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Review

Management of mechanical valve thrombosis during pregnancy, case report and review of the literature

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ABSTRACT

Anticoagulant therapy of the patients with mechanical heart valve prosthesis (MHV) in the course of pregnancy requires careful monitorization and well estimation of each step regarding benefits and handicaps of each treatment strategy in the particular trimester. Unfractioned heparin with close monitoring of activated thromboplastin time (APTT), low molecular weight heparin with close monitoring of anti Xa levels or warfarin with close monitoring of INR are the main options. It may be challenging most of the sometimes because of the procoagulant nature of pregnancy as well as physiological changes like increased glomerular filtration rate. During the follow up, any recent onset symptom should call prompt and careful investigation beginning with transthoracic echocardiography and planning further transesophageal echocardiography and fluoroscopic studies if needed. If MHV thrombosis is detected, management of patients differs due to the presence of obstruction, critical illness, thromboembolic events or thrombus size. Thrombolytic therapy and the surgical thrombectomy are the options for critically ill patients. International guidelines suggest surgical approach as a first line therapy if the risk of surgery is not too high. However, the complication and success rates of studies with fibrinolytic agents are encouraging. Each strategy comes with its own particular risk and regardless of the selected strategy MHV thrombosis during the pregnancy is a high risk situation. In this paper, we report a 26 year old patient presented with recent onset dyspnea due to MHV thrombosis in the mitral position. After the failure of unfractioned heparin, and because of hemodynamic deterioration she was referred for urgent surgery. She recovered after the surgery, however baby was found to have congenital diaphragmatic hernia and is still monitored in the intensive care unit. This report includes, treatment strategies of anticoagulant medication for the pregnant patients with MHV prosthesis and management of MHV thrombosis during the pregnancy.

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Introduction

Mechanical valve thrombosis during pregnancy is a life threatening situation. Accurate treatment is unclear and management should be personalized to find the lowest acceptable risk both for the fetus and the mother. Each strategy has its own particular risk and potential

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benefit. Clinicians should estimate the risk of each step carefully on this blurry road while trying to reach final cure for their patients.

Case

Twenty six year old woman at her 36 week of pregnancy presented to our emergency department with dyspnea and fatigue. The patient had a history of mechanical mitral valve implantation because of rheumatic disease in 2012. Transthoracic echocardiography (TTE) showed prosthetic valve dysfunction with high transvalvular gradient (max: 30 mm Hg, mean 18 mm Hg) without significant regurgitation. Pulmonary artery systolic pressure was calculated to be 68 mm Hg (from the tricuspid valve velocity). She was taking subcutaneous 80 mg (equivalent to 8000 IU anti-Xa activity) enoxaparin two times a day and was taking no other anticoagulant medications. Her anti Xa levels was measured and found to be in therapeutic range (1.3 IU/ml). However, transesophageal echocardiography (TEE) revealed thrombus on the atrial side to cause restriction of leaflet motions (Fig. 1). Intravenous continuous infusion of unfractionated heparin (UFH) to maintain activated partial thromboplastin time (APTT) 1,5 to 2 times higher than the upper normal threshold of controls was begun. However urgent surgical consultation was made in the second day due to deteriorating clinical status. She was also consulted to the gynecology department. The decision to take baby via cesarean section and to continue with the extirpation of thrombus in the same operation session was made. Just after the delivery, the baby was resuscitated and intubated and found to have right pulmonary hypoplasia and congenital diaphragmatic hernia. After the extraction of thrombus, mother was okay and extubated in the second day of operation. She was discharged in the tenth day with 100 mg acetyl salicylic acid (ASA) and adjusted warfarin, while baby was still under monitorization in the intensive care unit.

Discussion

Anticoagulant options

Management of the anticoagulant regimen of women with mechanical heart valves (MHV) during pregnancy is a challenging problem because of the procoagulant nature of pregnancy. Especially in the second and third trimesters, increased levels of factors VII, VIII, and X and decreased levels of protein S lead to a hypercoagulable state.[1] On the other hand thrombotic complications of MHV mostly occur during the first trimester where anticoagulant regimens are switched from one regimen to another.[2] Oral vitamin K antagonists (VKA) are the most effective regimen proven to prevent thrombosis of MHVs. However, VKA are shown to cross placental barrier and cause a group of embryonal pathology known as warfarin embryopathy.[3,4] These include nasal hypoplasia and stippled epiphyses, ocular and neurological abnormalities. VKA was also shown to cause late fetal loss and stillbirth.[5] The risk of embryopathy is dose dependent, with a low risk (<3%) if the dose of warfarin is ≤5 mg per day.[5] Moreover in the first trimester, the risk of fetal loss and abortion is same in the course of low dose warfarin, UFH or low molecular weight heparin (LMWH) usage.[5,6] Thus, if ≤5 mg warfarin dose can maintain therapeutic INR levels, it may be possible not to switch the anticoagulant regimen to another option. But if higher doses are needed to achieve therapeutic levels, then switching the therapy to another anticoagulant regimen other than VKA is needed. At that point the risk of valve thrombosis and related complications begins to rise. It is possible to use subcutaneous UFH throughout the pregnancy not to meet any embryonal pathology. However this strategy was shown to be related to high incidence (up to 33%) of MHV thrombosis.[7] Current guideline of the American College of Cardiology/American Heart Association (ACC/AHA) valvular heart disease guidelines suggests that if therapeutic targets of INR is achieved with <5 mg/day warfarin usage, then it should be used throughout pregnancy.[5,6] However, if the dose to achieve therapeutic INR exceeds 5 mg/day, changing the anticoagulant regimen from warfarin to LMWH or continuous UFH during the first trimester is recommended.[5,6] After substitution to a VKA, it is recommended until 36 weeks, when it should be replaced with LMWH or UFH mainly to prevent fetal intracranial hemorrhage as well as uncontrolled bleeding of the mother during the vaginal delivery. Dose-adjusted continuous intravenous UFH (with an aPTT at least 2 times control) during the first trimester is suggested for pregnant patients with a mechanical prosthesis if the dose of warfarin exceeds 5 mg/day to achieve a therapeutic INR.[5] On the other hand, if LMWH is the preferred agent in the first trimester, it is recommended to adjust the dosage not depending on weight but to maintain peak anti-Xa levels between 1.0 and 1.2 U/ml that was checked after 4–6 h of the last dose because of the fact that dose requirements may increase by as much as 50% over the course of pregnancy especially due to increased glomerular filtration rates.[5,8] LMWH provides better bioavailability, longer half-life, and a more predictable anticoagulation response, and it does not cross placental barrier.[5] It is known that monitoring anti-Xa levels in patients under LMWH regimen reduces complication rates as it was reported that maternal thromboembolic events were 22% versus 8.64% and death was 4% versus 0% with and without monitoring.[9–11] Moreover, with use of this anti-Xa dependent dosing regimen, the incidence of valve thrombosis is lower than with UFH.[5] On the other hand, it was shown that despite appropriate anti-Xa levels, MHV thrombosis risk is still a problem in patients under management of LMWHs.

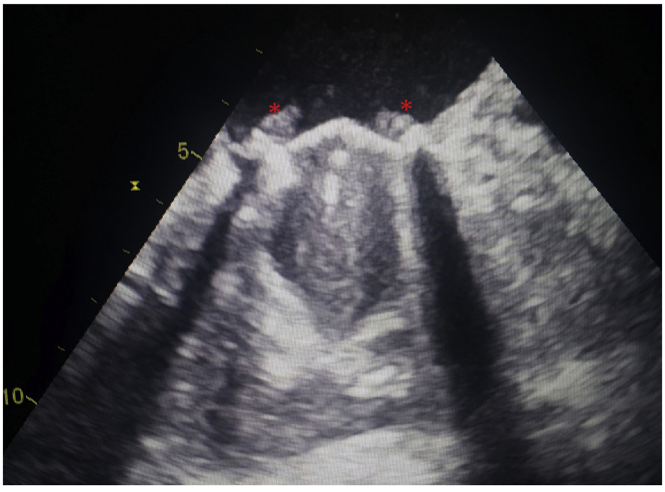

Fig. 1. Transesophageal echocardiography image depicting diffuse thrombus particles on the atrial side of mitral mechanic prosthetic valve. (Red asterisk on the both sides). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Mechanical heart valve thrombosis

It is usually hard to decide about MHV thrombosis during the pregnancy as cardiac output increases throughout the pregnancy which leads to limited increment of mean pressure gradient across the prosthetic valves. However, MHV thrombosis should be promptly suspected in cases presented with recent onset dyspnea and/or embolic events.[12] First TTE and then, if suspicion is high TEE should be performed.[13] If it is still required, fluoroscopy may be performed with limited fetal risk.[13] In a review, MHV thrombosis rates were reported to be 3.9% when oral anticoagulants (OACs) are selected throughout the pregnancy and 9.2% when UFH is used in the first and OACs are used in the second and third trimesters.[7] The rate is high as 33% when UFH is selected to be used throughout all trimesters.[7]

MHV thrombosis is a high risk situation, and this is regardless of the selected management strategy. Fibrinolytic therapy comes with the risks of bleeding and embolic events and surgery carries high maternal and fetal risks as it will be held in emergency situation and is a

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