Patients typically have aggressive arterial aneurysms (mean age of death, 26.0 years) and a high incidence of pregnancy-related complications [1]. It has been reported that patients with LDS undergo cardiovascular operations earlier (mean age, 16.9 years) and die earlier (mean age, 22.6 years) but have a lower intraoperative mortality rate compared with patients with vascular Ehlers-Danlos syndrome or Marfan’s syndrome [2].

An 18-year-old female patient was discovered to have a cardiac murmur during a school medical examination. Physical examination was otherwise unremarkable. There were no abnormal findings on a previous chest roentgenogram performed at age 15 years (Fig 1). She had a height of 166 cm, weight of 53.5 kg, and body mass index of 21.1 kg/m². There was no relevant family history of cardiovascular disease. She did not have any

Acute Dilatation of the Ascending Aorta and Aortic Valve Regurgitation in Loey-Dietz Syndrome

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Loeys-Dietz syndrome (LDS) is a recently recognized connective tissue disorder caused by mutations of the transforming growth factor (TGF)-β receptors. It is an autosomal dominant syndrome characterized by the triad of arterial tortuosity and aneurysms, hypertelorism, and bifid uvula or cleft palate. We treated an 18-year-old woman with a 100-mm-diameter aortic root aneurysm and severe aortic valve regurgitation. She underwent urgent aortic root replacement and bioprosthetic valve implantation. LDS was diagnosed by postoperative genetic screening results. Histopathologic examination of the aortic wall showed diffuse degeneration and elastin fragmentation in the media.

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characteristics of Marfan’s syndrome. Imaging examinations showed severe aortic valve regurgitation with left ventricular dilatation and a 100-mm-diameter massive aneurysm of the ascending aorta (Fig 2). Computed tomography showed tortuosity of the vertebral arteries, a 15-mm-diameter superior mesenteric artery, and a 21-mm-diameter left deep femoral artery. She was referred to our cardiovascular surgery department for urgent operation. A connective tissue disorder was suspected, and Ehlers-Danlos syndrome was ruled out by skin biopsy results. Blood was drawn for genetic screening, but there was a delay of a few months before results would be available. We discussed the timing of operation during a heart team conference and decided to operate as soon as possible to avoid rupture of the ascending aorta.

Results

Under general anesthesia with endotracheal intubation, the patient was placed supine. The pericardium was opened. A massive ascending aortic aneurysm occupied the majority of the pericardial space. After systemic heparinization, cardiopulmonary bypass was instituted by means of cannulation of the aorta and superior vena cava and inferior vena cava through the right artery. The distal anastomosis was performed using hypothermic circulatory arrest with retrograde cerebral perfusion. A retrograde cardioplegia cannula was placed in the coronary sinus for retrograde continuous cold blood cardioplegia. The aortic valve was carefully observed to consider the possibility of aortic valve-sparing surgery. However, the non-cusp valve was severely degenerated, and we decided to perform aortic valve replacement. Aortic root replacement was performed using a valve-graft conduit, consisting of a 25-mm bioprosthetic valve (Carpentier-Edwards PERIMOUNT Magna Ease aortic heart valve; Edwards Lifesciences, Irvine, CA) and a 28-mm Valsalva graft (Gelweave Valsalva graft; Vascutek, Renfrewshire, Scotland). After resection of the aortic valve leaflet, 12 everting pledgeted 2-0 polyester sutures were attached to the aortic valve annulus and were passed through a skirt portion of the composite valve-graft, not through the prosthetic valve ring. After ligation of all valve threads, continuous suturening with 4-0 polypropylene was performed, attaching the skirt portion of the graft to both 5-mm felt and the left aortic root wall. Coronary reimplantation was performed with 5-0 polypropylene running suture. After confirming hemostasis, the aortic cross-clamp was released. The heart spontaneously resumed beating, and the patient was easily weaned from cardiopulmonary bypass. All cannulas were removed in the conventional manner, and she was transferred to the intensive care unit. The postoperative course was uneventful. Pathologic examination of the ascending aorta showed medial necrosis and tears of the elastic fibers. The genetic screening results showed a TGF-β receptor 1 mutation, which led to the diagnosis of LDS. She continues school life without any problems.

Comment

Based on clinical experience, it has been suggested that variants of genetic aneurysmal diseases that are similar to but distinct from Marfan’s syndrome exist. Recently, several genetic mutations have been shown to account for a variety of aneurysmal disorders. Some are still being characterized, such as bicuspid aortic valve disease and familial thoracic aortic aneurysm and dissection syndromes. LDS is now known to be caused by TGF-β receptor mutations [3], which increase the downstream signaling of cytokine TGF-β in blood vessels, leading to overproduction of collagen, loss of elastin, and disarray of elastic fibers. LDS is characterized by vascular symptoms—such as aortic aneurysm, cerebral aneurysm, and arterial tortuosity—and skeletal symptoms—such as funnel chest, pigeon breast, and scoliosis. These patients are often initially diagnosed with other conditions. Our patient had an aneurysm of the ascending aorta, bilateral vertebral artery tortuosity, and peripheral artery dilatation. Compared with Marfan’s syndrome, the vascular disease in LDS tends to be more generalized and aggressive. Many patients present in childhood or young adulthood [4]. Rupture can occur at an early age and at an aortic diameter that usually would not cause rupture [5]. For this reason, patients with LDS should undergo vascular surgical intervention at an earlier age than those with Marfan’s syndrome [6]. Once the diagnosis is made, aortic imaging is indicated at least once per year [7]. Staged replacement of affected aortic segments is indicated, which sometimes leads to replacement of the entire aorta. Because this is an autosomal dominant disorder with variable clinical expression, genetic counseling and screening of family members is recommended. In this case, our patient had a 100-mm massive ascending aortic aneurysm. Aneurysms of this size are very rare until the aorta is dilated in the case of LDS.
In most of the cases, the aorta ruptures or dilates up to this size. Histopathologic examination of the aortic wall showed diffuse degeneration and elastin fragmentation in the media [8]. Because these changes are observed in both LDS and Marfan's syndrome, genetic screening is needed to diagnose LDS.

It is controversial whether we should perform total aortic arch replacement in these patients. Total aortic replacement is a major surgical procedure that has been associated with significant mortality and morbidity in the past. Recent advances in intraoperative management have greatly improved outcomes. We considered total aortic arch replacement in our patient, but eventually performed only replacement of the aortic root and ascending aorta, because her aortic arch was not dilated. We need to follow the patient carefully at least every 6 months.

The patient has a deep desire to have children in the future, which is another issue to be considered. Aortic root replacement and bioprosthesis valve implantation were performed after fully informed consent was obtained. Postoperatively, the diagnosis of LDS was finally confirmed. We explained to the patient that patients with LDS would likely have pregnancy-related complications. However, we need time to inform female patients at an early age that having no children is a better option.

In summary, LDS is caused by mutations in the TGF-β receptor 1 and 2 genes and is characterized by progressive aortic aneurysmal disease and dissection. Patients present at an early age and require vigilant monitoring of all vascular segments because of the rapidly progressive nature of the aortic disease. We need to follow our patient carefully.

References

Hypertrophic cardiomyopathy and anomalous origin of the coronary artery from the opposite sinus are common causes of sudden cardiac death. These entities have rarely been reported together. Here we present the case of a 48-year-old woman with hypertrophic cardiomyopathy and significant left ventricular outflow tract obstruction. She was referred for septal reduction therapy for symptomatic left ventricular outflow tract obstruction refractory to medical therapy. Cardiac catheterization and coronary artery computed tomography angiogram revealed a single coronary artery arising from the right sinus of Valsalva, coursing between the aorta and the right ventricular outflow tract. The patient underwent septal myectomy and placement of an implantable cardioverter defibrillator.


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