Alkaptonuric Ochronosis

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Abstract

Alkaptonuria is an autosomal recessive metabolic disorder characterized by joints and spine involvement, ochronosis and presence of homogentisic acid in urine and its deposition in cartilage, intervertebral disc and other connective tissues, leading to disabling arthritis in elderly individual.

Introduction

Alkaptonuria (AKU) is a rare, autosomal recessive congenital metabolic disorder, characterized by accumulation of homogentisic acid (HGA) in blood and tissues. Patients may remain asymptomatic with black discoloration of urine on exposure to air or may have disabling arthritis of axial skeleton. Slate blue discoloration of sclera, face, pinna or oral mucosa is also the feature of this disorder.

Herein, we report a rare case of AKU who presented to the Rheumatology Clinic of our hospital.

Case Report

A 50 year old female presented with complaints of back pain for approximately 13 years. The pain was localized to lumbar region and was gradual in onset and progression, non-radiating and was aggravated on movement and relieved by rest. There was no history of trauma, morning stiffness or any local deformity. On examination the patient was found to have black coloured spots on sclera on the medial as well as lateral side of cornea with black discoloration of skin of the face (Figure 1) and pinna (Figure 2). There was no evidence of any local tenderness or deformity of spine. On investigation her haemoglobin, ESR, leukocyte count and platelet count were within normal limits. Blood glucose, liver, kidney and thyroid tests were normal. X-ray of the lumbar sacral spine revealed multilevel intervertebral disc calcification (Figure 3).

On the basis of chronic backache, black spots on sclera, black discoloration of pinna and intervertebral disc calcification, a provisional diagnosis of ochronosis was made. The diagnosis was confirmed by positive urine test for HGA. Patient was treated symptomatically with analgesics, physiotherapy and tablets of vitamin C 500mg twice daily.

Discussion

Alkaptonuria (AKU) is a rare (1:250,000 to 1 million live-births, male:female 1:1) autosomal recessive congenital metabolic disorder.¹ It results from a gene mutation. Pollak et al used homozygosity mapping to locate the alkaptonuric gene to chromosome 3q 2 in a 16 centimorgan
region. This mutation results in deposition disease (Table 1).

Alkaptonuric patients are usually, asymptomatic as children or young adults. The earliest sign of the disorder is the tendency for diapers to stain black. In the fourth decade of life, external signs of pigment deposition, called ochronosis, begin to appear. The slate blue, gray, or black discoloration of sclerae and ear cartilage is indicative of widespread staining of the body tissues, particularly cartilage. Pigmentation may also be seen in the teeth, buccal mucosa, nails or the skin, as a dusty coloration.

Arthritis is the only disabling effect of this condition, and occurs in almost all patients with advancing age. It is a progressive, degenerative type of arthritis with a waxing and waning course. It may resemble crystalline arthritis with a waxing and waning course. The most commonly affected joints are hips, knees, shoulders and intervertebral discs (particularly at the thoracic and lumbar levels, in about 50% cases). Typically, significant back pain begins from the age of 30 years. Achilles tendon involvement is also common and may result in tearing.

Rarely cardiovascular (valvular dystrophic calcification, aortic stenosis, coronary arteries calcifications) genitourinary (kidney stones, ochronotic nephropathy) involvement may occur.

The treatment includes symptom relief (analogesics and physiotherapy) along with anti-osteoporotic therapy. Mild antioxidant nature of ascorbic acid helps to retard the process of conversion of homogentisate to the polymeric material that is deposited in cartilaginous tissues, therefore Vitamin C is recommended in older children and adults. Dietary restrictions of food containing phenylalanine and tyrosine have proved to be successful in alleviating the symptoms and reducing HGA excretion. Nitisinone (Orfadin), a potent inhibitor of 4-hydroxyphenylpyruvate dioxygenase, remarkable tolerability and biochemical efficacy in reducing production and urinary excretion of HGA.

In conclusion, AKU a metabolic disorder, though not life threatening, disability and pain forms the major complaint of these patients. Arthritis can be treated symptomatically. Surgical intervention might be necessary in advanced stages.

References


Table 1: Causes of intervertebral disc calcification

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<thead>
<tr>
<th>Category</th>
<th>Causes</th>
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<tbody>
<tr>
<td>Degenerative</td>
<td>Ochronosis (nucleous pulposus calcification)</td>
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<td>Ankylosing spondylitis</td>
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<td>Hemochromatosis</td>
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<td>Pseudogout (calcium pyrophosphate dihydrate deposition disease)</td>
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<td>Hyperparathyroidism</td>
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<td>Amyloidosis</td>
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