

Successful management of a patient with Marfan syndrome complicated with acute aortic dissection using landiolol during Cesarean section

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Abstract Aortic dissection is a lethal complication in pregnant women with Marfan syndrome. To decrease arterial wall stress, beta-blockers have been used as standard treatment, although uterine contractions caused by beta-2-adrenergic receptor antagonism may result. Herein, we report a patient with Marfan syndrome who was given landiolol, a selective beta-1-adrenergic receptor antagonist with a short half-life, for management during a Cesarean section procedure following development of acute aortic dissection. A 30-year-old pregnant woman with Marfan syndrome in the 38th week of gestation was referred to our department for an emergency Cesarean section because of development of acute aortic dissection. Blood pressure (BP) decreased from 157/70 to 128/64 mmHg after giving nicardipine and nitroglycerin. However, heart rate (HR) increased from 112 to 145 bpm, which was reduced to 105 bpm with landiolol, while BP was maintained. A Cesarean section was performed without complications under combined spinal–epidural anesthesia. Hemodynamic state, uterine contraction, and the extent of aortic dissection remained stable. The postoperative course was uneventful, and the patient and her baby were discharged safely. Landiolol was useful for reduction of HR without affecting BP or uterine contractions during a Cesarean section procedure in our patient with aortic dissection.

Keywords Marfan syndrome · Cesarean section · Aortic dissection · Landiolol

Introduction

Mortality associated with Marfan syndrome is primarily affected by cardiovascular complications, with aortic dissection a lethal complication that can occur during pregnancy [1–4]. To protect against aortic root dilatation caused by stress placed on the aortic wall, beta-blockers are often administered [5, 6]. However, these may not be appropriate for pregnant women as they have effects on uterine contraction because of beta-2-receptor antagonism [7]. Landiolol, a selective beta-1-adrenergic receptor antagonist with a short half-life, has been reported to be useful for treatment of pregnant women with Marfan syndrome [8]. Herein, we present a patient with Marfan syndrome given landiolol for tachycardia that appeared during a Cesarean section procedure following the development of acute aortic dissection.

Case report

The patient was a 30-year-old pregnant woman (height 160 cm, weight 52 kg). She had been diagnosed with Marfan syndrome with mitral valve regurgitation (MR) at the age of 10 years, dislocation of crystalline bodies at 11, and spontaneous pneumothorax at 15, 16, and 18 years old. In addition, her parents, brothers, and uncle had also been diagnosed with the syndrome.

During the 35th week of gestation, the patient informed her gynecologist of the presence of Marfan syndrome; an echocardiography examination of her cardiovascular system was then conducted, which revealed mild aortic regurgitation (AR) and MR. Because the ascending aorta was not enlarged (width 28 mm) and blood pressure (BP) was not elevated (120/60 mmHg), the patient was

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followed without medication. However, when labor began in the 38th week of gestation, she felt severe pain in her back, at which time BP was increased to 158/72 mmHg and a CT scan showed aortic dissection. She was then transferred to our institute with an infusion of nicardipine at 1 mg h⁻¹.

Upon arrival at the ICU, BP was still elevated (157/70 mmHg); thus, we increased the dose of nicardipine to 6 mg h⁻¹ and added nitroglycerin at 1.5 mg h⁻¹. The patient had a regular sinus rhythm, and echocardiography revealed normal left ventricular contractions with mild MR; however, the diameter of the ascending aorta was increased to 36 mm. CT scanning showed the aortic dissection (DeBakey type IIIb), and bullae in the bilateral apexes of the lungs were also noted. Because the aortic dissection was below the ascending aorta, and the fetus was matured and stable, we planned an emergency Cesarean section with control of BP and cardiac surgeons ready. To avoid severe stress against the aortic wall during and after the procedure, combined spinal-epidural anesthesia using vacuum delivery was planned. When the patient arrived in the operating room, BP was decreased to 128/64 mmHg by nicardipine and nitroglycerine; however, HR was increased from 112 to 145 bpm. We administered landiolol, a beta-1-selective blocker with a short half-life, at a rate of 10 mg h⁻¹, after which HR decreased to 105 bpm within 15 min and BP remained stable at 118/62 mmHg. After placement of an epidural tube between T12 and L1, spinal anesthesia with 2.2 ml 0.5% isobaric bupivacaine was given. The level of spinal anesthesia was T6 by a cold sign test, and BP and HR were decreased to 90/40 mmHg and 80 bpm, respectively. Therefore, the doses of nicardipine and landiolol were decreased from 9 to 5 mg h⁻¹ and from 10 to 5 mg h⁻¹, respectively, while nitroglycerine was discontinued. A boy weighing 3202 g was delivered using vacuum with an Apgar score of 8 at 1 min and 9 at 5 min. The amount of bleeding was 670 g, and uterine contractions were good with an intrauterine injection of 5 U oxytocin, followed by 0.2 mg ergometrine i.v. and 20 U oxytocin d.i.v.

The patient was transferred to the ICU for cardiovascular monitoring and given a continuous infusion of landiolol at 5 mg h⁻¹, nitroglycerin at 2 mg h⁻¹, and nicardipine at 9 mg h⁻¹. One day later, CT scanning revealed that the aortic dissection had not progressed and bilateral renal blood flow was maintained. The infused agents were then reduced and gradually changed to oral medications. The postoperative course was uneventful, and the patient and her baby were discharged in healthy condition at 38 days after birth. Twenty months after surgery, neither the aortic dissection nor AR showed further progression.

Discussion

Pregnancy is believed to contribute to the pathogenesis and progression of aortic dissection, although there is some controversy [9], because multiple factors are thought to be involved, such as increased blood volume, HR, and BP, whereas the strength of aortic connective tissue is decreased by estrogen [10, 11]. During labor, various events affect circulatory status, i.e., increases in venous return by uterine contractions, BP by labor pain, and intrathoracic pressure by breathholding. Especially in patients with increased diameter of the ascending aorta, moderate aortic or mitral valve lesions, or aortic dissection, pregnancy is not recommended. On the other hand, an ascending aorta diameter less than 40–45 mm has been reported to be associated with a safe pregnancy [1–4, 12]. However, aortic dissection occurred in another patient without increased aortic dilatation [3] and in the present case without hypertension, indicating that all pregnant women with Marfan syndrome have a risk of aortic dissection. Although administration of antihypertensives in pregnant women with normal BP is controversial, their use may be reasonable for high-risk patients, such as those with Marfan syndrome, especially in the third trimester [5].

Management of pregnant women with an aortic dissection is determined by the type of dissection and development of the fetus, namely, whether surgical treatment is needed for the aortic dissection and the maturity of the fetus for delivery [5, 13, 14]. The present patient was in the 38th week of gestation; thus, we chose an emergency Cesarean section procedure with cardiac surgeons ready, because the fetus was matured enough for delivery and the degree of aortic dissection allowed conservative treatment.

Although regional anesthesia is recommended for a Cesarean section procedure, both regional and general anesthesia have been applied for emergency Cesarean section patients with aortic dissection [5, 13, 14]. Particularly in those undergoing general anesthesia, an increase in BP, which can progress to aortic dissection, should be avoided. Furthermore, during anesthetic care for a patient with Marfan syndrome, various problems other than aortic dissection should also be considered. As for the cardiovascular system, AR, MR, left ventricular hypertrophy, cardiac failure, and arrhythmia have been reported, and airway and respiratory disorders are also known, such as a difficult airway, dislocation of cervical and mandibular joints, a restrictive respiratory disorder caused by thoracic deformity, and pneumothorax. Scoliosis and dural ectasia should also be considered in the patient with regional anesthesia [14, 15]. In the present case, hemodynamic stabilization was required during and after the Cesarean section; thus, we applied a combined spinal epidural technique, which provides several advantages over spinal or epidural anesthesia alone [16]. Hypotension and bradycardia are known to be

disadvantages of regional anesthesia during a Cesarean section procedure. However, the changes in BP and HR were mild in the present case, suggesting that vascular tone and HR were already reduced, and attenuated by the titration of vasodilators and landiolol.

To control BP during a Cesarean section procedure for a matured fetus, it is conceivable that antihypertensives should be selected, not because of teratogenicity, but on the basis of their effects on placental circulation and uterine contractions, as well as controllability. In the present patient, we used nicardipine, nitroglycerin, and landiolol, and the control of both BP and HR was satisfactory, while there were also no adverse effects on uterine contractions or the status of the fetus. In Marfan syndrome patients, it is also important that hemodynamic management should not be discontinued immediately after the Cesarean section because aortic dissection can occur even after delivery [3].

We administered landiolol to reduce HR that was increased after vasodilator administration. HR control in addition to BP control has been reported to improve the outcome of patients undergoing acute aortic dissection [17]. Landiolol is thought to be safe for pregnant woman because it has no adverse effects on the fetus [18]. In addition, because its ratio of (beta-1)/(beta-2) is as high as 251, the effects on uterine contractions are thought to be minimal [19]. The efficacy of landiolol has been reported in scheduled Cesarean section procedures for patients with Marfan syndrome [8]. In the present patient, in whom acute aortic dissection appeared during labor, landiolol effectively reduced HR without showing adverse effects on BP, uterine contraction, or the fetus, with the result that aortic dissection did not progress. Esmolol, another beta-1-selective blocker with a short half-life, can also be used. However, BP is important when choosing between these two agents because the negative inotropic effect is higher with esmolol than landiolol [20]. Following delivery, agents such as oxytocin and PGF_{2α} can be used to maintain uterine contractions, while it is also reasonable to administer PGE₁, a potent vasodilator known as an uterotonic agent for use after delivery, to prevent the elevation of BP and atonic bleeding [13].

In conclusion, landiolol, with a short half-life and beta-1-selective properties, was helpful to attenuate tachycardia without adverse effects on BP, the fetus, and uterine contractions in the present patient. We consider that the drug is useful for treatment of tachycardia during a Cesarean section procedure in patients who have developed an acute aortic dissection.

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