Case Reports

Ochronotic Involvement of the Aortic and Mitral Valves

in a 72-Year-Old Man

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Ochronosis, an autosomal recessive metabolic disorder, causes an excess of homogentisic acid that results in adverse pigmentation, calcification, and inflammation of cartilaginous and other tissues. Cardiovascular abnormalities are less frequently reported than are other manifestations. In rare cases, ochronosis can cause valvular heart disease. We report the case of a 72-year-old man with aortic stenosis and mitral insufficiency who was diagnosed with ochronosis while undergoing surgical aortic and mitral valve replacement. We discuss the history and surgical management of alkaptonuric ochronosis. ***(Tex Heart Inst J 2015;42(1):84-6)***

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Ochronosis is a rare metabolic disorder associated with a homogentisate 1,2-dioxygenase deficiency.[1] The transmission is autosomal recessive, and homogentisic acid (HGA) is the end product of the tyrosine and phenylalanine metabolism. Accumulated HGA is observed in connective tissue and in eliminated urine.[1] The usual clinical signs include arthropathy; manifestations affecting the ears, eyes, and skin; and genitourinary and cardiovascular complications. The accumulation of HGA can involve cardiac structures, especially the aorta, coronary vessels, and heart valves. In the elderly, the pericardium can be involved.[2] Pathologic examinations of the aortic valve and ascending aorta have revealed intracellular and extracellular deposits of ochronotic pigments. The extracellular deposits are, in part, degenerated cells that resemble valvular calculus.[3] Few reports have described ochronotic patients with severe cardiac involvement. We present the case of a man in whom ochronosis of the aortic and mitral valves was diagnosed intraoperatively.

Key words: *Alkaptonuria/complications/diagnosis/pathology; aortic valve/pathology; calcinosis/radiography; heart diseases/diagnosis; heart valve prosthesis implantation; homogentisic acid/urine; ochronosis/diagnosis/pathology*

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Case Report

In May 2013, a 72-year-old man who had severe aortic stenosis and mitral insufficiency presented at our clinic with dyspnea. He had no history of endocarditis or rheumatic fever. His medical history included progressive degenerative arthritis affecting his knees and spine, confirmed by means of musculoskeletal examination. Results of routine laboratory tests were normal. Echocardiograms revealed severely calcified aortic valve leaflets and a mean aortic valve gradient of 55 mmHg. The calculated aortic valve area was 0.5 cm^2. Mitral valve leaflet malcoaptation and grade 4/4 mitral insufficiency were detected. The patient's left ventricular function was normal. Cardiac catheterization yielded normal coronary arteries.

The patient underwent surgery to replace his aortic and mitral valves. A dark-green sternum was initially noted. The aortic and mitral valve leaflets, intima of the ascending aorta, and left ventricular outflow tract all contained black pigment (Fig. 1). Alkaptonuria was suspected. We replaced the native valves with a 25-mm mechanical aortic prosthesis and a 29-mm mechanical mitral prosthesis (Medtronic, Inc.; Minneapolis, Minn). The patient recovered uneventfully and was discharged from the hospital on postoperative day 10.

After surgery, the patient revealed that he had noticed dark discoloration of his urine since early childhood. Results of a general examination included black pigmentation of the sclera of both eyes and the cartilage of the outer ears (Fig. 2). Radiographs of the knees and spine showed calcification and severe degeneration of the vertebral discs.

Pathologic examination of the explanted native aortic and mitral leaflets revealed ochronosis (Fig. 3), and high HGA levels in the patient's urine confirmed the diagno-

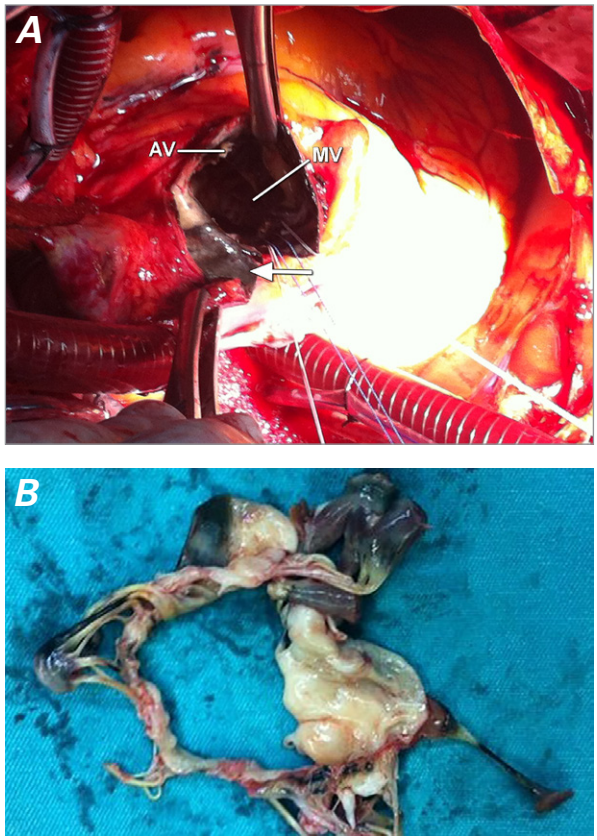


Fig. 1 *A) Intraoperative photograph shows black discoloration of the intima of the aorta (arrow). B) Photograph of operative specimen shows black discoloration of the mitral valve.*

AV = aortic valve; MV = mitral valve

sis of alkaptonuria (1,600 mmol/mol creatinine). There was no history of alkaptonuria in the patient's family.

Discussion

Alkaptonuria is a rare congenital metabolic disorder caused by a deficiency of HGA oxidase. This enzyme is responsible for the metabolic degradation of tyrosine that results in black discoloration of connective tissues.[1] The earliest verified case of ochronosis occurred in an ancient Egyptian.[4] The term alkaptonuria was first used in 1859 to describe urine discoloration caused by a reducing compound.[5] The compound was identified as HGA in 1891.[6]

Accumulated HGA causes a classical clinical triad: homogentisic aciduria, which presents at birth; the deposition of polymers of oxidized HGA in connective tissues, which leads to intensive pigmentation of the skin, sclera, and cartilage after 20 to 30 years of life; and degenerative ochronotic arthropathies, usually in the 4th decade of life. Another important but rarer consequence of alkaptonuric ochronosis is cardiovascular involvement. It is generally accepted that aortic valve stenosis is the most frequent cardiac manifestation of

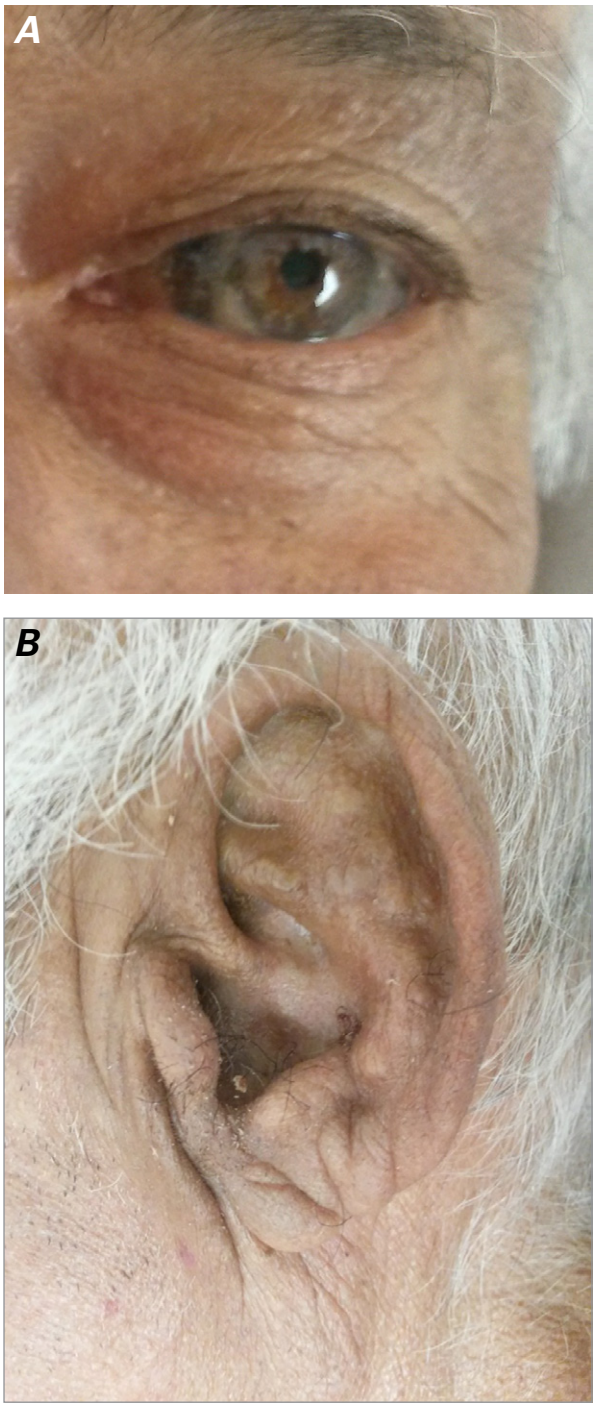


Fig. 2 *Photographs of the patient show ochronotic pigmentation of the A) sclera of the eye and B) outer ear cartilage.*

the disease; aortic and mitral regurgitation are less often diagnosed.[7] Our patient had aortic stenosis and mitral regurgitation.

Numerous investigators have suggested that cardiovascular calcification and stenosis are associated with pigment deposition in the aortic and mitral valves, endocardium, pericardium, aortic intima, and coronary arteries. Butany and colleagues[8] reported that the

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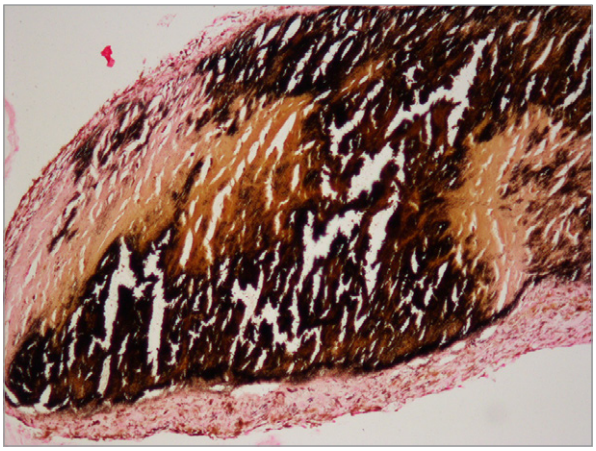


Fig. 3 *Photomicrograph of a section of valvular leaflet shows ochronotic pigment deposition (H & E, orig. ×100).*

pigmentation leads to an inflammatory reaction and to progressive valvular dysfunction. Some authors have reported that the site of ochronotic pigmentation is different from the site of calcification within the valve.

Gaines and Pai[3] suggested that ochronotic pigment in the aortic valve serves as a stimulus for dystrophic calcification that eventually leads to aortic valve stenosis. Mitral and tricuspid involvement does not seem to increase the prevalence of valvular disease; however, as in our patient, it might be that chronic ochronosis can cause leaflet thickening, calcification, and eventual mitral valve dysfunction.

In cardiac ochronosis, there is no consensus regarding the selection of prosthetic valves; the use of biological and mechanical devices has been described. We are unaware of any investigations into the optimal prosthetic valve for these patients. However, bioprostheses might degenerate over time because of ochronosis. For this reason, we used mechanical prosthetic valves in our patient.

Although cardiac ochronosis is rare, surgeons should be aware that they might be confronted with its typical signs during cardiac surgery for other conditions.

References

1. Phornphutkul C, Introne WJ, Perry MB, Bernardini I, Murphey MD, Fitzpatrick DL, et al. Natural history of alkaptonuria. N Engl J Med 2002;347(26):2111-21.
2. Cobos Soler FJ, Molero Cabrilla R. Ochronosis: a case report with multisystemic affectation, including pericardium [in Spanish]. An Med Interna 2002;19(11):583-5.
3. Gaines JJ Jr, Pai GM. Cardiovascular ochronosis. Arch Pathol Lab Med 1987;111(10):991-4.
4. Stenn FF, Milgram JW, Lee SL, Weigand RJ, Veis A. Biochemical identification of homogentisic acid pigment in an ochronotic Egyptian mummy. Science 1977;197(4303):566-8.
5. Boedeker C. Ueber das Alcapton: ein neuer Beitrag zur Frage: welche Stoffe des Harns können Kupferreduction bewirken [in German]? Z Ration Med 1859;7:130-45.
6. Wolkow M, Baumann E. Ueber das Wesen der Alkaptonurie [in German]. Z Physiol Chem 1891;15:228-85.
7. Gould L, Reddy CV, DePalma D, De Martino A, Kalish PE. Cardiac manifestations of ochronosis. J Thorac Cardiovasc Surg 1976;72(5):788-91.
8. Butany JW, Naseemuddin A, Moshkowitz Y, Nair V. Ochronosis and aortic valve stenosis. J Card Surg 2006;21(2):182-4.

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