Taiwanese Journal of Obstetrics & Gynecology 60 (2021) 145–147

Contents lists available at ScienceDirect

Taiwanese Journal of Obstetrics & Gynecology

journal homepage: www.tjog-online.com

Case Report

Postpartum Stanford type B aortic dissection in a woman with Loeys-Dietz syndrome who underwent a prophylactic aortic root replacement before conception: A case report

Rieko Shitara [a, b], Takayuki Iriyama [a, *], Seisuke Sayama [a], Norifumi Takeda [c], Takeshi Nagamatsu [a], Yutaka Osuga [a], Tomoyuki Fujii [a]

[a] Departments of Obstetrics & Gynecology, Faculty of Medicine, University of Tokyo, Tokyo, Japan
[b] Departments of Obstetrics & Gynecology, Japan Community Health Care Organization Tokyo Shinjuku Medical Center, Tokyo, Japan
[c] Department of Cardiovascular Medicine, Faculty of Medicine, University of Tokyo, Tokyo, Japan

ARTICLE INFO

Article history:
Accepted 27 August 2020

Keywords:
Aortic dissection
Aortic root replacement
Loeys-Dietz syndrome
Postpartum period
Pregnancy

ABSTRACT

Objective: Loeys-Dietz syndrome (LDS) is associated with a higher risk of aortic dissections (ADs) during pregnancy and postpartum. However, there is limited evidence about the perinatal management of LDS patients who have undergone prophylactic aortic root replacements (ARRs) before conception.
Case report: We present the case of a 28-year-old nulliparous pregnant woman with LDS with a pathogenic variant within exon 5 of *TGFBR2* (c.1379G > T, p.[Arg460Leu]), who underwent an ARR at 20 years of age. Cardiac echocardiography did not show any significant changes in the aorta during pregnancy, and her blood pressure remained normal. She had a cesarean section at 37 weeks of gestation. She developed an acute Stanford type B AD extending from the aortic arch to the infrarenal aorta 8 days postpartum and underwent a total arch replacement.
Conclusion: This case report suggests that patients with LDS after prophylactic ARRs still possess a risk for Stanford type B ADs.

Introduction

Loeys-Dietz syndrome (LDS) is a systemic connective tissue disease with an autosomal dominant inheritance pattern. This syndrome has overlapping clinical features with Marfan syndrome (MFS), which is caused by pathogenic variants in the *FBN1* gene encoding the major component of the extracellular matrix protein, fibrillin-1 [1]. The distinctive disease concept of LDS was first proposed by Dr. Bart Loeys and Dr. Hal Dietz in 2005 [2], who identified pathogenic variants in genes encoding transforming growth factor-β (TGF-β) receptors 1 and 2 (*TGFBR1* and *TGFBR2*, respectively) in a subset of MFS type 2 patients who had prominent aortic/arterial aneurysms and dissections without ectopia lentis. Compared to MFS, patients with LDS have a higher risk of early cardiovascular events, including aortic aneurysms and aortic dissections (AD), even in peripheral vessels. Although women with MFS and LDS are both at a higher risk for pregnancy-associated aortic dissections (ADs) [3,4], LDS patients present more frequently with ADs during pregnancy and the postpartum period [4,5]. The Japanese Circulation Society (JCS) recommends aortic root replacements (ARRs) in MFS patients with aortic root dilations of ≥45 mm to prevent Stanford type A ADs involving the ascending aorta, a leading cause of death in patients with MFS. Moreover, MFS patients with aortic root diameters of >40 mm should undergo preconception counseling for ARR [6]. Optimal management of LDS during pregnancy, however, has not yet been established because of the limited number of reported cases of pregnant women with LDS. In addition, reports on the perinatal outcomes of LDS patients who have undergone prophylactic ARRs before pregnancy are even more limited. Here, we present the case of an extensive postpartum Stanford type B AD in LDS patient after prophylactic ARR.

Case presentation

A 28-year-old pregnant female (G1P0, 167.5 cm, 51 kg) with LDS presented to our hospital. At 6 years of age, she underwent a coil

* Corresponding author. Department of Obstetrics & Gynecology, The University of Tokyo Hospital, 7-3-1 Hongo, Bunkyo-ku, Tokyo, 113-8655, Japan. Fax +81 3 5800 8728.
E-mail address: iriyama-tky@umin.ac.jp (T. Iriyama).

https://doi.org/10.1016/j.tjog.2020.10.005

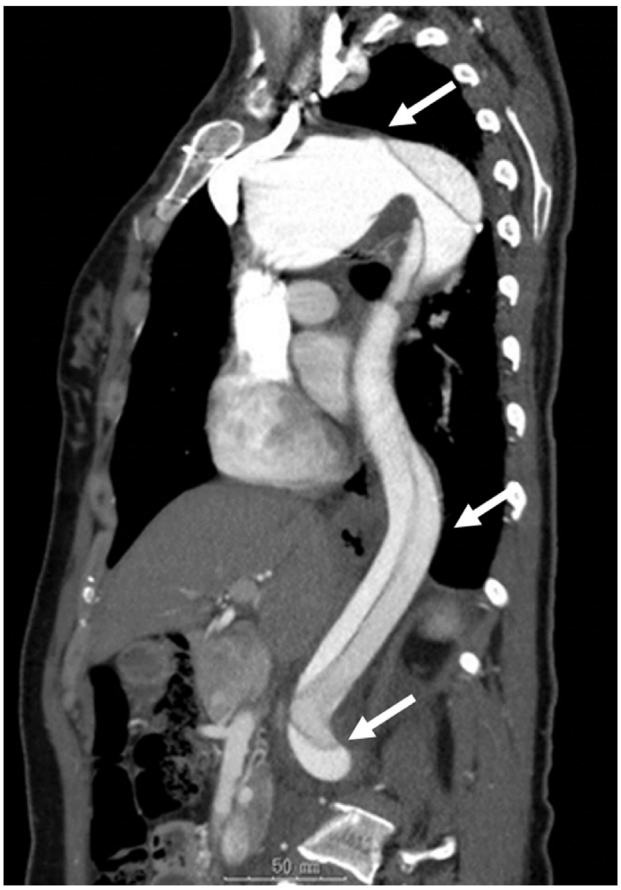

Fig. 1. Contrast-enhanced computed tomography scans revealed a Stanford type B aortic dissection. Arrows indicate the location of dissection extending from the aortic arch to the infrarenal aorta.

embolization for a patent ductus arteriosus (PDA). An aortic root aneurysm was followed conservatively by a general hospital. At the age of 20 years, she was first suspected to have LDS because she had the diagnostic triad of a rapidly progressive aortic aneurysm (the sinus of Valsalva: 55 mm), hypertelorism, and a bifid uvula. She was referred to our hospital and underwent an aortic valve-sparing aortic root replacement (David V-UT procedure). Losartan, an angiotensin II receptor blocker (ARB), was prescribed thereafter, without hypertension or dilatation of the remaining aorta. At 25 years of age, she chose to try to conceive and stopped taking the losartan. At 27 years of age, a genetic analysis for thoracic aortic aneurysm-related genes was conducted, and a previously reported pathogenic variant for LDS was identified within exon 5 of *TGFBR2* [c.1379G > T, p.(Arg460Leu)], after which she was definitely diagnosed with LDS. Her blood pressure was kept within normal range and the remaining aorta was not dilated before conception without any antihypertensive medication. She conceived with clomiphene treatment at a fertility clinic and was referred to our hospital for perinatal care at 10 weeks of gestation. During pregnancy, her blood pressure remained below 120/80 mm Hg. At 18 and 36 weeks of gestation, cardiac echocardiography evaluations did not show any aortic insufficiency or significant changes in the remaining aorta, including the thoracic arch or descending aorta. The diameter of Valsalva was 36 mm and a trivial aortic regurgitation was seen. Chest X-ray at 36 weeks of gestation didn't show the dilation of ascending aorta.

At 37 weeks of gestation, an elective cesarean section was performed under spinal and epidural anesthesia because of a breech presentation. The total blood loss was 1015 mL. The baby weighed 2410 g and had Apgar scores of 2 and 7 at 1 and 5 min, respectively. The patient was monitored in the intensive care unit (ICU). On postpartum day 1, she received cabergoline, and she chose not to breastfeed after being informed about the potential risk of lactation-related blood pressure elevation. She was treated with enough epidural anesthesia and non-steroidal anti-inflammatory drugs to avoid elevated blood pressures due to pain. Without any antihypertensive drugs, her blood pressure remained at around 120/60 mm Hg until postpartum day 8, when it suddenly increased to 130/80 mm Hg. The patient was administered losartan, and an unenhanced computed tomography (CT) scan detected a 54-mm aortic arch aneurysm. Four hours later, she suddenly developed back pain and her blood pressure readings exceeded 150/90 mm Hg. An acute AD was highly suspected, and an emergency contrast-enhanced CT scan revealed a Stanford type B AD extending from the aortic arch to the infrarenal aorta (Fig. 1). Due to the extensive type B AD and the risks associated with emergency surgery, our cardiovascular surgeons advocated watchful waiting and conservative medical therapy with antihypertensives and pain medications for management. A total aortic arch replacement and an open stent implantation were performed 37 days after the AD. The postoperative course was unremarkable, and she was discharged on postoperative day 15 with prescriptions for an ARB, a beta-blocker, and a calcium channel blocker.

Discussion

Reports on the perinatal outcomes of patients with LDS who have undergone prophylactic ARRs prior to conception are limited, with only three reported cases from Braverman et al. and one case from Fujita et al. at our institution [7,8]. The clinical outcomes of six pregnancies in five women are shown in Table 1, including the present case (Case 1). All patients had undergone prophylactic ARRs by their early 20s, with larger diameters than the surgical indication (40 mm) [4], and thus were aggressively managed. We previously reported a serious case of a patient with LDS who experienced two ADs during the early postpartum periods (Table 1, Case 2). The patient presented with an acute Stanford type A AD

Table 1
Review of outcomes of pregnancy cases after ARR in LDS.

Case	Age at delivery (y)	Genetic mutation	History of ARR	Age of ARR (y)	Aortic root diameter at ARR (mm)	Use of β-blocker during pregnancy	Weeks at delivery	Mode of delivery	Onset of AD	References
1	28	*TGFBR2*	VSARR	20	55	no	37	CS	8 day postpartum	This report
2	23	*TGFBR2*	(−)	n/a	n/a	no	38	CS	3 day postpartum	Fujita et al. [7].
	29	*TGFBR2*	VSARR	23	50	yes	37	CS	5 day postpartum	
3	43	*TGFBR1*	VSARR	25	48	yes	35	CS	2 day postpartum	Braverman et al. [8].
4	37	*TGFBR2*	VSARR	17	50	yes	34	CS	One day after discharge	Braverman et al. [8].
5	26	*TGFBR2*	VSARR	21	45	yes	34	CS	(−)	Braverman et al. [8].

ARR, aortic root replacement; LDS, Loeys-Dietz syndrome; AD, aortic dissection; VSARR, Valve-sparing aortic root replacement; CS, Cesarean section.

after delivering her first child by cesarean section in another hospital, and an aortic valve-sparing David V-UT procedure was performed in our hospital (Table 1, 1st pregnancy of case 2). Five days after the delivery of her second child by cesarean section in our hospital, the patient had a fatal AD extending to the vertebrobasilar arteries, and she died at 20 days postpartum (Table 1, 2nd pregnancy of case 2) [7]. Both cases of pregnant women with LDS after ARRs presented with Stanford type B ADs in the postpartum period. The high rate of complications observed in our hospital is consistent with previously reported cases from Braverman et al. (Table 1, Cases 3–5), in which two out of three post-ARR LDS patients suffered acute ADs in the postpartum period, while there were no complications in 13 LDS women without ARRs (31 pregnancies) [8]. In patients with MFS, Sayama et al. reported that three out of five patients (60%) who had previously undergone ARRs had a type B AD in the third trimester or postpartum period, whereas only one of 10 patients (12 pregnancies) without an ARR had an AD [9]. Thus, our current report provides valuable information that pregnant women with LDS after ARRs are at a high risk for type B ADs.

As there is limited information in the literature about the outcomes of pregnancy after ARRs in patients with LDS, no consensus has yet been reached on the management of these patients during pregnancy. While strict control of blood pressure during pregnancy and the postpartum period is critical to prevent ADs [5,10], our patient's blood pressure was kept below 120/80 mm Hg throughout the postpartum period. The patient had discontinued losartan before pregnancy and had not taken any other antihypertensive drugs during her pregnancy. Even in cases with MFS, no consensus has yet been reached on whether beta-blockers reduce the risk of ADs in pregnant women with MFS [6,11]. In the above-mentioned case series by Braverman et al. [8], all three LDS patients received a beta-blocker after ARR, though two of them developed ADs, one with a type A AD and the other with a type B AD [8]. With regards to the duration of hospital stay, pregnant women with MFS or LDS after ARR are routinely hospitalized for 2 weeks after delivery as our management policy, based on the experience reported in our previous study [9]. However, further studies are needed to clarify the perinatal outcomes of LDS patients to establish the optimal management strategies.

In conclusion, we have presented a case of a postpartum Stanford type B AD in a patient with LDS after a prophylactic ARR. Our results highlight the need for preconception counseling for post-ARR LDS patients wishing to conceive. It is important to emphasize that the prophylactic ARR is to avoid fatal Stanford type A AD and high risk for Stanford type B ADs during perinatal periods still remains, even under strict management policies including strict blood pressure control and longer duration of hospital stay after delivery. Given the life-threatening consequence of AD in these patients, giving up conception is an option. Counseling should also include a hereditary risk to their offspring. We consider that it is essential to provide counseling not only to the patients but also to their family members as well to let them decide what is the best decision for the family.

Declaration of competing interest

The authors declare no conflict of interest.

Acknowledgments

We are grateful to doctors in the Departments of Cardiovascular Surgery, Cardiovascular Medicine, and Anesthesiology at our institution for the successful management of this patient.

References

[1] Dietz HC, Cutting GR, Pyeritz RE, Maslen CL, Sakai LY, Corson GM, et al. Marfan syndrome caused by a recurrent de novo missense mutation in the fibrillin gene. Nature 1991;352(6333):337–9.
[2] Loeys BL, Chen J, Neptune ER, Judge DP, Podowski M, Holm T, et al. A syndrome of altered cardiovascular, craniofacial, neurocognitive and skeletal development caused by mutations in TGFBR1 or TGFBR2. Nat Genet 2005;37(3):275–81.
[3] Katsuragi S, Ueda K, Yamanaka K, Neki R, Kamiya C, Sasaki Y, et al. Pregnancy-associated aortic dilatation or dissection in Japanese women with Marfan syndrome. Circ J 2011;75:2545–51.
[4] MacCarrick G, Black 3rd JH, Bowdin S, El-Hamamsy I, Frischmeyer-Guerrerio PA, Guerrerio AL, et al. Loeys-Dietz syndrome: a primer for diagnosis and management. Genet Med 2014;16(8):576–87.
[5] Frise CJ, Pitcher A, Mackillop L. Loeys-Dietz syndrome and pregnancy: the first ten years. Int J Cardiol 2017;226:21–5.
[6] JCS Joint Working Group. Guidelines for diagnosis and treatment of aortic aneurysm and aortic dissection (JCS 2011): digest version. Circ J 2013;77(3):789–828.
[7] Fujita D, Takeda N, Morita H, Kato M, Nishimura H, Inuzuka R, et al. A novel mutation of TGFBR2 causing Loeys-Dietz syndrome complicated with pregnancy-related fatal cervical arterial dissections. Int J Cardiol 2015;20:288–90.
[8] Braverman AC, Moon MR, Geraghty P, Willing M, Bach C, Kouchoukos NT. Pregnancy after aortic root replacement in Loeys-Dietz syndrome: high risk of aortic dissection. Am J Med Genet 2016;170(8):2177–80.
[9] Sayama S, Takeda N, Iriyama T, Inuzuka R, Maemura S, Fujita D, et al. Peripartum type B aortic dissection in patients with Marfan syndrome who underwent aortic root replacement: a case series study. BJOG 2018;125(4):487–93.
[10] Melissa LR, Neelima S, Mathur Veena, Morris SA. Obstetric management of Loeys-Dietz syndrome. Obstet Gynecol 2018 June;131(6):1080–4.
[11] Gersony DR, McClaughlin MA, Jin Z, Gersony WM. The effect of beta-blocker therapy on clinical outcome in patients with Marfan's syndrome: a meta analysis. Int J Cardiol 2007;114(3):303–8.