Case Report

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A Rare Case Report of Ochronotic Arthritis

Balasundararajan Uma[*], Ganapathy Shivashekar[**], Kalaivani Amit Kumar[***], Bhuvanamha Devi Ramamurthy[****]

*Postgraduate **Professor and head ***Associate Professor ****Assistant Professor, Department of Pathology, SRM Medical College and Research Centre, Chennai,Tamil Nadu.

Abstract

Introduction: Alkaptonuric ochronosis is a rare autosomal recessive metabolic disorder resulting from deficiency of homogentisic acid oxidase enzyme leading to deposition of homogentisic acid in various tissues of the body (ochronosis). The most common clinical features are arthritic changes in weight-bearing joints, lumbosacral degenerative disc disease, dark brown discoloration of urine on air exposure, ocular and cutaneous pigmentation, coronary and valvular calcification and renal calculi formation. Histopathological examination from cutaneous/bony lesion is confirmatory. *Case History:* 52 year old female sustained a stress fracture of the right femoral neck, necessitating surgical repair, which showed black pigmentation of the femoral head and glenoid labrum. On examination pigmentation of the sclera and ear lobe was also noted. Further work up and histopathological examination with histochemistry confirmed it as a case of Ochronotic arthritis. *Conclusion:* The case is being presented for its rarity.

Keywords: Ochronosis; Homogetisic Acid Oxidase.

Introduction

Ochronosis or Alkaptonuria was named by Virchow in 1866 [1], an inborn error of metabolism with autosomal recessive pattern of inheritance [2]. There is a defect in the metabolism of homogentisic acid caused by a mutation in the homogentisic acid oxidase (HGO) gene on chromosome 3 q. Incidence is less than 1 in 2,50,000 to 1 million live births [1].The clinical manifestations are due to the accumulation of black pigment of polymerized form of homogentisic acid in various tissues of the body mainly in skin, cartilage and connective tissue.

Case Report

52 year old female had reported to the orthopedic out patient department with complaints of chronic vague, dull aching pain in the right hip for the past two years. She also gave history of trivial fall two weeks ago. No history of exogenous topical/ oral drug intake. Patient had no other co-morbidities. She gives no history of smoking / alcoholism.No significant family history was noted.

On general examination she was moderately built and nourished, greyish blue pigmentation of the sclera(Figure 1) and ear lobe (Figure 2) was noted. Systemic examination of central nervous system, cardiovascular system, respiratory system and abdomen were unremarkable.

No abnormality in posture was detected. Right hip joint showed tenderness with restricted range of motion. Straight leg raise test was restricted to 80 degrees.

X-ray of the bilateral hip joints showed lytic lesions with areas of sclerosis in articular surface of the right hip joint suggestive of chronic arthritis (Figure 3). Urine oxidation test showed blackish discoloration of urine after six hours of oxidation in air (Figure 4).

Corresponding Author: Balasundararajan Uma, E-904, Purva Swan Lake, Old Mahabalipuram Road, Kelambakkam, Chennai – 603103 Tamilnadu.
E-mail: umarajan_86@yahoo.co.in

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She underwent total hip replacement of the right hip and specimen was sent for histopathological examination.

Gross Findings

Head of femur (Right) measured 6.5x5x6 cm . It showed black pigmentation along the articular surface both on external surface and cut surface (Figure 5 and Figure 6).

Microscopic Findings

Multiple well defined ochre coloured deposits (Figure 7 and 8) were noticed interspersed with bony trabeculae, cartilage, hyperplastic synovial tissue, attached fibrovascular tissue and skeletal muscle fibers associated with partial replacement of articular cartilage and synovium by foreign body granulation tissue. Pigment laden macrophages with areas of calcification was also appreciated elsewhere. To confirm the findings and also to rule out other pigmentary lesions a panel of histochemical stains was done. Methylene blue was found to be positive highlighting the deposits (Figure 9) and other stains found to be negative were Perls prussian blue, Massons fonatana and Von geison to rule out haemosiderin, melanin pigmentation and collagen respectively (Figure 10,11,12).

Combining the clinical, radiological and histopathological findings the final impression was given as Ochronotic arthritis involving the right femoral head. Further evaluation of the patient included Echocardiography for cardiac lesions and USG abdomen which did not show any significant findings.

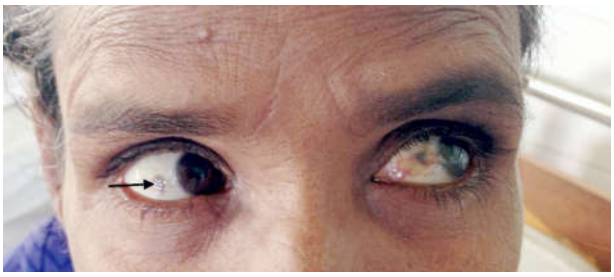

Fig. 1: Blackish scleral pigmentation

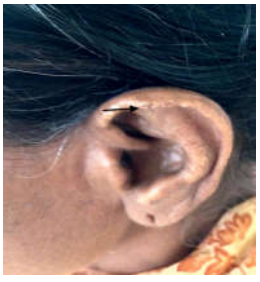

Fig. 2: Blackish pigmentation of ear lobe

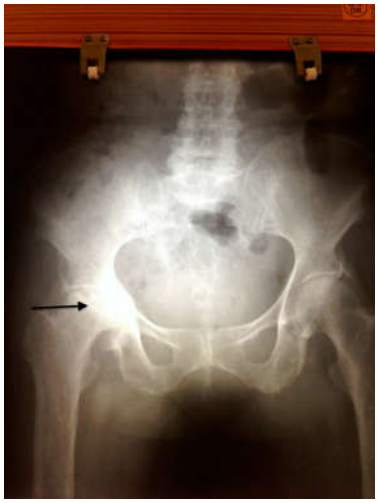

Fig. 3: X ray of hip joint showing lytic lesion in right hip

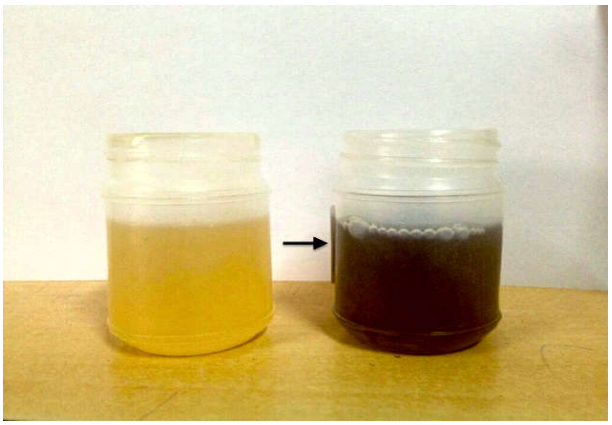

Fig. 4: Urine turns black on oxidation

Fig. 5: Blackish pigmentation on the head of femur

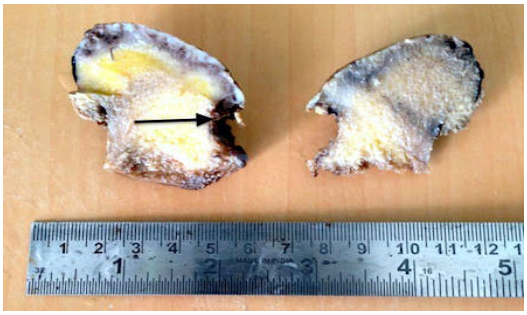

Fig. 6: Cut surface of femoral head showing blackish pigmentation of neck of femur

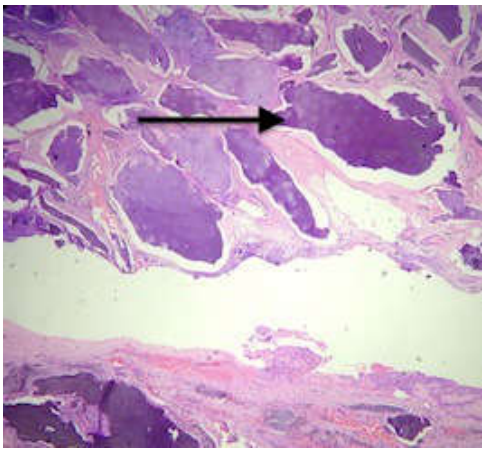

Fig. 7: Ochre coloured deposits on haematoxylin and eosin, 400x

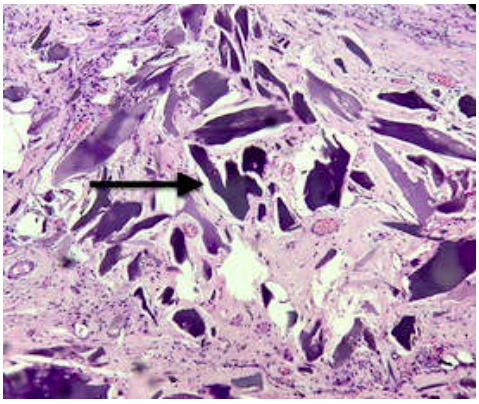

Fig. 8: Ochre coloured deposits on haematoxylin and eosin,400x

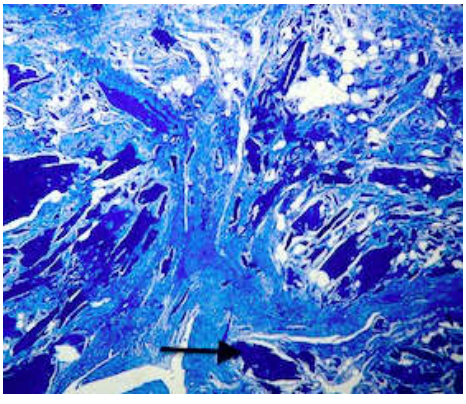

Fig. 9: Methylene Blue stain highlighting the deposits, 400x

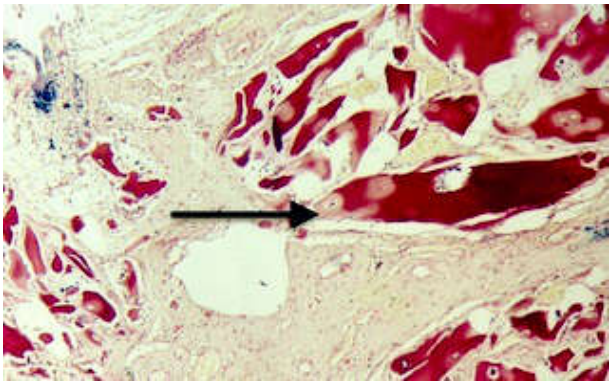

Fig. 10: PerlsPrussion blue stain negative in deposits, 400x

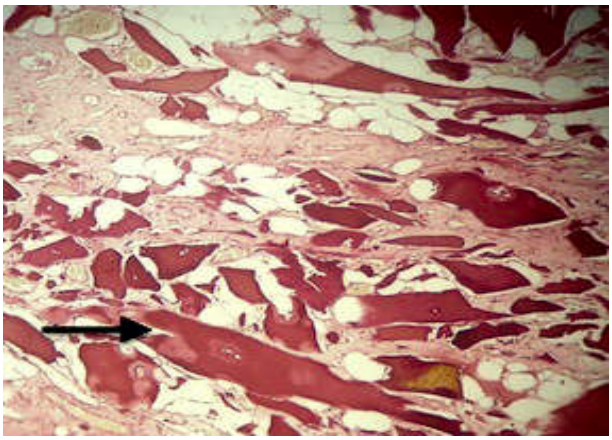

Fig. 11: Masson's Fontanna stain negative in deposits, 400x

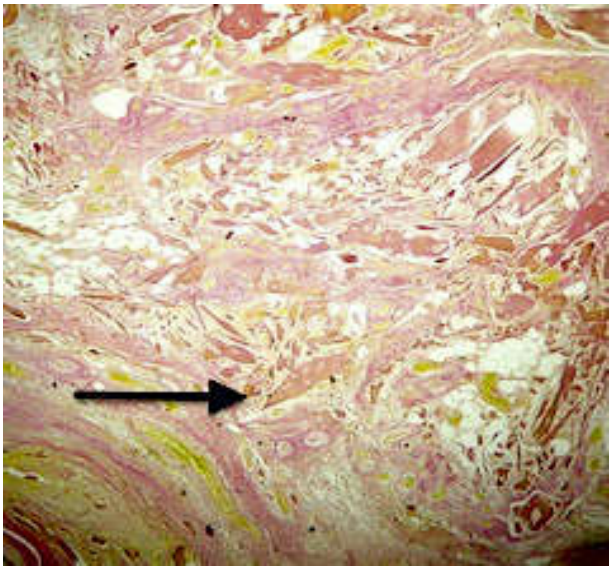

Fig. 12: Von Geison stain negative in deposits, 400x

Discussion

Ochronosis is also referred to as Alkaptonuria and is an inborn error of phenylalanine metabolism [3]. "Alkapton" is an Arabic word which means to suck up oxygen by alkali, based on the findings seen in the

patients where the urine in alkaline condition on oxidation turned black [3]. Ochronosis is generally seen in the 4th to 5th decade of life (our case 52 years of age) with slight male predominance. Since homogentisic acid has a high renal clearance (400-500 microns/ml) and low plasma levels(50 – 400 micromol/ml) it takes nearly 20 to 30 years for the manifestations to occur [4]. The pathogenesis of disease shows pigment deposition, induces an inflammatory reaction which is superadded with dystrophic calcification [5]. The colour of the pigment is brownish yellow (ochre) when viewed on the haematoxylin and eosin slides

The first case was diagnosed by Boedker in 1859 [4]. Usual clinical presentation is with lumbosacral degenerative disease which mimics ankylosing spondylitis and osteoarthritis . There is a triad of clinical presentation which includes homogentisic aciduria, pigmentation of connective tissue and degenerative ochronotic arthropathy. Other features are pathological fractures, calcification and stenosis of aortic valve, renal calculi with ochronotic nephropathy and connective tissue pigmentation [4]. It is of two types-Exogenous and Endogenous [6]. Exogenous ochronosis is due to prolonged exposure to drugs like antimalarials and hydroquinone. Endogenous ochronosis is the result of HGO deficiency. To diagnose the disease with only clinical and radiological features is difficult, hence confirmation with biochemical and histopathological examination is mandatory. The diagnostic workup includes urine oxidation test and silver nitrate test (qualitative assay) along with other routine investigations like complete blood count, renal function test, serum calcium and phosphorous, alkaline phosphatase, C reactive protein, X ray of the spine and pelvis, ECG and Echocardiogram.

There is no definitive treatment for Ochronosis, currently the treatment is only symptomatic which includes pain reduction and physiotherapy and conservative treatment using low protein diet, high dose vitamin C and Nitisinone have proved to be beneficial [1]. Total joint replacement helps reducing pain and increasing joint activity [7]. Tendon repair is the treatment of choice in cases of tendon rupture [2]. Nitisinone is a drug that inhibits hydroxyl phenyl pyruvate which is an enzyme involved in the conversion of hydroxyl phenylpyruvate to homogentisic acid. It is presently used in the treatment of type 1 herditary Tyrosinemia. Less is known about its advantage in the treatment of alkaptonuria.

Conclusion

The case is being reported for its rarity. The case report also emphasizes on the salient clinical features, various diagnostic modalities available to clinche the diagnosis at the earlier stage. Though no specific treatment is available, conservative management with regular follow up can improve the quality of life.

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