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Case Report

Biochemistry Section

Myocardial Infarction with Alkaptonuria: A Case Report

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ABSTRACT

Alkaptonuria is an autosomal recessive disorder due to deficiency of homogentesic acid oxidase, an important enzyme in the catabolism of aromatic amino acids. Homogentesic acid is finally converted to fumarate and acetoacetate. Reduced activity of this oxidase causes accumulation of homogentesic acid in the cells and body fluids. Here we describe an interesting case of alkaptonuria in a 50-year-old man, previously diagnosed as osteoarthritis who succumbed to myocardial infarction, which is one of the complications of alkaptonuria.

Keywords: Alkaptonuric patient, Ankylosis, Homogentesic acid

CASE REPORT

A 50-year-old male patient was admitted with pain in the shoulders, knees and hips. At the time of admission his blood pressure, pulse, Electrocardiogram (ECG), Pulmonary Function Tests (PFT) were normal. Routine haemogram, blood glucose and other clinical parameters were normal. He was diagnosed with osteoarthritis of pelvic joint for which he was advised surgery.

He was posted for total hip replacement under general anaesthesia. His general condition after surgery was good. But two weeks later, he developed difficulty in passing urine and his bladder was distended. His urine was noticed to darken on standing [Table/Fig-1].

The patient was investigated further to evaluate the cause of the darkening of urine. A transient blue colour was noticed on addition of 10% ferric chloride to a sample of the urine. The Benedict's test showed a dark brownish black precipitate. The silver nitrate test was positive. Thin layer chromatography of plasma and urine using cellulose acetate sheets in butanol, acetone, acetic acid and water (12:3:5) showed the presence of large amounts of homogentesic acid. Based on the presence of homogentesic aciduria, the patient was diagnosed as having alkaptonuria.

During the second week of his hospital stay the patient complained of excessive sweating and pain in the chest followed by restlessness. His pulse was feeble, but heart sounds and air entry was adequate. Emergency ECG showed inferior wall infarct and the cardiac monitor showed ventricular fibrillation. Intravenous xylocard was given and cardiac massage was done. Patient was intubated and ventilated. Inspite of all these efforts patient revival was not possible.

DISCUSSION

Alkaptonuria is a rare hereditary metabolic disorder in which urine darkens on standing due to the presence of homogentesic acid, a substance not normally found in urine [1]. It is characterised by a triad of homogentesic aciduria, arthritis and ochronosis. Although, asymptomatic during childhood, clinical manifestations such as large joint arthritis, black and ochronotic pigmentation of cartilage and collagenous tissue develop during later life [2].

The urine of an alkaptonuric patient appears normal on passing but darkens on standing due to oxidation and polymerisation of the homogentesic acid. This process is enhanced in an alkaline pH. Therefore, urine of an alkaptonuric patient does not darken, if it is acidic and hence goes undetected many times. As a result, diagnosis may be delayed until arthritis or ochronosis develops [2]. Hence, the patients commonly complain of arthritic symptoms involving spine, hips and knees.

Alkaptonuria is the first defined human genetic disease with recessive trait [3]. Alkaptonuria is a very rare condition, with an incidence of 1 in 2,50,000 to 1 in 10,00,0000 population. Very few cases are reported in India [4]. Alkaptonuria results from a hereditary deficiency of the enzyme homogentesic acid oxidase in liver and kidney. The gene is transmitted in an autosomal recessive fashion. Inability to convert homogentesic acid to maleylacetoacetic acid results in accumulation of the former. Homogentesic acid is subsequently converted to benzoquinone acetic acid and spontaneously polymerised. These polymers are deposited in the cartilage, causing damage and impairing its normal function [5].

Homogentesic acid is a strong reducing agent that produces a positive reaction with Fehling or Benedict reagent. Enzymatic spectrophotometry [6] and gas liquid chromatography [7] can be used to confirm the diagnosis of alkaptonuria. High pressure liquid chromatography is used for the quantitation of homogentesic acid and its derivative benzoquinone acetic acid [8]. Excretion of homogentesic acid in the urine is usually massive, and as much as 4 to 8 gm of this compound is excreted daily in the urine and very little is found in the plasma [9].

Arthritis occurs in almost all patients, seen with advancing age [10,11]. The large weight bearing joints like hips, spine and knees are the earliest to be involved. The characteristic changes in lumbar spine include narrowing of joint spaces and ankylosis of vertebral bodies resulting in marked restriction of movements.

[Table/Fig-1]: Gross appearance of normal urine and cola coloured urine of alkaptonuric patient.

A high incidence of heart disease in alkaptonurics, commonly due to mitral and aortic valvulitis has been reported [12]. Secondary calcification of the aortic valve may be so severe as to necessitate urgent aortic valve replacement [13]. Ischaemic heart disease with ultimate myocardial infarction is a common cause of death. There are reports of calcification and stenosis of the aortic annulus leading to coronary artery disease and the incidence of myocardial infarction is higher than normal in older patients with ochronosis [14]. Incidence of myocardial infarction is also increased later in life. Hence, a chest X-ray and electrocardiography is advisable to assess for any signs of myocardial insufficiency in all older patients with alkaptonuria.

Atherosclerosis and valve changes are documented in alkaptonuria. ECG alone will not help in detecting these abnormalities. Echocardiogram could have helped in this direction; however, it was not done in this patient as alkaptonuria was detected incidentally postoperatively and postmortem examination was not conducted as the patient's relatives did not give consent. Patient was not a known diabetic or hypertensive which is the major risk factors for myocardial infarction. Therefore, the patient could have succumbed to myocardial infarction as a complication of alkaptonuria.

Urinary tract infections, obstructions and finally failure are common in patients with alkaptonuria due to accumulation of homogentesic acid, which leads to the formation of renal calculi. Hence, a complete renal evaluation should be done so that the dosages of the drug can be modified according to the renal dysfunction [15]. Renal manifestation in this patient could be just a postoperative complication.

CONCLUSION

Alkaptonuria was diagnosed in our patient who had features of osteoarthritis and later died of myocardial infarction. So this brief case report emphasises the role of thorough cardiac workup in a patient with alkaptonuria, as there is high incidence of mitral and aortric valvulitis, ischaemic heart disease and myocardial infarction in these patients. A thorough cardiac workup could delay the complications and improve the life span.

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