Journal of
Cardio - Thoracic Medicine

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Ochronotic Heart Disease: A Case Report of Aortic Valve Replacement and Coronary Artery Bypass Grafting in a Patient with Alkaptonuria

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ARTICLEINFO

Article type:
Case Report

Article history:
Received: 22 December 2024
Revised: 29 December 2024
Accepted: 31 December 2024

Keywords:
Alkaptonuria
Coronary Artery
Ochronotic

ABSTRACT

Introduction: Alkaptonuria is an autosomal recessive genetic disorder that disrupts tyrosine metabolism, causing the buildup of homogentisic acid and its oxidized derivatives in tissues, including the heart, leading to potential health issues. Understanding Alkaptonuria pathophysiology and clinical manifestations is crucial for early recognition and appropriate management .

Case Report: A 53-year-old man with severe aortic stenosis (AS) and coronary artery disease is scheduled for coronary artery bypass grafting (CABG) and aortic valve replacement (AVR) surgery. After median sternotomy and cardiopulmonary bypass, the aortotomy showed black discoloration of the aortic wall and valve .

Conclusion: The patient's echocardiogram indicated very severe AS with thickened and calcified leaflets, moderate aortic regurgitation (AR), and mild mitral regurgitation (MR). The aortotomy revealed significant black discoloration of the aortic wall and valve, indicating a critical issue that demands immediate attention. These findings underscore the necessity for thorough preoperative assessment and careful perioperative management to improve outcomes.

► *Kahrom, M., Tabari, M., Rezaeian Deloei, S., Shaarbaf Eidgahi, E. Ochronotic Heart Disease: A Case Report of Aortic Valve Replacement and Coronary Artery Bypass Grafting in a Patient with Alkaptonuria. J Cardiothorac Med. 2024; 12(4): 1435-1438. Doi : 10.22038/jctm.2025.84836.1480*

Introduction

Alkaptonuria, a rare autosomal recessive disorder of phenylalanine and tyrosine metabolism caused by deficiency in homogentisate 1,2-dioxygenase activity, leads to accumulation of large amounts of homogentisic acid. This is reported to affect 1 in 250,000 individuals (1, 2). This condition often presents with distinctive clinical features, including joint and spine degeneration, dark pigmentation of the skin and sclera, and urinary excretion of homogentisic acid.

Alkaptonuria can also manifest as cardiovascular and ophthalmologic complications. Understanding the pathophysiology and clinical manifestations of ochronosis is crucial for its early recognition and appropriate management. In

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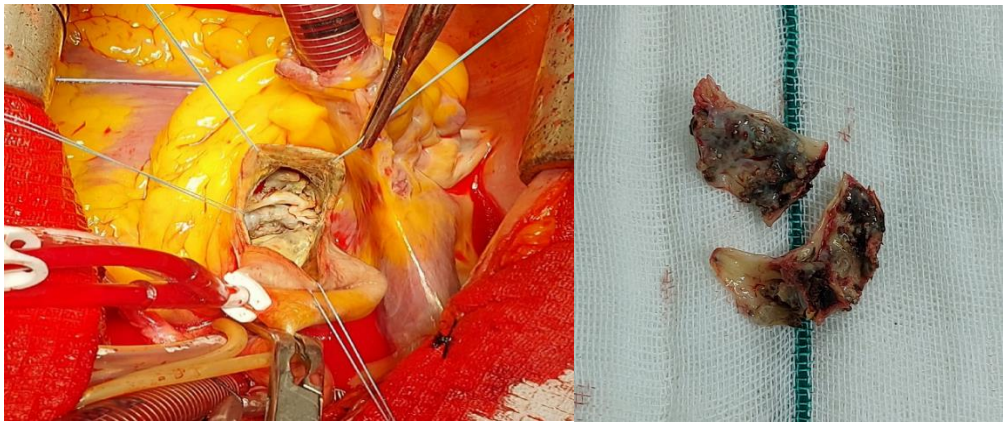
this case report, we present a patient with ochronosis and its implications in the context of a surgical intervention.

Case Reports

A 53-year-old man was diagnosed with severe aortic stenosis (AS) and coronary artery disease. He was a candidate for coronary artery bypass grafting (CABG) and aortic valve replacement (AVR) surgery. The patient had newly diagnosed hypertension and no significant past medical history. He was taking Amlodipine 5mg daily, Pantoprazole 40mg daily, and Alprazolam 0.5mg daily. The patient had no previous social history, anesthesia history, or surgical history. His METS score was under 4. Renal function indicators, such as urea and creatinine levels, were within normal ranges prior to the surgery.

Echocardiography revealed left ventricular ejection fraction (LVEF)=55-60%, mild diastolic dysfunction, moderate concentric left ventricular hypertrophy (LVH) with basal septal hypertrophy (15 mm), mild mitral regurgitation (MR), very severe AS (peak gradient=114 mmHg) with severely thickened and calcified leaflets resulting in restricted motion, moderate aortic regurgitation (AR), mild tricuspid regurgitation (TR), and mild perfusion index (PI). Angiography confirmed severe AS and significant obtuse marginal (OM) artery stenosis. ABG was normal. Upon arrival at the operating room, the patient was fully awake and received thorough monitoring, including invasive blood pressure measurement through a left radial artery arterial line. A 16-gauge (intravenous) IV access was promptly inserted. The patient's vital signs were as follows: blood pressure (BP): 115/75, pulse rate (PR): 78. Following preoxygenation, induction with Etomidate, Fentanyl, and Cisatracurium was expertly administered. Subsequently, a central venous line was inserted to ensure optimal care for the patient.

After the median sternotomy and establishment of cardiopulmonary bypass and cardioplegic arrest, the aortotomy was performed, revealing black discoloration of the aortic wall and valve (see Figure. 1). Aortic valve replacement with a mechanical St. Jude No. 23 valve, combined with partial septal myectomy and CABG using saphenous vein graft (SVG) to OM, was performed. Post-valve replacement echocardiography revealed peak and mean gradients of 20 and 13 mmHg, and LVEF of 55%. Also, During the procedure, the patient's eyes were carefully examined, revealing the presence of dark areas in the sclera (Figure. 2). The postoperative recovery was uneventful, and the patient was discharged home on the 6th day after the operation with satisfactory condition and a good target international normalized ratio (INR).



(a) (b)

Figure 1.(a) Intra-operative photo showing black discoloration of aortic wall and aortic valve leaflets after aortotomy. (b) Aortic valve leaflets after removal showing ochronotic black discoloration.

Figure 2. Ocular ochronosis

The aortic valve exhibited a change in color in the macroscopic view and fibromyxoid degeneration with multiple calcifications in the microscopic view It's important to emphasize that the postoperative echocardiogram and mean gradients following the surgery were within normal limits, indicating a successful outcome.In pathology, the aortic valve showed fibromyxoid degeneration and numerous calcifications, and it appeared discolored.

Discussion

Alkaptonuria is a rare metabolic disorder caused by a deficiency in the enzyme homogentisate 1,2-dioxygenase, leading to the accumulation of homogentisic acid (HGA) (3). The oxidized form of HGA can polymerize and deposit in connective tissues, causing a condition known as ochronosis. This deposition can lead to discoloration of tissues and is associated with various complications, including arthritis, heart disease, and renal problems (4).

In a separate case, a 70-year-old male patient was diagnosed of Alkaptonuria with AS and has been under observation for 4 years. The results of the echocardiogram indicate severe calcific aortic stenosis with an aortic transvalvular mean gradient of 51 mmHg. The innominate artery junction just below the innominate artery was replaced with a 24-mm Dacron tube graft. The anastomosis was performed using polytetrafluoroethylene (Teflon) felt on either side of the aorta. The deposition of HGA in joints, the aorta, and the base of the aortic valve suggests that areas of increased pressure or turbulence may be more prone to microvascular damage and subsequent ochronosis. This phenomenon could serve as an early indicator of cardiovascular complications in patients with alkaptonuria, potentially explaining the myocardial septal involvement observed in this patient, who has a history of hypertension (5).

In previous case reports and studies on ochronotic cardiovascular disease, it has been observed that older patients with alkaptonuria often exhibit aortic and intracardiac calcification, regardless of traditional cardiac risk factors. This discovery raises questions about the necessity of specialized cardiovascular screening in this population and the potential predictive value of age in identifying cardiovascular complications.

In another case report , mentioned the individual under examination is a 51-year-old man. Upon physical examination, severe knee osteoarthritis, thoracic kyphosis, and limited motion in the thoracolumbar spine were observed. Additionally, there was noticeable blue-black discoloration of both ears. Laboratory tests revealed the presence of mitral valve calcification. Furthermore, within the family, the patient's siblings also tested positive for a urinary condition (6).

The case of a 53-year-old man diagnosed with severe AS and coronary artery disease (CVD) presents several clinical challenges and considerations. The patient's comorbidities, including newly diagnosed hypertension (HTN), and the need for CABG and AVR surgery, emphasize the complexity of managing cardiovascular conditions in the presence of concurrent medical issues.

The patient's echocardiogram revealed a mixed valvular pathology, including very severe (AS) with severely thickened and calcified leaflets, moderate AR, and mild MR. These findings highlight the importance of thorough preoperative assessment and careful perioperative management to optimize outcomes.

The presence of moderate concentric LVH and mild diastolic dysfunction further complicate the patient's hemodynamic status. These factors could affect the patient's cardiac function during and after surgery, so close monitoring and tailored interventions may be necessary to reduce the risk of decompensation.

The patient's medication regimen includes amlodipine for controlling blood pressure, pantoprazole for protecting the gastrointestinal system, and alprazolam for managing anxiety. It is crucial to carefully assess the potential interactions and effects of these medications on perioperative hemodynamics, anesthetic requirements, and postoperative recovery to ensure the best perioperative management.

Conclusion

In conclusion, this case emphasizes the significance of a multidisciplinary approach involving cardiovascular specialists, anesthesiologists, and perioperative care teams to tackle the unique challenges presented by severe valvular heart disease alongside concurrent medical conditions. Close perioperative monitoring, customized anesthetic management, and proactive measures to optimize cardiac function are crucial to ensure positive surgical outcomes for patients with similar complex cardiovascular profiles.

The successful use of ochronotic venous conduits in bypass surgery for this patient showed no signs of deterioration in the postoperative follow-up. This suggests that such interventions can be safe and effective for patients with alkaptonuria. Nevertheless, more extensive research is needed to understand the long-term effects of alkaptonuria on cardiovascular health and the outcomes of cardiac surgery for this patient group.

This discussion emphasizes the crucial considerations and challenges involved in managing patients with severe valvular heart disease who undergo complex cardiovascular surgeries. It underscores the importance of a thorough preoperative evaluation, personalized anesthetic management, and careful intraoperative monitoring to improve patient outcomes.

Acknowledgements

This case report was obtained from a patient at Ghaem Hospital at Mashhad University of Medical Sciences.

Conflict of interest

The authors declare that they have no conflict of interest.

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