Impaired Systolic Function in Loeys-Dietz Syndrome
A Novel Cardiomyopathy?

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Loeys-Dietz syndrome (LDS) is a recently described autosomal dominant genetic syndrome caused by mutations in the gene encoding transforming growth factor-β receptor 1 or 2 with no known cardiac involvement. Common characteristics include aortic and arterial aneurysms or dissections, orbital hypertelorism, and cleft palate or bifid uvula. We report the first case of a cardiomyopathy associated with LDS in a patient with a novel transforming growth factor-β receptor mutation and pathological evidence of microvascular coronary artery dysplasia.

Case Report
A 44-year-old tall, thin, white man with “borderline” hypertension and sleep apnea developed a severe, painful stabbing sensation in his throat while walking. He presented to a local hospital and was found to have an acute thoracoabdominal aortic dissection (Stanford type A) without involvement of the coronary arteries. He underwent emergent ascending aortic replacement and resuspension of the aortic valve; left ventricular function was not evaluated perioperatively. Although his perioperative course was uneventful, he developed fatigue and experienced syncope on postoperative day 31. Echocardiogram revealed impaired systolic function (left ventricular ejection fraction, 25%). He had no family history of cardiomyopathy or sudden death, did not consume alcohol, and had normal thyroid function. He was treated with a β-blocker and an angiotensin-converting enzyme inhibitor and followed with serial echocardiograms. He was also referred to a geneticist for suspicion of connective tissue disease. He was of normal intelligence, 185 cm tall, had normal arm span:height ratio, wide uvula, high arched palate, ankyloglossia, retrognathia, malar flattening, a pinched nasal bridge, mild joint laxity, and pectus carinatum noted on examination. Suspicion for LDS was confirmed by genetic testing, which identified a novel c. 1303G>C transversion in exon 8 of TGBFR1 in the serine threonine kinase domain of the gene. His fatigue and left ventricular systolic function initially improved to 40% with medical therapy, but his aorta continued to dilate, and he required composite root and valve graft ~6 months later with bypass of left coronary artery and reimplantation of the right coronary artery. Clinical deterioration was accompanied by decline in his left ventricular systolic function, and he ultimately developed cardiogenic shock. He underwent emergency heart transplantation, and the explanted heart had interstitial and replacement fibrosis of the left ventricular myocardium and dysplastic medium-to-

Figure. Light micrograph of a medium size muscular-type coronary artery (atrioventricular node artery). There is intimal proliferation with reduplication of the internal elastic lamina forming multiple small, thin, fragmented lamellae instead (right image and inset). In addition, the bundles of smooth muscle in the media show lack of a parallel, circumferential orientation of these fascicles. These changes were commonly seen in medium and small size muscular-type arteries (hematoxylin-eosin, ×75; Movat pentachrome, ×75; inset, ×500).
small size muscular-type coronary arteries (including the artery to the atrioventricular node and small branches of the epicardial coronary arteries) but patent epicardial arteries (Figure). The involvement of the medium size coronaries was more prominent than the involvement of the small size (<1 mm in diameter) arteries.

Discussion

Vascular coronary artery dysplasia is a distinctly uncommon finding in cardiac tissue explanted for transplant. Previous descriptions seem to be limited to focal fibromuscular dysplasia of small arteries in hypertrophic cardiomyopathy and dysplasia of in the sinus node artery after sudden death. The transforming growth factor-β receptor mutation in LDS is known to cause macrovascular disease, but microvascular dysplasia in LDS has not previously been described to the best of our knowledge. Microvascular dysplasia would be expected to impair myocardial blood flow and eventually cause myocardial dysfunction. Although it is possible that the 2 rare conditions are unrelated, it seems plausible that the transforming growth factor-β receptor mutation in LDS could cause microvascular dysplasia and subsequent cardiomyopathy. A careful examination of future pathological specimens may provide an opportunity to clarify the significance of this finding.

Disclosures

None.

References

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