Valve-sparing root replacement in a patient with a filamin A variant

Naoto Fukunaga, MD, Michael A. Seidman, MD, PhD, and Tirone E. David, MD, Toronto, Ontario, Canada

From the Division of Cardiovascular Surgery and Pathology, Peter Munk Cardiac Centre, Toronto General Hospital, University of Toronto, University Health Network, Toronto, Ontario, Canada.

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Address for reprints: Naoto Fukunaga, MD, Division of Cardiovascular Surgery, Peter Munk Cardiac Centre, Toronto General Hospital, University of Toronto, University Health Network, 200 Elizabeth St, Toronto, Ontario, Canada M5G 2C4 (E-mail: naotowakimachi@hotmail.co.jp).

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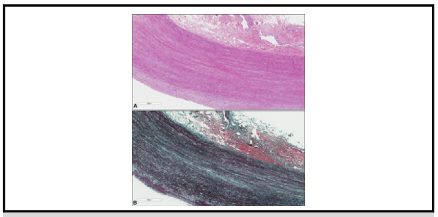

Histologic images from the resected aortic root (A and B).

CENTRAL MESSAGE

FLNA gene mutations are associated with more severe form of degenerative changes, and additional surgical care is needed to manage patients.

See Commentaries on pages e357 and e358.

Mutations in loss of function at the encoding filamin A (FLNA) locus lead to X-linked periventricular nodular heterotopia and are associated with some anomalies, including vascular, joint hypermobility, and variable skin characteristics.[1] We report a case of a patient with a de novo FLNA gene variant who underwent aortic valve-sparing root replacement (VSRR) and ventricular septal defect (VSD) repair.

CLINICAL SUMMARY

An asymptomatic 32-year-old woman, who had de novo FLNA gene variant c.676C>T (p.Arg266), was admitted for elective VSRR and VSD closure. Intraoperative transesophageal echocardiography showed moderate aortic insufficiency (AI) due to aortic root aneurysm (52 mm) and a restrictive subaortic VSD (Figure 1, *A* and *B*).

At surgery, the aortic valve was tricuspid and all 3 cusps were overstretched and thinned. The annulus was dilated to 30 mm. There was a VSD at the nadir of the right aortic cusp and membranous septum, and the intervalvular fibrous body was thinner than normal. The VSD orifice was closed with 2 interrupted 4-0 polypropylene sutures. The coronary arteries were detached from the aortic sinuses. The 3 sinuses were excised, leaving 3 to 4 mm of sinus wall attached to the aortic annulus. A tubular Dacron graft of 28 mm was sutured to the left ventricular outflow tract with 12 interrupted horizontal mattress sutures of 2-0 polyester with soft Teflon felt pledgets. These sutures were place close together along the fibrous component of the left ventricular outflow tract, that is, from the lateral to medial fibrous trigones. The commissures were resuspended in the graft, and the remnants of sinus wall and aortic annulus were sutured to the graft with running 4-0 polypropylene sutures. These sutures were also placed closer together than usual because of the fragility of the remnants of the aortic sinuses and aortic annulus. In addition, 3 horizontal mattress sutures of 4-0 polypropylene were used to fix the subcommissural triangles of the noncoronary aortic cusp to the Dacron graft because they were also paper-thin (Figure 2). The left and right coronary arteries were reimplanted into the respective neoaortic sinuses. All 3 cusps were prolapsing, and the free margins were shortened by plication along the nodule of Arantius with 5-0 polypropylene sutures. The graft was trimmed 15 mm above the commissures and anastomosed to the distal ascending aorta. Transesophageal echocardiography showed trace to mild central AI with preserved function (Figure 1, *C*). Postoperative transthoracic echocardiography showed trivial AI and a coaptation height of 12 mm and coaptation length of 5 mm. Another transthoracic echocardiography 14 weeks after surgery showed intact reconstructed aortic root and trivial AI. Pathological findings revealed severe medial degeneration (Figure 3, *A* and *B*). Informed consent was obtained.

DISCUSSION

To our knowledge, this is the first report describing a detailed surgical perspective with histology from a resected aortic root in a patient with de novo FLNA gene variant. Our experience with our first case cautions surgeons who may encounter patients with FLNA mutations.

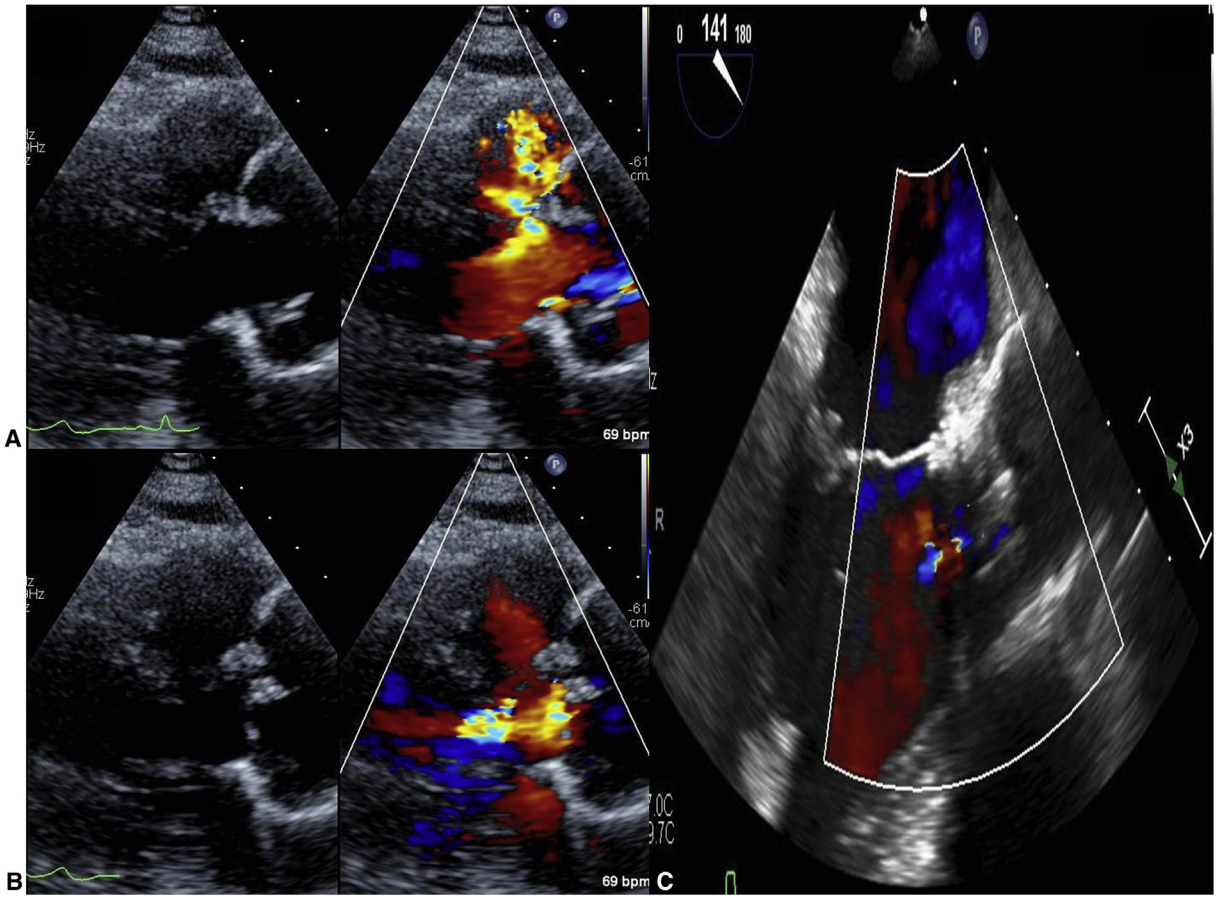

FIGURE 1. Preoperative transthoracic echocardiography shows a restrictive subaortic VSD with a peak gradient of 148 mm Hg (A) and moderate AI due to aortic root aneurysm (52 mm). The aortic valve was trileaflet (B). Left ventricular function was preserved, and no other valvular disease was noted. Intraoperative transesophageal echocardiography after VSRR revealed trace to mild central AI (C).

A large cohort of 114 patients with FLNA mutations demonstrated that most frequently involved parts of the thoracic aorta are the aortic root and ascending aorta.[2]

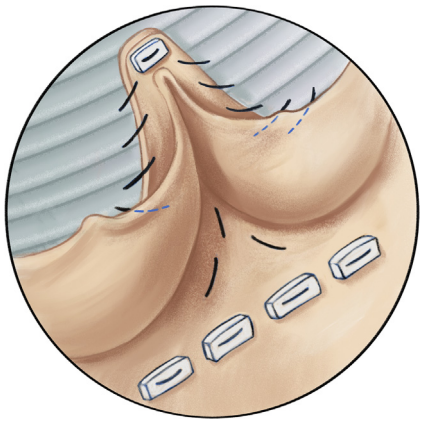

FIGURE 2. Three horizontal mattress sutures of 4-0 polypropylene used to fix the subcommissural triangles of the noncoronary aortic cusp to the Dacron graft to prevent dehiscence and development of a false aneurysm.

Also, there is a risk for a rupture at an aortic diameter smaller than current guidelines.[2] These guidelines did not comment on the fragility of tissue or the surgical perspectives.[1] In our 32-year-old patient, the subcommissural triangles were tearing when the commissures were suspended into the graft, and we had to reinforce those areas by placing additional sutures to prevent dehiscence and development of a false aneurysm. Normally, we do not place additional sutures in the subcommissural triangles of the noncoronary cusp. However, a life-threatening complication associated with aortic VSRR is a pseudoaneurysm due to tearing of the subannular tissues. Liu and colleagues[3] reported 4 cases of pseudoaneurysm formation after VSRR in children with severe subset of Loeys–Dietz syndrome. They found that pseudoaneurysms occurred as the result of tearing of tissue. Those surgeons used 3 sutures to secure the Dacron graft to the left ventricular outflow tract.[3] We have published on the late outcomes of patients with Marfan syndrome and VSRR. No pseudoaneurysm was observed in that series.[4]

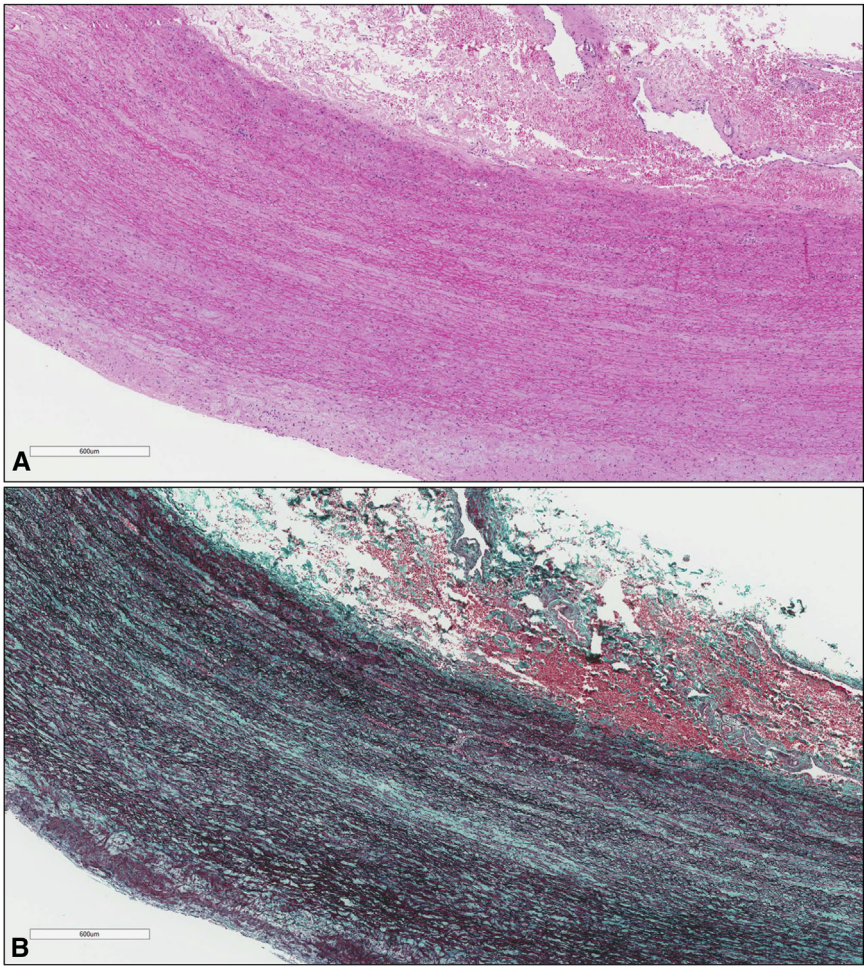

FIGURE 3. The images shown are from histologic sections taken from the resected portion of the aortic root. These demonstrate severe medial degeneration, as characterized by smooth muscle nuclear loss (fewer cells in the medial wall with visible nuclei compared with normal), intralamellar and translamellar myxoid extracellular matrix accumulation (characterized by increased intercellular material, colored *light pinkish blue* in A and *light green* in B), smooth muscle and elastic fiber disarray (nonlaminar organization of the medial layers, most evident in B as demonstrated by intersecting black elastic fibers), and elastic fiber fragmentation (gaps in the black elastic fibers seen in B; in other foci, these fibers are almost completely lost). A, Hematoxylin–eosin stain. B, Elastic-trichrome stain. Scale bar as indicated (600 μm).

CONCLUSIONS

FLNA gene mutations have not been well known as Marfan or Loeys–Dietz syndromes in the field of cardiovascular surgery. Although the patient described is our first to undergo VSRR, we were surprised by the fragility of the connective tissues in the aortic root. It is possible that FLNA gene mutations are associated with a more severe form of degenerative changes. Additional surgical care is needed, and patients have to remain under medical surveillance with periodical images of the aortic root.

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