Intracranial Hemorrhage in Pregnancy

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Abstract

A pregnant woman with a mechanical prosthetic mitral valve was anticoagulated with low-molecular-weight heparin in the first trimester followed by warfarin until 36 weeks' gestation. She was then switched to intravenous unfractionated heparin infusion to allow for regional anesthesia in anticipation of vaginal delivery. She developed severe headache on hospital day 2 that was refractory to pain medications. Cranial imaging demonstrated a large subdural hematoma with midline shift. She delivered a healthy baby girl by cesarean section. Eventually, symptoms and intracranial abnormalities resolved over time. In conclusion, subdural hematoma is a relatively rare complication that requires multidisciplinary management plan.

Keywords
- anticoagulation
- pregnancy
- prosthetic heart valve
- heparin

Prosthetic heart valves in pregnancy present a unique clinical challenge. Adequate anticoagulation is mandatory in such patients to prevent catastrophic complication of valve thrombosis with up to 40% risk of maternal mortality.[1] Other less feared complications include hemorrhage and/or endocarditis. The goal in pregnancy is to maintain adequate maternal anticoagulation while minimizing the deleterious effects of anticoagulants in the developing fetus. Overall, the risk for anticoagulation-related complications is ~3% per patient year.[2] We present a patient with a mechanical prosthetic mitral valve who developed intracranial hemorrhage while on intravenous unfractionated heparin (UFH) infusion in the third trimester.

Case Report

A primigravida was referred to our University Medical Center with a history of prosthetic mitral valve replacement (St. Jude No. 32, St. Paul, MN) 2 years prior to this pregnancy due to severe rheumatic mitral stenosis. The patient was otherwise healthy with no chronic medical conditions. The patient was being treated with warfarin anticoagulation prior to pregnancy without sequelae. As soon as the pregnancy was confirmed, the patient was switched to enoxaparin (1 mg/kg subcutaneously twice daily) and was followed with serial enoxaparin levels. At 14 weeks' gestation, she was converted to daily warfarin therapy (dose range between 5 and 7.5 mg) to maintain international normalized ratio (INR) between 2.5 and 3.5. The patient had an uneventful prenatal course.

Warfarin dose was held for 2 days and the patient was admitted at 36 weeks for conversion to UFH infusion in anticipation for regional anesthesia and vaginal delivery. She received a 5000 U UFH intravenous bolus followed by an infusion at a rate of 1000 U per hour. Activated partial thromboplastin time (aPTT) was monitored and infusion adjusted to maintain aPTT between 55 and 80 seconds. Within 24 hours of initiation of UFH infusion, the patient complained of a persistent headache that was refractory to pain medications. The patient was afebrile and hemodynamically stable with a blood pressure of 110/70 mm Hg. Given the clinical suspicion for an intracranial pathology, a cranial computed tomography (CT) scan was obtained that revealed an acute subdural hemorrhage with a 6-mm left-to-right midline shift. The patient's aPTT at the time of diagnosis was 49 seconds (normal $\leq$35 seconds), platelet count 162,000, and hemoglobin of 11.4 mg/dL. Of note, aPTT of 120 seconds was observed 12 hours prior to the onset of headache that was managed in the standard way by holding off the infusion until the aPTT normalized over a period of 2 hours. Heparin infusion was immediately discontinued and

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consultations with neurosurgery and cardiology were obtained. The aPTT normalized within 3 hours of intravenous heparin cessation. The patient remained hemodynamically stable and alert and oriented without neurological deficits. She was transferred to the neurological intensive care unit for close neurological monitoring. Neurosurgery team obtained magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA) of the brain to delineate the source of bleeding and to rule out potential vasculature malformations. Both MRI and MRA confirmed a stable left extra-axial hemorrhage localized to the subdural and subarachnoid areas without evidence of abnormal brain vasculature. The patient was expectantly managed without anticoagulation with plans to intervene surgically in the event of clinical deterioration.

A multidisciplinary discussion was held between maternal-fetal medicine, neurosurgery, and cardiology teams to outline further management including delivery plan. Given her stable neurological status and a relatively late preterm gestational age of 36 weeks, the decision was made to proceed with cesarean delivery. We performed an uncomplicated primary low transverse cesarean section under general anesthesia, delivering a vigorous female infant with Apgar scores of 8 at 1 minute and 9 at 5 minutes and weighing 2669 g. The infant was transferred to the newborn nursery.

Following delivery, the patient returned to the neurological intensive care unit for telemetry and serial neurological evaluations. In addition, the patient was followed closely with serial cardiac evaluations to confirm normal function of the prosthetic valve. The patient remained clinically stable and neurologically intact, and the headache gradually resolved over the next 12 hours. A repeat CT scan remained stable and no cardiac complications were encountered in the postpartum period. UFH infusion was restarted without a loading dose ~72 hours following her delivery to aPTT level between 55 and 65 seconds (low therapeutic range). Once therapeutic on intravenous UFH, she was started on low-dose warfarin. On hospital day 16, the patient was therapeutic on warfarin (INR 3.0), and the UFH drip was discontinued. The patient was discharged to home in stable condition. Subsequent serial CT scans demonstrated gradual but complete resolution of the hematoma over the next couple of weeks.

Discussion

There are no reported cases in the literature of this devastating complication of anticoagulation in pregnancy to our knowledge. To maintain a sustained and stable anticoagulation profile in a pregnant woman may be challenging due to the inherent physiological changes in coagulation profile. Prosthetic heart valves in pregnancy are particularly at high risk of complications such as valve thrombosis, thromboembolism, and bleeding. The estimated risk of thromboembolic complication in patients with prosthetic heart valves in pregnancy ranges from 7 to 23%; Mortality rate may be as high as 40% in a setting of valve thrombosis.[1]

The baseline risk for thrombosis without anticoagulation in a patient with prosthetic mechanical heart valves is 4% per patient year, and therefore, use of anticoagulants is mandatory. Agents used for anticoagulation may pose significant maternal and fetal risks. Currently, the commonly used drugs in such patients include warfarin, UFH, and low-molecular-weight heparin (LMWH). Warfarin is considered an ideal agent in nonpregnant patients; however, it is teratogenic. Warfarin is associated with embryopathy if used in the first trimester, spontaneous abortion, and fetal intracranial hemorrhage. It may also restrict the use of regional anesthesia at the time of delivery. UFH is a reliable drug when given intravenously and minimally crosses the placenta; however maintaining adequate anticoagulation with subcutaneous administration is difficult and is associated with higher maternal risk for thromboembolic complications.[3] Last, LMWH has a better pharmacokinetic profile and may be considered an option for anticoagulation in pregnancy as suggested by the American Heart Association/American College of Cardiology guidelines.[4,5]

Intracranial bleeding is a challenge in the presence of prosthetic heart valve as there is an increased risk of thrombotic complications in pregnancy. The immediate treatment of the subdural hemorrhage warrants cessation of anticoagulant therapy. We considered reversal of heparin anticoagulation with protamine sulfate; however, we were concerned about the potential risk of rebound hypercoagulability leading to valvular thrombosis, heart failure, thromboembolism, and even maternal mortality.[6] The options for management of valve thrombosis include clot lysis with thrombolytic agents or emergency valvular surgery.[7] However, in the setting of intracranial hemorrhage, thrombolytic therapy is absolutely contraindicated and the surgical option would have required intravenous UFH infusion during and following surgery that could be fatal in a setting of intracranial bleeding. And therefore, the team decided against that option.

There are a few reports in the literature regarding the management of intracranial hemorrhage and prosthetic heart valves in nonpregnant patients on warfarin. Phan and colleagues retrospectively analyzed data on 141 patients with "high-embolic risk" over a 23-year period. Of them, 52 had prosthetic heart valves. In this group, discontinuation of warfarin therapy for 1 to 2 weeks had a relatively low probability of embolic events.[8] Bertram et al validated this seemingly "safe" window of 1 to 2 weeks of discontinuation of anticoagulation following an intracranial bleed. However, in the same report, the authors observed a higher rate of rebleeding nearing 20% when therapeutic values were achieved. Interestingly, 20% of patients also had evidence of embolism recurrence if therapeutic levels were not attained, emphasizing the importance of timing of reinitiation of anticoagulation as well as targeting the appropriate level of anticoagulation so as to avoid clinical mishap.[9] Unfortunately, none of these series included gravid patients who are inherently more hypercoagulable than their nonpregnant counterparts.

In conclusion, we conducted a Medline and PubMed search from 1980 to 2010 with the search terms "prosthetic valves," "intracranial hemorrhage," and "pregnancy" and found no case reports. Our goal is to raise awareness and potential

management strategy of this relatively rare adverse effect of anticoagulation in pregnancy. Such cases mandate a coordinated multidisciplinary approach for a favorable maternal and fetal outcome.

References

1 Born D, Martinez EE, Almeida PA, et al. Pregnancy in patients with prosthetic heart valves: the effects of anticoagulation on mother, fetus, and neonate. Am Heart J 1992;124:413–417

2 Vongpatanasin W, Hillis LD, Lange RA. Prosthetic heart valves. N Engl J Med 1996;335:407–416

3 Srivastava AR, Modi P, Sahi S, Niwariya Y, Singh H, Banerjee A. Anticoagulation for pregnant patients with mechanical heart valves. Ann Card Anaesth 2007;10:95–107

4 American College of Obstetricians and Gynecologists. ACOG Committee Opinion: safety of Lovenox in pregnancy. Obstet Gynecol 2002;100:845–846

5 Bonow RO, Carabello BA, Chatterjee K, et al. American College of Cardiology/American Heart Association Task Force on Practice Guidelines. 2008 focused update incorporated into the ACC/AHA 2006 guidelines for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to revise the 1998 guidelines for the management of patients with valvular heart disease). Endorsed by the Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. J Am Coll Cardiol 2008;52:e1–e142

6 Elkayam U, Bitar F. Valvular heart disease and pregnancy: part II: prosthetic valves. J Am Coll Cardiol 2005;46:403–410

7 Choi C, Midwall S, Chaille P, Conti CR. Treatment of mechanical valve thrombosis during pregnancy. Clin Cardiol 2007;30: 271–276

8 Phan TG, Koh M, Wijdicks EFM. Safety of discontinuation of anticoagulation in patients with intracranial hemorrhage at high thromboembolic risk. Arch Neurol 2000;57:1710–1713

9 Bertram M, Bonsanto M, Hacke W, Schwab S. Managing the therapeutic dilemma: patients with spontaneous intracerebral hemorrhage and urgent need for anticoagulation. J Neurol 2000;247:209–214