Ochronotic arthritis of knee

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ABSTRACT

Ochronotic arthropathy of the knee is a common manifestation of alkaptonuria and may present before symptoms of spondylitis. The joint disease can be rapidly progressive and crippling, necessitating early total joint replacement. The clinical features of this inborn error of metabolism are often overlooked and hence remain undiagnosed until the onset of spondyloarthropathy.

Keywords: Ochronosis, alkaptonuria, arthritis.

Ochronosis is a condition in which a black melanin-like pigment is deposited in the connective tissues due to an inherent disorder of tyrosine metabolism. We report here a patient with ochronosis who presented for the first time with left knee swelling and pain at the age of 50 years, with minimal radiological changes, but then rapidly progressed to gross degenerative arthritis during the span of 2 years.

Case Report. A 50 year old laborer presented with progressive pain and swelling of the left knee of 1 year duration. The pain was aggravated by movements of the joint and his walking distance was reduced to about 100 yards. The pain was only partially responding to NSAIDs. There was no associated locking or giving way, nor any fever, chills or urinary symptoms. There was no history of low back pain, hip or abdominal pathology or any past history of tuberculosis or trauma to the knee. He was born of consanguineous marriage with no history of arthritic problems in any family member.

On examination, the patient was afebrile. Both eyes showed black scleral pigmentation. Left knee was grossly swollen warm tender with moderately tense effusion. There was no ligamentous laxity. There was moderate wasting of left quadriceps muscle. Extension was full and flexion limited to 90 degrees due to pain. Hip movements were normal. The lumbar spine showed normal lordosis and was not tender, but movements were about 60% of normal.

Investigations were as follows: WBC 17,700/mm3 with neutrophil leucocytosis, coagulation screen normal. ESR 110mm/hr. C-Reactive Protein 24mg/l, rheumatoid factor and ASO titre negative, serum uric acid 2.5mg%. X-rays of both knees showed moderate degenerative changes. The knee aspirate was a turbid transudate; microscopy did not show any crystals and culture (including AFB) was negative. Because of the persistent swelling and pain, partial synovectomy was carried out. The histologic picture was suggestive of ochronosis with brownish staining of the cartilage tissue with hematoxylin and eosin while giving negative results for melanin and iron staining (Figure 4). Urine screening by silver nitrate reduction test was strongly positive for homogentistic acid (HGA). X-rays of the lumbar and thoracic spine showed degenerative changes and calcification of the invertebral discs.
The symptoms improved significantly following partial synovectomy and further conservative treatment was continued for a short while with physiotherapy, NSAIDs and ascorbic acid. The patient was subsequently lost to follow up until 2 years later when he returned with increasing pain and swelling of the left knee. His mobility was severely restricted due to pain and he had to abandon his job. The left knee was swollen and painful on movements. There was loss of extension by 15° with flexion to 60°. There was no ligamentous instability. Movements showed severe patellofemoral and tibiofemoral crepitus. X-rays of the left knee showed marked destruction of the articular surfaces and subchondral cyst formation (Figure 1).

Discussion. Alkaptonuria is an autosomal recessive disorder of tyrosine metabolism due to the absence of the gene responsible for the production of homogentisic acid oxidase. Homogentisic acid (2,5-dihydroxyphenylacetic acid) (HGA) produced during the metabolism of phenylalanine and tyrosine cannot be further metabolized and accumulates. It is excreted in the urine which, on standing is oxidized and turns black (alkaptonuria).\(^1\) The polymerization of homogentisic acid into a melanin like pigment and its deposition in the connective tissues result in the clinical syndrome of ochronosis.\(^2\) The term ochronosis was coined in 1866 by Virchow who described the pigment as having an ochre (yellow brown) color microscopically.\(^2\) The connective

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**Figure 1** - Showed marked destruction of the articular surfaces and subchondral cyst formation.

**Figure 2** - Showed wafer thin lines of calcification or ossification in the intervertebral discs.

**Figure 3** - The pathological feature showed at surgery and the black color of articular cartilage, synovium & joint capsule.

**Figure 4** - Ochronosis with brownish staining of the cartilage tissue with haematoxylin and eosin while giving negative results for melanin and iron staining.
tissues like cartilage, ligament, tendons, sclera and pinnae show a bluish black appearance. The pigment deposition in the intervertebral discs and articular cartilage can produce spondylosis and peripheral arthropathy resembling ankylosing spondylitis and osteoarthritis.³

Spondyloarthropathy is the most disabling manifestation of ochronosis.⁴ The arthropathy is due to pigment deposition in the articular cartilage leading to destruction of the joint. Knee, shoulder and hip are the joints commonly involved apart from the intervertebral discs.³ Arthritic complications are often severe and painful, crippling the patient. During the first 25 years of life, the symptoms are related to the urine turning dark on standing with the staining of the underpants (armpits etc.). By 35 to 45 years of age, these patients develop ochronotic spondylitis characterized by stiffness, low back pain, increasing rigidity and obliteration of the normal lumbar lordotic curve. The clinical picture is very similar to that of ankylosing spondylitis with dorsal kyphosis, loss of lumbar lordosis, flexed hips and knees and low back pain and stiffness. However, the radiological features are very different from the typical bamboo spine and sacroiliac joint changes of ankylosing spondylitis.⁶

The earliest radiographic change that is pathognomonic of ochronosis consists of wafer thin lines of calcification or ossification in the intervertebral discs (Figure 2). The most evident pathological feature is seen at surgery and is the black color of articular cartilage, synovium and joint capsule (Figure 3). Microscopy reveals HGA deposits in these tissues (Figure 4). Erosion of the articular cartilage is obvious in the areas of pigment deposition. Biochemically there is irreversible linkage of HGA with collagen, proteoglycans and other extracellular macromolecules. The mechanism by which the pigment induces the degenerative changes in the joint is not clear; it may be direct chemical irritation or indirectly through the generation of oxygen radicals by auto-oxidation of homogentisic acid.⁷ Maintenance of relatively high tissue concentration of ascorbic acid delays and possibly reduces the degree of pathologic change in the connective tissues. Ascorbic acid protects the lysyl hydroxylase from inhibition by sulphydryl binding agents, by maintaining the iron in the reduced form.

Our patient did not have any clinical symptom related to spondylosis. Diagnosis was reached after the synovial biopsy which showed histological evidence of ochronotic arthropathy.⁸ Urinary abnormalities of alkaptonuria are frequently overlooked. The dark skin complexion (racial) which made the skin pigmentation unnoticeable and the absence of any medical consultation until the onset of knee arthritis are the factors that caused the delay in diagnosis. Screening of other family members and offspring of this patient by urine test proved impractical as the rest of his families were abroad. Unlike rheumatoid arthritis, synovectomy has minimal effect in relieving symptoms or arresting progression of the disease and in retrospect, was unnecessary in this patient. Rapid progression with extensive destructive changes in the joint makes a total joint replacement the only remedial option.⁹

In conclusion, clinical manifestations of alkaptonuria may often be overlooked in early years until the patient develops symptoms of spondyloarthropathy. Arthropathy of major weight bearing joint can be the first manifestation of ochronosis. The disease can be disabling and rapidly progressive necessitating early total joint replacement.

Reference


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