diagnosis and treatment of shoulder ochronotic arthropathy – A case report

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ARTICLE INFO

Article history:

Received 30 July 2016

Received in revised form 5 November 2016

Accepted 17 November 2016

Available online xxx

Keywords:

Ochronosis

Shoulder

Arthroscopy

Alkaptonuria

ABSTRACT

Alkaptonuria is a rare inherited metabolic disorder, caused by the deficiency of homogentisate 1,2 dioxygenase enzyme. The three major features of alkaptonuria are the presence of homogentisic acid in urine, ochronosis (bluish-black pigmentation in connective tissue) and arthritis of the spine and large joints.

We present a 48 years old female presented with pain, restriction of movements of right shoulder. Arthroscopy was suggestive of ochronotic arthropathy. The definitive diagnosis of ochronosis was subsequently confirmed by laboratory and pathologic evaluation.

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1. Introduction

Alkaptonuria is a rare genetic disorder caused by deficiency of homogentisate 1,2-dioxygenase (HGD) leading to failure in processing of amino acids phenylalanine and tyrosine, thus causing accumulation of an intermediate substance homogentisic acid (HGA) in blood and tissues. This HGA and its oxidated form *alkapton* are excreted in urine leading to darkening of urine on long exposure to air. HGA oxidizes to benzoquinone acetic acid, which in turn form melanin like polymer which is deposited in collagen causing ochronosis. This leads to damage to cartilage which causes early joint destruction and painful degenerative arthritis involving knee, spine and shoulder.

We present a patient presented with shoulder pain and stiffness, who was diagnosed as a case of ochronosis on shoulder arthroscopy.

2. Case report

A 48 years old female presented with pain and limitation of movements in the right shoulder for 3–4 months duration which gradually worsened with time. Her activities of daily living were

severely affected and she was unable to get sound sleep because of pain. She took analgesics regularly but was unable to get satisfactory relief of symptoms. She also had mild pain in her both knees and left shoulder.

On clinical examination, significant wasting was seen around shoulder. Diffuse tenderness was present all around the shoulder. Active shoulder movements were painful and grossly restricted. Passive range of motions was: abduction of 60°, forward flexion of 80°, external rotation of 10°, and internal rotation up to gluteal area (30°).

Laboratory tests including complete blood counts, ESR, CRP, Serum uric acid were normal and RA factor, HLA B27 were negative. Radiograph of right shoulder showed superior migration of the humeral head, decreased joint space and degenerative changes in the humeral head (Fig. 1). MRI of the right shoulder demonstrated joint effusion, synovial thickening, articular erosion and flattening of the humeral head possibly because of chronic inflammatory process with degenerative changes (Fig. 2).

Non-operative treatment in the form of NSAID and rehabilitation followed by local corticosteroid injection failed to improve the symptoms. Hence it was decided to go ahead with an arthroscopic examination.

Arthroscopy of the right shoulder was performed under general anaesthesia in using standard posterior and anterior portals. Dark brown-black, soot like pigmentation of the synovial tissue and cartilage was noted. Also there was erosion of the glenoid, labrum and humeral head, synovial hyperplasia and osteochondral loose bodies in the joint (Fig. 3). Debridement of the hypertrophied

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Fig. 1. Radiograph of right shoulder showing superior migration, decreased joint space and degenerative changes in the humeral head.



Fig. 2. MRI of the right shoulder demonstrated joint effusion, synovial thickening, articular erosion and flattening of the humeral head possibly because of chronic inflammatory/infective process with degenerative changes.

synovium and pathological tissue along with removal of loose bodies was done. A biopsy of synovium and frayed tissue was taken. Postoperatively, the patient was given cuff and collar sling for two days and rehabilitation was started.

Based on arthroscopic findings, provisional diagnosis of alkaptonuria was thought and patient re-evaluated in light of

fresh findings. Clinically, she showed blue discoloration of the auricular cartilage (Fig. 4), kyphoscoliosis of the dorsolumbar spine, thickening and tenderness in left Achilles tendon. Radiographs of spine revealed narrowed disc spaces with wafer like horizontal bands of calcification of each space (Fig. 5). The knee joint radiographs showed gross narrowing of the joint space

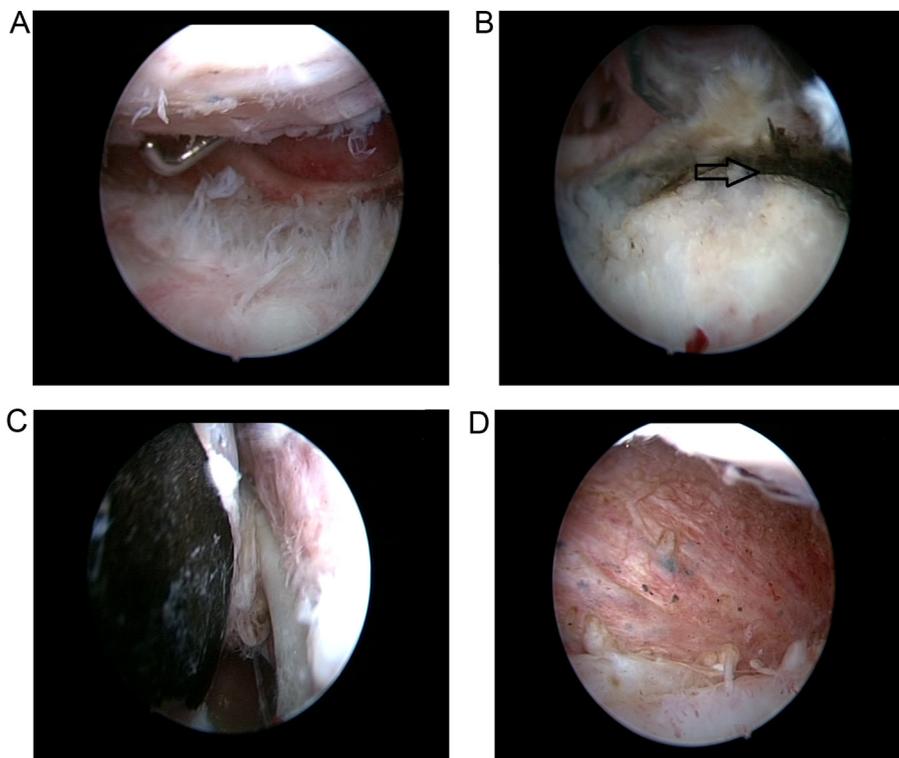


Fig. 3. (A) Arthroscopic view of the right shoulder showing erosion of glenoid and head. (B) Arthroscopic view of the right shoulder showing pigment behind anterior and superior labrum. (C) Arthroscopic view of the right shoulder showing pigment over posterior superior part of head. (D) Arthroscopic view of the right shoulder showing pigmentation of anterior capsule and labrum.



Fig. 4. Auricular cartilage showing bluish discoloration.



Fig. 6. Radiograph of knee joint showing diminishing of joint spaces.



Fig. 5. Radiograph of dorsal and lumbar spine showing narrowed disc spaces with wafer like horizontal bands of calcification of each space.

(Fig. 6). Her urine turned dark on long exposure to air. Her mother also had similar symptoms of multiple joint pains. Darkening of urine was also noted in other members of family.

Histopathologic examination of the synovial tissue showed nonspecific inflammation with focal coarse brown-black pigmentation which was negative for Iron stain (Fig. 7). Urine examination showed presence of HGA, thus confirmed the diagnosis of alkaptonuria.

She was advised low protein diet, ascorbic acid and gentle physiotherapy. Her symptoms of pain and stiffness in right shoulder started to improve. At one year after the arthroscopy, her pain VAS score improved from 8 to 3, while forward flexion from 30 to 115°, abduction from 20 to 95°, internal rotation from 30 to 50° and she is able to do her daily activities with little pain.

3. Discussion

In 1584, Scribonius reported a case of a young boy whose urine became dark when exposed to the air.¹ Boedeker in 1859 noted that this reaction can be accelerated by alkalinizing the urine hence he named the disease alkaptonuria,² from the Arab alqaliy (alkaline) and the Latin capere (take in). The term 'okronosis' (from Greek okhros, yellow and nosos, disease) has been used for the first time by Virchow³ to describe the dark-yellow colour taken by the tissue imbued with HA when treated with hematoxylin-eosine. In 1908, Sir Archibald Garrod had proposed that alkaptonuria was an inborn error of metabolism and the genetic defect for the enzyme was mapped to long arm of 3rd chromosome (3q21–q23) in 1996 [4].

HA displays a high affinity for collagen in the connective tissue. This leads to a progressive deposition of HA, as dark-bluish pigment in those tissues in which collagen is present in large concentrations, like the skin and the cartilage.⁵

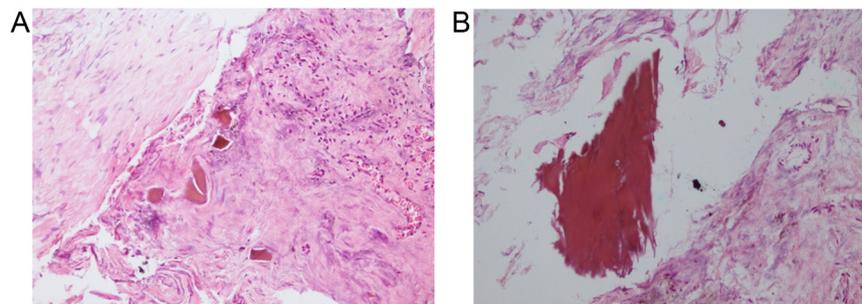


Fig. 7. (A) and (B) Histopathology of synovial tissue showing nonspecific inflammation with focal coarse pigmentation.

Clinically, the first sign is the presence of dark spots in diapers and underwears of the affected children. The patients suffering from this disease are usually asymptomatic till 4th Decade of the life, when they present with arthritis of large joints or as low back pain with stiffness.⁶ The arthritis is usually severe making the patient crippled with pain.

The radiological features in the joints include loss of joint space, subchondral bone sclerosis with few cystic lesions, no osteophytes and fragmentation, calcification of loose bodies. In the spine features are compression, narrowing and calcification of disc spaces. In the shoulder there is calcification of the cartilage tissue, increased density in the subchondral region with scattered areas of osteoporosis. The articular surface become irregular, the joint space becomes narrowed, asymmetrical, marginal osteophytes develop and flattening of humeral head is seen.

The extraarticular manifestations includes pigmentation of the ears, sclera and skin, darkening of urine after long exposure to air, aortic stenosis, nephrocalcinosis and renal failure,⁷ prostatic calculi, calcification of costal cartilage with an irregular spotty appearance.⁸ Laboratory investigation – shows elevation of urinary HGA excretion by a factor of 100–600.

The differential diagnosis of this disease includes mainly osteoarthritis, rheumatoid arthritis, ankylosing spondylitis and calcium pyrophosphate arthropathy. Discal calcification in the spine can also mimic hyperparathyroidism, haemochromatosis, amyloidosis, diffuse idiopathic skeletal hyperostosis (DISH).⁶

Unfortunately, currently there is no specific treatment available for the disease. Management is usually conservative which include reduction in protein intake and vitamin C has been used with limited success. Nitisinone – a triketone herbicide that inhibits 5-hydroxy phenylpyruvate dioxygenase by rapid, avid binding is under evaluation for long-term efficacy, and ophthalmic, neurologic, dermatologic complications.⁸ Sometimes, ochronotic arthropathy leads to rapid destruction of the articular surface and the need of salvage surgery in the form of total joint replacement [9].

Few case reports of arthroscopy in ochronotic joints including knee⁹ and shoulder^{9,10} have been published with excellent symptomatic relief achieved in follow-ups. In our case the debridement of the degenerated tissue on humeral head, the removal of hypertrophic synovium and loose bodies resulted in excellent pain relief and improvement of shoulder range of motion.

4. Conclusion

Arthroscopy is a valuable procedure to be used as an adjunct in the diagnosis of ochronosis. Arthroscopy is also a useful therapeutic tool in patients affected by ochronotic arthropathy for improving symptoms and range of motion.

Conflicts of interest

The authors have none to declare.

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