

Successful Thrombolysis of Mitral Valve Prosthesis by Streptokinase during Pregnancy

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A 37 year old female patient presented with the clinical picture of pulmonary edema while pregnant (13 weeks). Eight years earlier she underwent mitral valve replacement because of rheumatic mitral incompetence using bileaflet St-Jude prosthesis. Her oral anticoagulation maintenance therapy (Coumadin) was discontinued by her physician and shifted to subcutaneous unfractionated heparin 10 days prior to her presentation. Immediate 2D-echodoppler and cinefluoroscopy showed evidence of mitral prosthesis malfunction and stuck prosthetic valve leaflets. Successful restoration of proper prosthesis function was achieved by prolonged intravenous thrombolytic therapy (Streptokinase).

A normal vaginal delivery was performed at 36 weeks with no maternal or fetal complications. Her oral anticoagulation maintenance therapy was resumed in hospital and she was discharged two weeks later.

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Classical management of prosthetic valve thrombosis, a life-threatening condition, is a repeat prosthetic valve replacement or clot removal that requires cardio-pulmonary bypass and carries a high mortality. Successful restoration of valve function by thrombolytic therapy has been reported before. We describe the successful use of streptokinase for thrombosed mitral valve prosthesis in a pregnant woman.

THE CASE

A 37 year old mother of five children presented with progressive shortness of breath of four days duration. She had a history of rheumatic fever in early childhood. She underwent mitral valve replacement because of rheumatic mitral incompetence using bileaflet St-Jude prosthesis eight years prior to her presentation. Pregnancy was diagnosed at 11 weeks of gestation by her physician and her maintenance oral anticoagulation (Coumadin) was discontinued 10 days prior to the onset of her symptoms and she was shifted to subcutaneous unfractionated heparin (12.500 IU twice daily).

Her physical examination revealed a dyspneic afebrile woman with a blood pressure of 100/60 mmHg and regular pulse of 110/min. Chest examination showed bibasal crepitations. Heart auscultation revealed muffled prosthetic valve clicks. No focal neurological deficit was detected.

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Surface EKG showed sinus tachycardia but otherwise was normal and chest x-ray showed bilateral fluffy alveolar pulmonary edema. Transthoracic 2-D echocardiography (TTE) and color coded doppler showed malfunctioning mitral valve prosthesis with 25 mmHg gradient across the mitral prosthesis and Grade II transprosthetic mitral incompetence. There was no echocardiographic evidence of clot or vegetations or pannus formation by TTE.

Cinefluoroscopy, which is a rapid and easily accessible diagnostic tool and used frequently in our institute in the evaluation of prosthetic valves, revealed immobile mitral prosthetic leaflet in the open position.

Gestational age was evaluated by abdominal ultrasound at about 3 weeks.

After joint discussion between the attending cardiologist, cardiac surgeon and obstetrician, the decision was made to give her prolonged streptokinase infusion in an attempt to restore prosthetic valve function and to avoid repeat surgery. The streptokinase protocol was adopted. According to this protocol 250,000 iu of streptokinase are given by intravenous infusion over 30 minutes, followed by continuous streptokinase infusion at a rate of 100,000 iu/hr for 72 hours. Serial cinefluoroscopy was used to assess restoration of prosthetic valve leaflet motion.

On the second day, the patient demonstrated clinical improvement but developed signs of right leg ischemia which was managed conservatively. Symptoms and signs of limb ischemia vanished soon and the patient regained her limb pulses after 24 hours.

Cinefluoroscopy at 72 hours showed full restoration of prosthetic valve leaflet motion. Follow-up abdominal ultrasound revealed an alive fetus with normal fetal heart and a biparietal diameter of 25 mm that goes with 14 weeks of gestational age.

At this stage, streptokinase infusion was discontinued and intravenous unfractionated heparin therapy was initiated. Afterwards, warfarin therapy was resumed and titrated to achieve an INR between 3.0-3.5. She was discharged from hospital in an excellent condition.

At 36 weeks of pregnancy a standard vaginal delivery was performed. Both mother and newborn had an uneventful recovery. Tubal ligation was performed at a later stage.

DISCUSSION

Prosthetic heart valve disease may be complicated by thromboembolism, bleeding, endocarditis, valve dysfunction, re-operation or death and this affects the patients at a rate of 5% per year through their lives^{1,2}. Prosthetic valve obstruction may be caused by thrombus formation, pannus ingrowth, or a combination of both. The cause may be difficult to determine and requires knowledge of the clinical presentation and findings on echocardiography, including transesophageal echocardiography.

Pregnancy increases the risk of each of the above complications. The risk of pregnancy in women with a valve prosthesis is multifactorial. Potential problems

may be related to an increased hemodynamic load, hypercoagulable state of pregnancy and risk to the fetus due to anticoagulants. It should be noted that significant changes in the levels of coagulation factors increase the risk of thrombosis during gestation. Thrombosis of prosthetic valves during pregnancy has been reported in several cases despite adequate anticoagulation³.

Thrombolytic therapy has been used in pregnant women with deep vein thrombosis, pulmonary embolism and acute myocardial infarction⁴ and thrombosed tricuspid prosthetic valve⁵. Rinaldi JP, et al⁶ reported successful thrombolysis with rt-PA in a 28 year old pregnant woman with thrombosed St-Jude aortic valve prosthesis implanted two years earlier and delivered at term by cesarean section. Fleyfel M, et al⁷ reported a 32 year old patient whose pregnancy was complicated by two episodes of thrombosed St-Jude mitral prosthesis, first occurred at 20 weeks of pregnancy during shift from warfarin to heparin (as in our case); the patient was in cardiogenic shock and was treated by clot removal and the second episode was treated by thrombolysis (recombinant tissue plasminogen activator rt-PA). It was considered to be the first case in which pregnancy was carried to term and standard vaginal delivery performed.

Thrombolytic therapy for a prosthetic valve obstructed by thrombus is associated with significant risks and is often ineffective. Two extensive reviews^{8,9} of thrombolytic therapy for left-sided prosthetic valve thrombosis reported that thrombolytic therapy is ineffective in 16 to 18% and acute mortality is 6%. The risk of thromboembolism is 12%; stroke 3% to 10%; major bleeding episodes 5%; nondisabling bleeding 14% and recurrent thrombosis 11%.

Thrombolytic therapy is reserved for those in whom surgical intervention carries a high risk and those with contraindication to operation. Patients who have a large clot, those with evidence of obstruction and those with NYHA class III or IV should undergo early/immediate re-operation.

Pregnant patients with mechanical valve prostheses have an obligate need for anticoagulation. While some suggested that warfarin is an acceptable anticoagulant, most would advise avoidance particularly in the first trimester as warfarin is teratogenic and crosses the placenta. Some others advocated the use of warfarin through pregnancy despite increased fetal teratogenicity, the risk might be less if warfarin dose was less than 5 mg per day, nonetheless this approach is still very controversial despite the fact that fetal teratogenicity with warfarin has been over emphasized¹⁰.

Heparin does not cross the placenta and is generally considered safer. Its longer-term use, however, is complicated by sterile abscesses, osteoporosis, thrombocytopenia and bleeding. Numerous case series and patient registries attest to an unacceptable incidence of thromboembolic complications, including fatal valve thrombosis, in high-risk pregnant women managed with subcutaneous heparin has not been definitively established.

Low molecular weight heparin offers several potential advantages over unfractionated heparin, including greater bioavailability, easy administration, lack of need for laboratory monitoring and lower incidence of thrombocytopenia and osteoporosis.

Low molecular weight heparins may be a reasonable alternative but still are not well evaluated in patients with prosthetic valves¹¹. Therefore, it seems that there is no safe method of anticoagulation during pregnancy in women with a mechanical heart valve.

CONCLUSION

Thrombolysis of thrombosed prosthetic heart valve in pregnant women is feasible and relatively safe in selected cases and may allow continuation of pregnancy.

REFERENCES

1. Sbarouni E, Oakley CM. Pregnancy and prosthetic heart valves. *Br Heart J* 1994;71:196-201.
2. Cotrufo M, Deluca TSL, Calabro R, et al. Coumarin anticoagulant during pregnancy in patient with prosthetic heart valves. *Eur J Cardiothoracic Surg* 1991;27:1704-6.
3. Hurt's the heart text book. Clinical performance of prosthetic heart valve. Chapter 67, 1850-60. Miscellaneous disease and condilition. Chapter 92, 2400-2.
4. Schumacher B, et al. Successcul treatment of acute myocardial infarction during pregnancy. *Am J Obstet Gynecol* 1997;176:716-9.
5. Dio Roio C, et al. Thrombolytic therapy with rt-PA of recurrent thrombosis of tricuspid valve prosthesis during pregnancy. *Ann Fr Anesth Reanim* 1996;15:666-8.
6. Rinaldi et al. Successful thrombolysis on san aortic valve prosthesis by t-PA during pregnancy. *Arch Malcoeur Vaiss* 1999;92:427-30.
7. Flefyl et al. Recombinant t-PA treatment of thrombosed mitral valve prosthesis during pregnancy. *Can J Anasthe* 1997;44:735-8.
8. Lengyel M, Fuster V, Keltali 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.
9. Hurrel DG, Schaff HV, Tajik AJ. Thrombolytic therapy for obstruction of mechanical valve. *Mayo Clin Proc* 1996;71:605-13.
10. Elkayam U. Anticoagulation in pregnant woman with prosthetic valve. A double Jeopardy. *JAM Coll Cardiol* 1996;27:205-13.
11. Barbour LA. Department of medicine, university of Colorado health science center, Denver USA. Current concepts of anticoagulant in pregnancy. *Obst Gynecol Clin North AM* 1997;2:499-521.