A case report: mechanical mitral valve thrombosis in pregnancy

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Background

Pregnancy in women with mechanical valves has a high risk of both valve thrombosis and bleeding as well as adverse effects on the foetus. There is limited data on achieving optimal anticoagulation in pregnancy and management of valve thrombosis, to achieve a successful foetal outcome, while prioritizing the mother’s health. While warfarin may carry a lower risk of valve thrombosis, warfarin is teratogenic in the first trimester and is associated with increased foetal loss throughout the pregnancy. Heparin does not cross the placenta but is associated with increased maternal morbidity and mortality.

Case summary

We describe the case of a pregnant patient with thrombosis of a mechanical mitral valve presenting with an embolic stroke at 22 weeks of pregnancy. The stroke was treated with clot retrieval and resulted in no residual neurological deficit. Two previous pregnancies had been managed with low molecular weight heparin, and both resulted in foetal loss. The patient was determined to continue this pregnancy. She was treated with intravenous unfractionated heparin during the remainder of the pregnancy. She developed worsening heart failure due to persisting valve thrombosis despite maintenance of therapeutic anticoagulation. The patient deteriorated rapidly prior to a planned early elective delivery. Emergency Caesarean section was required followed by valve replacement using extracorporeal membrane oxygenation support with an ultimately successful maternal and foetal outcome. Anticoagulation regimes and treatment of mechanical valve thrombosis in pregnancy are discussed.

Discussion

The management of pregnant patients with mechanical valves is complex, especially when valve thrombosis and other complications occur. A multidisciplinary approach is essential and in this case led to successful outcome.

Keywords

Prosthetic valve thrombosis • Pregnancy • Anticoagulation • Thrombolysis • Case report

Learning points

• Anticoagulation in pregnant patients with a mechanical valve carries significant risk and the regime is individually based.
• Pre-pregnancy planning improves outcome. This includes selection of an appropriate prosthetic valve prior to pregnancy and anticoagulation in early pregnancy.
• Early multidisciplinary treatment in pregnancy with a mechanical valve (and complications) is essential for a good outcome for mother and baby.
**Introduction**

The risk of complications in pregnancy is high in patients with mechanical prosthetic heart valves. Up to 42% of these pregnant patients experience serious adverse events. The risk of mechanical valve thrombosis is increased due to haemodynamic changes and hypercoagulable status. Thrombotic and bleeding complications vary depending on the selected anticoagulation regime, but remain high.

While warfarin may carry a lower risk of valve thrombosis, warfarin is teratogenic in the first trimester and is associated with increased foetal loss throughout the pregnancy. Heparin does not cross the placenta but is associated with increased maternal morbidity and mortality.

**Timeline**

| Time          | Events                                                                 |
|---------------|------------------------------------------------------------------------|
| 14 years ago  | Endocarditis of mitral valve complicated by embolic stroke, treated with antibiotics and mechanical mitral valve replacement. Prosthetic mitral valve thrombosis, treated with thrombectomy. |
| 2 years ago   | First pregnancy complicated by premature labour at 20 weeks and foetal loss. |
| 1 year ago    | Second pregnancy complicated by retroplacental haematoma and foetal loss in second trimester. |
| Day 1, presentation, 22 weeks gestation | Hemiparesis due to left middle cerebral artery stroke, while on subcutaneous low molecular weight heparin (Enoxaparin), treated with thrombectomy. |
| Day 2         | Transoesophageal echo showed mitral valve thrombosis with normal leaflet opening. Anticoagulation with intravenous unfractionated heparin. |
| Day 6         | Transfer to tertiary hospital. Initially stable New York Heart Association (NYHA) Class II and increased mitral gradient. |
| Day 55        | Worsening heart failure, further optimization of medical treatment. |
| Day 60, 30 weeks pregnant | Acute pulmonary oedema. Transoesophageal echocardiography extensive thrombus on mitral valve and in left atrial appendage. Emergency Caesarean section, baby in good condition. Maternal deterioration and extracorporeal membrane oxygenation instituted. Bioprosthetic mitral valve re-replacement. |
| Day 74        | Discharge in good condition. |

**Case presentation**

A 23-year-old woman was referred from New Caledonia because of complications from thrombosis of a mechanical mitral valve during pregnancy.

In 2003, at the age of 9 years, she underwent a mechanical mitral valve replacement (ATS 26 mm) following endocarditis complicated by an embolic stroke. Later that year, she developed a thrombus on the prosthetic valve, while on warfarin and this was treated with thrombolysis. Valve function remained satisfactory until the first pregnancy. Her obstetric history was unfavourable. The first pregnancy in 2015 was complicated by premature labour at 20 weeks and foetal loss. The second pregnancy in 2016 was complicated by retroplacental haematoma and foetal loss in the second trimester.

At 22 weeks in her third pregnancy, whilst on subcutaneous low molecular weight heparin (LMWH) (Enoxaparin) commenced early in pregnancy, she presented with a middle cerebral artery stroke, which was treated by thrombolysis and clot retrieval at the major referral hospital in New Caledonia (Centre Hospitalier Territorial-Medipole). The patient had signs of heart failure. A transoesophageal echocardiogram showed a mitral mean gradient of 20 mmHg and two non-obstructive thrombi on the valve. Fluoroscopy showed apparently normal leaflet motion. Intravenous unfractionated heparin was commenced and the patient was transferred to a teaching hospital in Sydney with cardiothoracic services.

On admission, blood pressure was 95/60 mmHg, rhythm sinus with heart rate 85 b.p.m., and there was no clinical heart failure. A mitral diastolic murmur was heard. There was no residual neurological deficit. Transoesophageal echocardiogram was repeated and showed persisting valve thrombus and severe valve obstruction with a mean gradient of 18 mmHg and mild pulmonary hypertension (pulmonary artery systolic pressure 40 mmHg) (Figure 1A). Treatment with intravenous unfractionated heparin was continued with target activated partial thromboplastin time (aPTT) in the high therapeutic range and Metoprolol and oral Furosemide were maintained. Aside from a daily clinical assessment, the patient had weekly transthoracic echocardiograms and weekly foetal ultrasounds. Despite frequent aPTT measurements, maintaining therapeutic anticoagulation was challenging and the dose of heparin very variable (Figure 2). A multidisciplinary team, consisting of cardiologists, an obstetrician, cardiothoracic surgeon, obstetric, and cardiothoracic anaesthetists and a neonatologist, was involved in her treatment.

At 29 weeks of pregnancy, symptomatic heart failure developed in the setting of sinus tachycardia and frequent atrial ectopic beats and was treated with increasing diuretics and beta blockers. Foetal growth and wellbeing was monitored with regular clinical assessment, CTG monitoring and scans to assess growth and wellbeing. Steroid cover was achieved to improve foetal lung maturity. At 30 weeks, as the patient’s heart failure was rapidly progressive despite an increase in medical therapy, she proceeded to emergency Caesarean section. Prior to delivery, the patient was receiving Metoprolol 100 mg BD orally and Lasix 40 mg orally with IV boluses as required. Delivery was for maternal reasons and there was no foetal compromise. Heparin was stopped 6 h prior to Caesarean section. Intravenous magnesium was given (loading dose of 4 g IV over 15 min and...
maintenance of 1 g/h) to reduce the risk of foetal brain injury at delivery in a preterm infant but was ceased when sinus tachycardia worsened significantly after 2 h of the maintenance infusion. At this stage, the patient was gravely unwell, tachycardic, sitting upright in bed with acute pulmonary oedema despite accelerated medical therapy and oxygen through a Hudson mask at six litres per minute. Femoral venous and arterial access was obtained before the start of the Caesarean section for rapid institution of extracorporeal membrane oxygenation (ECMO) if needed. Intra-operative transoesophageal echocardiography showed thrombus on the mechanical mitral valve and in the left atrial appendage with severe pulmonary hypertension (Figure 1B), and this rapid progression of thrombus may have been promoted by heparin cessation. The Caesarean section was uncomplicated but the patient’s haemodynamics deteriorated over the next 2 h requiring institution of ECMO, without heparinization. Six hours after Caesarean section, when full anticoagulation could be used without prohibitive bleeding risk, an emergency mitral valve replacement was performed on cardiopulmonary bypass. The thrombosed mechanical valve (Figure 3) was excised and a 25 mm Perimount Tissue Valve was implanted. A bioprosthetic valve was selected to facilitate a further planned pregnancy. Extracorporeal membrane oxygenation was ceased after 24 h and the patient was extubated 2 days after surgery.

Apgars were 3 and 7 at 1 min and 5 min. The neonate required continuous positive airway pressure for 2 weeks for hyaline membrane disease and a patent ductus arteriosus was treated with oral Ibuprofen. Bedside ultrasound confirmed normal appearance of the neonatal brain and no haemorrhage. There was a normal clinical neurological examination of the baby prior to discharge at 19 days (32 weeks and 5 days corrected for gestational age) into the care of her mother. The mother was discharged 2 weeks after surgery, on aspirin.

Discussion

This case illustrates the complexity of the management of pregnant patients with mechanical valves.

The risk of mechanical valve thrombosis was 4.7% in the Registry of Pregnancy and Cardiac Disease (ROPAC) that included 212 pregnant patients. In a recent meta-analysis, the risk of valvular thrombi and extravalvular thromboemboli was 2.7–8.7%, dependent on the anticoagulation regime. Studies show that there is no ideal
anticoagulation regime.2–4 Treatment with vitamin K antagonists throughout pregnancy is associated with lower risk of valve thrombosis and maternal mortality compared with sequential treatment with unfractionated heparin or LMWH in the first trimester and vitamin K antagonists in the second and third trimester. The same is true for comparison with LMWH throughout pregnancy, even when adjusted for anti-Xa levels.1–3 However, vitamin K antagonists cross the placenta and have a higher risk of foetal adverse events. The patient in this case study was on Enoxaparin during her first trimester to reduce the risk of embryopathy and this was continued during her second trimester with doses adjusted according to anti Xa levels.

When mechanical valve thrombosis complicates pregnancy, anticoagulation therapy should be optimized and, in this patient, unfractionated heparin was started after thrombectomy.4,5 Aspirin crosses the placenta but is recognized as a safe drug during pregnancy. Some guidelines suggest the addition of low dose aspirin to warfarin for pregnant women with prosthetic heart valves at high thromboembolic risk, such as patients with an older generation prosthesis in mitral valve position, history of thromboembolism or atrial fibrillation.6 In the ROPAC study, aspirin was used in the second and third trimester in 13 patients in addition to other anticoagulation regimes and no mechanical valve thrombus occurred in this small subgroup. The bleeding risk is however higher1 and this was a relative contraindication in our patient with previous foetal loss due to retroplacental haematoma.

In critically ill patients, surgery is recommended when anticoagulation fails and thrombolysis when surgery is not available.4 Thrombolitics have a high bleeding and thromboembolic risk of 10%,7 including placental haemorrhage and are sometimes used in complicated pregnancy. Thrombolysis with low-dose tissue type plasminogen activator may be a safe and effective therapy, with foetal loss in 5 of 25 pregnancies, 1–5 weeks after thrombolysis, but no maternal morbidity or mortality.8 Valve surgery in pregnancy carries a high risk of maternal morbidity (24%) and mortality (6%) and foetal-neonatal morbidity (9%) and mortality (30%).9 The patient in this case report was New York Heart Association (NYHA) Class IV at the time of delivery which significantly increases maternal mortality and morbidity.9 An additional factor contributing to the lability of the patient at delivery was the persistent thrombus on the valve acting as a nidus for further thrombus formation despite therapeutic anticoagulation. Long-term heparin use induces antithrombin III deficiency and this may have resulted in a hypercoagulable state when heparin was ceased prior to Caesarean section. Furthermore, intravenous magnesium worsened the patient’s sinus tachycardia and we believe this contributed to the acute deterioration in this patient with an obstructed mitral prosthesis, with reduced diastolic filling time for mitral inflow.

Early referral to a tertiary hospital with both obstetric and cardiac surgical services is important because of the high risk of adverse events during pregnancy in women with prosthetic heart valves. A multidisciplinary team was essential for the successful outcome for this woman and her baby.

Supplementary material

Supplementary material is available at European Heart Journal - Case Reports online.

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Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

Consent: The author/s confirm that written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: none declared.

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