

## A Successfully Operated Case of Prosthetic Valve Thrombosis during Planned Pregnancy

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**The patient was a 29-year-old woman who, when she was an 8-year-old, had undergone atrial septal defect (ASD) closure and mitral valve replacement (MVR) using a Björk-Shiley valve (25 mm) for Lutembacher syndrome. Because of a planned pregnancy, warfarin had been replaced by heparin. During the 7th week of pregnancy, she was admitted to our hospital because of dyspnea. She was diagnosed with acute heart failure due to prosthetic valve thrombosis. Following termination of pregnancy, the mitral valve was replaced with an ATS valve (25 mm). She was discharged 10 days after surgery without complications. (Ann Thorac Cardiovasc Surg 2006; 1: 66–70)**

**Key words:** prosthetic valve, valve replacement, valve thrombosis

### Introduction

Recently, with advances in pediatric cardiac surgery technology<sup>1)</sup> and development of prosthetic valves,<sup>2)</sup> the procedure of prosthetic valve replacement has been extended to young patients. Many studies have been conducted on the pregnancy after valve replacement.<sup>3–6)</sup> Although pregnancy was thought to be contra-indicated for these patients, there have been a number of reports describing success after valve replacement.<sup>7)</sup> However, there is no established protocol for delivery safety. We report a case of a valve thrombosis during pregnancy after valve replacement.

### Case Report

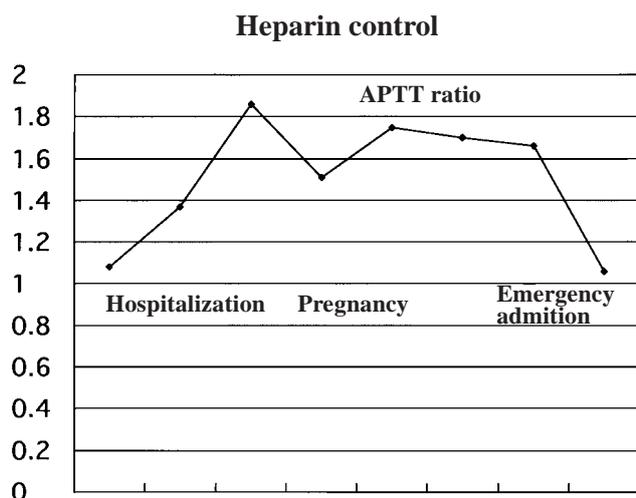
The patient was a 29-year-old woman who, when she was 8-year-old, had undergone atrial septal defect (ASD) closure and mitral valve replacement (MVR) using a Björk-Shiley valve (25 mm) for Lutembacher syndrome. One

month prior to the planned pregnancy, she was hospitalized to start a regimen of subcutaneous injection of heparin, to achieve an activated partial thromboplastin time (aPTT) ratio at 1.5~2.0. She was discharged with a control mechanism set with the procedure. Following discharge, she had been receiving subcutaneous injections of 15,000 units of heparin at home (Fig. 1). In the 7th week of pregnancy and a few days prior to her current hospitalization, she developed a fever and dyspnea on exertion. The blood pressure, heart rate, and temperature were 100/56 mmHg, 116 per minute, regular and 37.6°C, respectively. On admission, a white blood cell was 12,900/ $\mu$ l, C-reactive protein (CRP) was 1.89, prothrombin time was 10.8seconds [international normalized ratio (INR) 0.98], partial prothrombin time as 40.1seconds. Chest X-ray showed cardiac enlargement (cardiothoracic ratio 60%), and there was increase in pulmonary vascular shadow. On transthoracic echocardiography (TTE), the left atrial diameter was 50.2 mm, the peak pressure gradient across the mitral valve was 30.2 mmHg and the pressure half-time was 244 mseconds. The ejection fraction 39.6(%) and %FS 18(%) demonstrated normal cardiac functions. An attachment measuring 10 $\times$ 10 mm was found at the prosthetic valve at the side of the left ventricle (Fig. 2). The opening angle of prosthetic valve was limited to 45° by cinefluoroscopy. She was diagnosed with acute cardiac failure due to valve thrombosis. The condition

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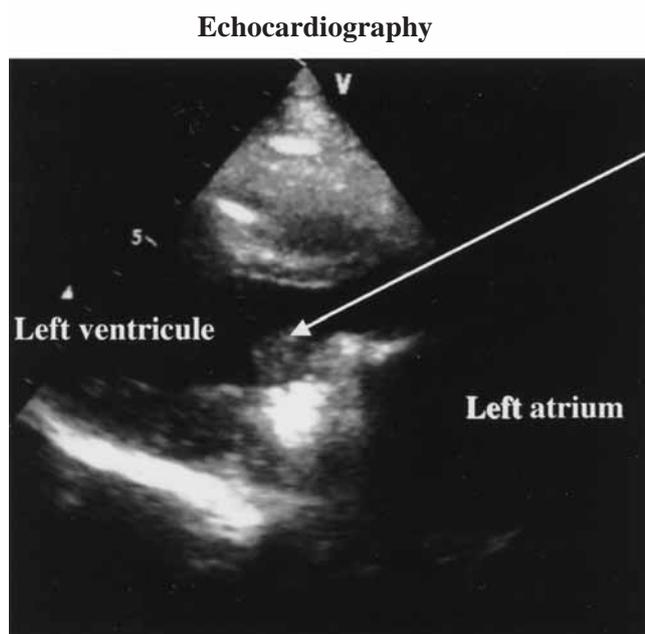
**Fig. 1.** She started a regimen of subcutaneous injection of heparin, with the goal of the activated partial thromboplastin time (aPTT) ratio set at 1.5~2.0.

improved slightly with the administration of anti-coagulants (intravenous injection of heparin) and furosemide but the thrombus did not reduce by TTE and transesophageal echocardiography (TEE). A re-MVR was scheduled. Upon consent of the patient and her family, her pregnancy was terminated first. On the next day after the termination, she underwent re-MVR (25 mm ATS mechanical valve: ATS Medical, Inc, Minneapolis, MN, USA). The prosthetic valve was covered with pannus (mainly around the pivotal region), while a fresh thrombus measuring about 10 mm in diameter was seen at the

side of the left ventricle (Fig. 3). The leaflet motion of the prosthetic valve was evidently restricted due to the presence of this thrombus. After operation, we administered warfarin and antiplatelet drugs for anticoagulant therapy. The postoperative course was uneventful and the patient was discharged on the 10th postoperative day.

## Discussion

When a patient who has had a valve replacement with a mechanical valve wishes to conceive, it is essential that she rely on anticoagulants during the entire course of her pregnancy. However, the use of anticoagulants may have many problems. The time of onset of these anti-coagulant-related complications may be divided mainly into that during pregnancy and after delivery; and the side effects may involve the mother or fetus. The teratogenic effects of warfarin are well known. Incidences of aplasia of the nasal cartilage and optic atrophy have been reported.<sup>8)</sup> Because of these side effects, at many institutions, warfarin is replaced by heparin at the initiation of pregnancy. It has been reported that the result of this substitution has been satisfactory.<sup>3,4,6,7)</sup> The following is given as the reason for successful replacement: heparin has a relatively large molecular weight (12,000~15,000); therefore it is unable to pass through the placenta. On the other hand, the molecular weight of warfarin is only 346 and can readily pass through the placenta, thus exerting a direct effect on the fetus.<sup>8)</sup> However, the teratogenic mechanism of warfarin has recently been studied and its dose-dependency

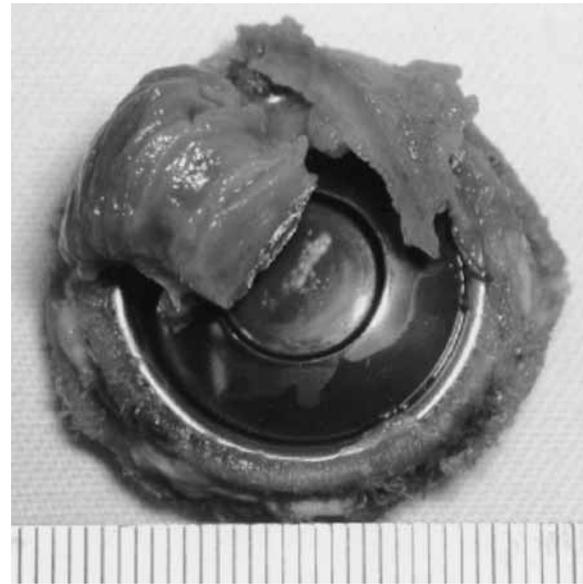


**Fig. 2.** On transthoracic echocardiography (TTE), the left atrial diameter was 50.2 mm. An attachment measuring 10×10 mm was found at the prosthetic valve at the side of the left ventricle.

### Thrombosed valve



Left atrium side



Left ventricle side

**Fig. 3.** The prosthetic valve was covered with pannus (mainly around the pivotal region), while a fresh thrombus measuring about 10 mm in diameter was recognized at the side of the left ventricle.

has been suggested. It has been said that oral administration of warfarin in a dosage under 5 mg is not likely to produce teratogenic results.<sup>9-11)</sup>

More serious side effects on mothers include prosthetic valve thrombosis. The condition is more likely to develop in those patients using mechanical valves. One of the reasons for the development of this complication: it is believed that pregnancy-related changes exaggerate the blood coagulation reaction in mothers, which leaves them more vulnerable to thrombosis. For this reason, more strict control of anti-coagulant therapy is necessary for those patients who have used a mechanical valve. In general, oral administration of warfarin is replaced by injection of heparin during the organogenetic stage of early pregnancy (6~12th week) and immediately before delivery to avert fetal teratogenicity or complications, such as a hemorrhage at delivery.<sup>3,4,6)</sup> However, it has been reported that compared with warfarin, the coagulating capacity of heparin is less stable and is more likely to cause prosthetic valve thrombosis.<sup>12)</sup> A safe and reliable protocol for anti-coagulation therapy has not been established. In planned pregnancy, the patient, her husband, and other family members should be sufficiently alerted to these risks and the procedure must be conducted with their full understanding.

The factors frequently cited as being responsible for the development of valve thrombosis are inadequate anti-coagulant therapy, arrhythmia and irregular blood flow. Other factors promoting the development of a valve are the site at which the valve was replaced and the type of prosthetic valve. In general, prosthetic valve thrombosis develops more frequently at the mitral valve than at the aortic valve, a mechanical valve rather than a bioprosthesis; and among the mechanical valves, more frequently in association with the tilting disc valve than the bileaflet valve. These tendencies are further exacerbated by pregnancy. Therefore in dealing with patients with prosthetic valves who expect to be pregnant, the most strict anti-coagulant management becomes necessary, giving due consideration to the site of valve replacement and type of valve used.

During pregnancy patients with prosthetic valves need regular tests such as aPTT and INR to monitor coagulation and to perform TTE to evaluate cardiac functions (including the valve's function). If the slightest abnormality is suspected, TEE or cinefluoroscopy is conducted for early identification of prosthetic valve insufficiency. In addition, for early diagnosis of maternal and fetal abnormalities, close contact should be maintained with the pediatric and gynecological departments.

During pregnancy following replacement with a prosthetic valve, valvular or systemic thrombosis may develop in spite of the anticoagulant therapy such as that described above. The treatment for valve thrombosis during pregnancy will depend on the facilities and the condition of each patient; but thrombolytic therapy or surgery (valve replacement or thrombectomy) is usually conducted.<sup>13-15</sup> Thrombolytic therapy is useful when the patient's condition is stable, or the thrombus is small. In fact, there is a report on a successful thrombolytic therapy culminating in the delivery of a normal infant.<sup>13</sup> However, this therapy is associated with a risk of causing abruption of the placenta and its effect on the fetus is still unknown. Lengyel et al. reported that about 12% of the patients who undergo thrombolytic therapy to treat prosthetic valve thrombosis develop a thromboembolism.<sup>16</sup> On the other hand, the success rate of the re-valve replacement is strongly influenced by the pre-operative hemodynamics. Instead of surgery, Lengyel et al. recommended thrombolytic therapy for patients with NYHA class III or IV.

At re-operation, one faces the problem of how to deal with the fetus. If the patient is in the early stage of pregnancy, an avenue for pregnancy termination is open: if she is in the late stage, the option of cesarean section exists. When the patient is in the mid-stage of pregnancy, however, the choice is limited and one is forced to conduct surgery while the fetus is left in place. There are occasional reports in which the survival of both the mother and fetus are described when extracorporeal circulation was conducted with the latter left in the uterus.<sup>15</sup> In such a state, the mortality of the fetus is very high (15~20%).<sup>17,18</sup> If it is possible to select the timing, re-operation should be avoided except for an emergency. The advisability of doing a cesarean section depends on whether the mother is capable of withstanding the burden of the surgical procedure.

In selecting a prosthetic valve in young women, the possibility of the patient becoming pregnant in future cannot be ignored. A bioprosthesis will not require anticoagulants and the performance of the valve remains relatively unaffected by pregnancy. Takahara et al. reported on the safe use of bioprostheses in women who wished to become pregnant.<sup>19</sup> However, it has been reported that the durability of these valves is limited so the patient has to undergo a re-valve replacement when the prosthetic valve malfunctions. In our case, if we choose a bioprosthesis for pregnancy, in the future, she would have to undergo a third operation. Therefore, it is difficult to choose an adequate valve.

In this case, the hemodynamic state was unstable and the thrombus depicted by echocardiography was large (about 1 cm). Following consultation with the patient's family, replacement with a mechanical mitral valve was conducted.

## References

1. Tsunemoto M. The present status of surgical treatment for congenital heart disease during infancy in Japan (2nd report)—a questionnaire report. *Rinsho Kyobu Geka* 1984; **4**: 130–44.
2. Akins CW. Mechanical cardiac valvular prostheses. *Ann Thorac Surg* 1991; **52**: 161–72.
3. Sbarouni E, Oakley CM. Outcome of pregnancy in women with valve prostheses. *Br Heart J* 1994; **71**: 196–201.
4. Ginsberg JS, Hirsh J. Use of antithrombotic agents during pregnancy. *Chest* 1995; **108** (4 Suppl): 305–11S.
5. Ginsberg JS, Barron WM. Pregnancy and prosthetic heart valves. *Lancet* 1994; **344**: 1170–2.
6. Fukuda T, Yokoyama T, Otaki M, et al. Successful planned pregnancy in a patient with St Jude medical prosthetic mitral valve. *Circ J* 2002; **66**: 204–6.
7. Nonoyama M, Kurosawa H. Anticoagulation in pregnant women with prosthetic heart valves. *Cardiovascular Med-Surg* 2002; **4**: 186–92.
8. Hall JG, Pauli RM, Wilson KM. Maternal and fetal sequelae of anticoagulation during pregnancy. *Am J Med* 1980; **68**: 122–40.
9. Vitale N, De Feo M, De Santo LS, et al. Dose-dependent fetal complications of warfarin in pregnant women with mechanical heart valves. *J Am Coll Cardiol* 1999; **33**: 1637–41.
10. Hung L, Rahimtoola SH. Prosthetic heart valves and pregnancy. *Circulation* 2003; **107**: 1240–6.
11. Ueno M, Masuda H, Nakamura K, et al. Antiplatelet therapy for a pregnant woman with a mechanical aortic valve: report of a case. *Surg Today* 2001; **31**: 1002–4.
12. Oakley CM. Anticoagulants in pregnancy. *Br Heart J* 1995; **74**: 107–11.
13. Anbarasan C, Kumar VS, Latchumanadhas K, et al. Successful thrombolysis of prosthetic mitral valve thrombosis in early pregnancy. *J Heart Valve Dis* 2001; **10**: 393–5.
14. Ramamurthy S, Talwar KK, Saxena A, et al. Prosthetic mitral valve thrombosis in pregnancy successfully treated with streptokinase. *Am Heart J* 1994; **127**: 446–8.
15. Sudoh Y, Takahara Y, Sunazawa T, et al. Emergent mitral valve replacement in the second trimester of pregnancy. *Nippon Kyobu Geka Gakkai Zasshi* 1997; **45**: 1034–8.
16. Lengyel M, Fuster V, Keltai M, et al. Guidelines for management of left-sided prosthetic valve thrombosis:

- a role for thrombolytic therapy. Consensus Conference on Prosthetic Valve Thrombosis. *J Am Coll Cardiol* 1997; **30**: 1521–6.
17. Pomini F, Mercogliano D, Cavalletti C, et al. Cardiopulmonary bypass in pregnancy. *Ann Thorac Surg* 1996; **61**: 259–68.
18. Westaby S, Parry AJ, Forfar JC. Reoperation for prosthetic valve endocarditis in the third trimester of pregnancy. *Ann Thorac Surg* 1992; **53**: 263–5.
19. Takahara Y, Sudoh Y, Sunazawa T, et al. Carpentier-Edwards pericardial valve in the aortic and the mitral positions: 12-year follow-up. *Jpn J Artif Organs* 1998; **27**: 174–7.