Minimally invasive surgical aortic valve replacement in setting of pseudoxanthoma elasticum

Devon Anderson, MD, a,b Joshua Gustafson, MD, b,c and Elaine E. Tseng, MD, a,b Bethesda, Md

Pseudoxanthoma elasticum (PXE) is an autosomal-recessive disease that leads to ectopic mineralization of elastic fibers and calcium deposits in the eyes, skin, and vascular walls due to mutations in ABCC6 gene. The prevalence of PXE is unknown and ranges between 1:25,000 and 100,000. PXE manifests clinically as yellow skin papules, ophthalmologic angioid streaks, and calcium deposits in small/medium-sized arteries. Most common cardiovascular complications include hypertension, coronary artery disease (CAD), and peripheral vascular disease. However, a paucity of information exists about PXE and its effect on the aortic valve. We present the case of a patient with history of PXE and severe aortic stenosis (AS).

CASE REPORT
Our study was approved by the Committee on Human Research at University of California San Francisco and institutional review board of the San Francisco Veterans Affairs, which allows us to retrospectively review and publish case outcomes without consent ( CHR approval: 11-06811; consent waived). A 61-year-old man with a history of PXE presented in decompensated congested heart failure and was referred for transcatheter aortic valve replacement after echocardiogram showed severe AS, mean gradient of 50 mm Hg, and aortic valve area (AVA) of 0.73 cm². Catheterization revealed nonobstructive CAD. On preoperative imaging, areas of calcification were seen in the ascending aorta but much more extensive in abdominal aorta to the periphery (Figure 1). After a heart team discussion, it was determined that transcatheter aortic valve replacement was inappropriate, given the patient’s age and extensive calcification, and minimally invasive surgical aortic valve replacement (SAVR) was chosen.

At operation, obtaining arterial access for hemodynamic monitoring was challenging, given his diffuse atheromatous plaques, so after unsuccessful bilateral radial artery cannulation attempts, an ulnar arterial line was achieved. An epiaortic ultrasound scan demonstrated areas of calcification in the ascending aorta and arch, which were avoided to safely cannulate and crossclamp the aorta. The ascending aorta was used for the arterial cannulation site, and the right atrium was used as the venous cannulation site. Through a mini-sternotomy at the level of the fourth intercostal space based on imaging, he underwent an uncomplicated minimally invasive SAVR, which is our all-comers approach for isolated SAVR. Native aortic...
valve was noted to be trileaflet, extremely calcified, with crumbly calcium on the leaflets (Figure 2 and Figure E1). Meticulous dissection was performed to safely remove the valve, and a 27-mm Edwards INSPIRIS valve was sutured in place. Postcardiopulmonary bypass echocardiogram showed good ventricular function and a well-seated valve. While he was weaned from cardiopulmonary bypass, ulnar arterial line read 10 to 15 mm Hg lower than the central aortic pressure. He was transferred to the intensive care unit for recovery.

The postoperative course was complicated by intermittent atrial fibrillation, for which we restarted his rivaroxaban for anticoagulation that he was on preoperatively for deep venous thrombosis prophylaxis. He otherwise had an unremarkable hospital course. A short review of the case can be seen in Video 1.

**DISCUSSION**

Cardiac complications associated with PXE are found in case reports and focus on advanced CAD rather than AS.3,4 Prunier and colleagues3 performed a prospective study focusing on cardiac findings in patients with PXE and found 2 patients (3%) who had AS: a 61-year-old male patient with severe AS (mean gradient 63 mm Hg, AVA 0.7 cm²) who underwent SAVR and a 73-year-old female patient with moderate AS (mean gradient 10 mm Hg, AVA 1.5 cm²) who did not undergo surgery. However, the study did not explore management or complications that may arise in patients with PXE and AS.
Another case report, by Farmakis and colleagues, detailed a 46-year-old female patient with AS and thalassemia-related PXE who underwent SAVR with mechanical valve. The valve thrombosed 6 months later, despite therapeutic anticoagulation with warfarin (international normalized ratio 3.0-3.5), which led to a redo-SAVR and ultimately death from postoperative complications. Thalassemia-related PXE is similar clinically and histologically to the inherited form of PXE, but the relationship between warfarin use in PXE and valve thrombosis is not established. What has been shown in mouse models deficient in \textit{ABCC6} gene normally mutated in PXE is that worsening disease severity occurred after being started on a warfarin diet. The study by Li and colleagues showed a 16-fold increase in ectopic mineralization in ABCC6 knockout mice on a warfarin diet. This was due to warfarin preventing activation of local inhibitors of mineralization in peripheral tissues. These findings highlight the importance of anticoagulation choice in patients with PXE, as warfarin can lead to worsening of the disease process.

A multidisciplinary approach is essential for perioperative management. Intraoperative hemodynamic monitoring can pose a challenge in patients with PXE due to the amount of calcification in the arterial walls, as demonstrated in our patient. The ulnar arterial line did not accurately reflect the direct aortic pressure reading intraoperatively, which led to the need for increased vasopressor support at times during the operation. Thus, sufficient planning is required to determine the best intraoperative monitoring option.

**CONCLUSIONS**

PXE is a rare disease, and it is even more rare to find it combined with severe AS. This case report demonstrates the importance of the collaboration between different specialties, preoperative evaluation and imaging, intraoperative findings, and postoperative management.

**References**

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FIGURE E1. Hematoxylin and eosin section of valvular tissue showing marked myxoid degeneration, extensive calcification, and chronic inflammation.