Fetal Hydrocephaly Induced by Warfarin in the Second Trimester

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ABSTRACT
Managing a patient with a mechanical prosthetic heart valve during pregnancy is problematic. The use of vitamin K antagonists such as warfarin, even after the period of embryogenesis, is associated with fetal abnormalities. A patient with a mechanical prosthetic heart valve was managed according to recent guidelines indicating to resume warfarin therapy after the period of embryogenesis. The fetus sustained an intraventricular hemorrhage with resultant obstructive hydrocephaly. In view of warfarin-induced fetal abnormalities after the first trimester, consideration should be given to maintaining patients with mechanical prosthetic heart valves on unfractionated heparin or low molecular weight heparin throughout pregnancy.

INTRODUCTION
Management of a patient with a mechanical prosthetic heart valve during pregnancy is problematic. Full anticoagulation is required throughout pregnancy to prevent thromboembolic complications that can lead to significant maternal morbidity and mortality. Most patients are managed with warfarin or other vitamin K antagonists prior to pregnancy. The goal of therapy is to keep the international normalized ratio (INR) between 2.5-3.5. Once pregnancy is confirmed, most guidelines recommend that warfarin be discontinued from 6 weeks of gestation until the end of the first trimester to avoid warfarin embryopathy. Unfractionated heparin (UFH) or low molecular weight heparin (LMWH) is substituted during the first trimester and then after 36 weeks gestation.

Warfarin embryopathy is characterized by nasal hypoplasia, depressed nasal bridge, stippling of uncalcified epiphyses, hypoplastic distal phalanges, small-for-gestational age, and other associated anomalies including central nervous system abnormalities such as hydrocephaly, Dandy-Walker malformations, and microcephaly. Teratogenic effects are thought to be directly due to warfarin embryopathy or from hemorrhage into fetal organs from vitamin K deficiency caused by warfarin. In addition to induction of fetal anomalies, warfarin exposure may lead to fetal demise.

CASE REPORT
A 24-year-old primagravida female presented at 6 weeks gestation for prenatal care. Her medical history was remarkable for mitral valve replacement with a mechanical prosthetic heart valve, Starr-Edwards type, for mitral stenosis due to rheumatic fever. She was on warfarin 5 mg each day for thromboembolism prophylaxis. After confirmation of pregnancy, her cardiologist switched her to UFH to prevent warfarin-induced embryopathy. At 18 weeks gestation, a targeted fetal anatomical survey was done and no fetal anomalies were identified. After this exam, her cardiologist discontinued heparin therapy and re-instituted warfarin therapy after conferring with the patient’s obstetrician. Her warfarin was adjusted to maintain a therapeutic INR.

At 24 weeks gestation, an ultrasound exam was performed for fetal growth. Fetal hydrocephaly was present. The biparietal diameter measured 8.0 cm and the head circumference was 30.5 cm, consistent with an estimated gestational age of 32 and 33 weeks, respectively. Less than 5 mm of cerebral cortex was present. No other gross fetal anomalies were noted.

After counseling, the patient elected to terminate the pregnancy. Induction of labor was performed with prostaglandin E2 (dinoprostone) after pre-induction cervical ripening with laminaria. The fetal presentation was breech and during labor a cephalocentesis was performed to facilitate vaginal delivery. Amniotic fluid was obtained for karyotyping prior to the cephalocentesis, which was normal (46XX). Cultures of the amniotic fluid were negative. TORCH titers were also negative. No gross anomalies were present of the fetus other than the hydrocephaly. The parents declined an autopsy.

DISCUSSION
The patient was managed according to the 2006 guidelines of the American College of Cardiology and the American Heart Association. Warfarin was discontinued until after the first trimester and then re-instituted. In spite of adhering to the guidelines, the fetus sustained a warfarin-induced intracerebral hemorrhage. Recent guidelines (2012) from the American College of Chest Physicians continue to recommend vitamin K antagonists after 13 weeks gestation in addition to adjusted-dose LMWH or UFH for patients with mechanical prosthetic heart valves during pregnancy. For women with older generation mitral valve prostheses or a history of thromboembolism, warfarin and its derivatives may be more efficacious than heparin derivatives in preventing thromboembolic phenomena during pregnancy.

Heparin, because of its molecular weight (9,000-12,000 daltons), does not cross the placenta to any extent as does warfarin with a lower molecular weight (308 daltons) and it does not possess the ability to cause a similar warfarin-induced embryopathy. This case demonstrates that warfarin can cause fetal abnormalities after the first trimester by hemorrhage into fetal tissues. The

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ciology of the hydrocephaly was most likely due to warfarin-induced vitamin K deficiency leading to intraventricular hemorrhage and subsequent obstructive hydrocephaly. Patients with mechanical prosthetic heart valves should be extensively counseled concerning anticoagulation therapy during pregnancy. Even though warfarin and other vitamin K antagonists are still recommended as an alternative to LMWH or UFH, the patient and her fetus may be better served by not using warfarin during pregnancy without full disclosure of the potential risks and benefits.

REFERENCES


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