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Letter to the Editor

Anticoagulation strategy and management of patients with mechanical prosthetic heart valves during pregnancy

To the Editor,

We have read with great interest the article by Komatsu et al. entitled "A case of thrombolytic therapy with recombinant tissue plasminogen activator for mechanical valve thrombosis at 9 weeks of pregnancy in a Japanese woman" [1]. The authors have reported the management of a pregnant patient with mechanical prosthetic valve thrombosis in mitral position. We congratulate the authors for achieving a successful outcome in such a high-risk patient for prosthetic valve thrombosis (PVT). However, we believe that the management strategy proposed by the authors during pregnancy requires further discussion.

Mechanical heart valves (MHVs) are thrombogenic, necessitating long-term anticoagulation to prevent adverse outcomes such as valve thrombosis, stroke, or death. Hence, anticoagulation for MHVs during pregnancy is essential to prevent thromboembolic events. The optimal type, dose, and route of anticoagulation therapy, however, remains unclear. Current evidence indicates that the administration of a vitamin K antagonist (VKA) throughout pregnancy is the most favorable approach, with a PVT risk as low as 3.9% [2]. However, a VKA crosses the placental barrier, and at high doses (i.e. >mg) can cause embryopathy when used in the first trimester, as well as other adverse fetal outcomes beyond the first trimester. But this risk has been reported to be as low as 0% to 2.6% at low doses. On the other hand, although unfractioned heparin (UFH) during the first trimester is safe for the fetus, it is associated with an unacceptable PVT risk. The highest risk strategy in terms of PVT should be noted, which is as much as 33% when pregnant patients are continuously administered with adjusted-dose UFH [2]. Therefore, it is reasonable to continue with VKA treatment throughout a pregnancy if the required dose before pregnancy is low. For the reasons described above, European Society of Cardiology/European Association for Cardiothoracic Surgery guidelines regarding the management of cardiovascular diseases during pregnancy recommend the use of low-dose warfarin in women who are able to maintain therapeutic international normalized ratios (Class IIa) over the use of either low molecular weight heparin or UFH in the first trimester (Class IIb) [3]. In the present case reported by Komatsu et al. [1], it was debatable that UFH was used as anticoagulation therapy in the first trimester in a patient needing low-dose warfarin (4 mg/day) for anticoagulation. Furthermore, continuous intravenous infusion made the patient prone to additional risks such as catheter-associated bacteremia. Also, the patient had to stay in the hospital unnecessarily throughout the first trimester of pregnancy.

Although no evidence-based guidelines for pregnant patients complicated with PVT are currently available, recommendations of guidelines for this complication are similar to the management of PVT in nonpregnant patients and missing definitive class I recommendations due to lack of randomized controlled trials. We have previously reported that low-dose (25 mg) and slow-infusion (6 h) of tissue type plasminogen activator (t-PA) is safe and associated with high thrombolytic success in pregnant patients with PVT [4]. In this single-center prospective study including a relatively large number of pregnant patients with PVT, this strategy was associated with successful thrombolysis in all patients with lower maternal and fetal adverse events compared with surgery or anticoagulation based on the available published data. This strategy includes repeated thrombolytic therapy (TT) sessions of low-dose (25 mg) slow infusion (6 h) of tPA without bolus under the guidance of serial transesophageal echocardiography (TEE) [4]. The lack of TEE guidance during TT is a major drawback of the current report. Despite the fact that transthoracic echocardiography (TTE) examination is a crucial part of the diagnosis of patients with prosthetic valves, TTE findings are usually insufficient due to acoustic shadowing of prosthetic valves. TEE may provide valuable data with regards to the assessment of mobility, location, and thrombus size. Moreover, real time 3-dimensional (RT-3D) TEE plays an essential role as a complementary imaging tool to 2-dimensional (2D) TEE in the diagnosis and evaluation of PVT [5]. We have previously shown that nonobstructive PVT (Doppler-silent) could often be overlooked during TTE study. Patients with PHV, even if they are asymptomatic, should be evaluated with TEE at least every trimester during pregnancy. In this case report, Komatsu et al. mentioned that echocardiography was performed at the first visit and when indicated, but there are no data regarding detailed evaluation of PVT with 2D TEE and RT-3D TEE. In the present case report, TT was performed after the evaluation of mitral prosthetic valve by TTE. After the first session of TT, the resolution of the stuck leaflet was visualized by TTE and cine fluoroscopy (CF) and TT was stopped. There were no data regarding the size of the residual thrombus. Was there an indication (>10 mm or 0.8 cm^2) to continue the TT for a nonobstructive PVT? TTE and CF are noninvasive tools, but have limited ability in evaluating thrombus burden and mechanism of valvular obstruction [5]. On the other hand TEE with its high resolution may differentiate thrombus from pannus formation and vegetation in PVT patients. TEE also has an indispensible value to assess thrombus size, mobility, and location which may help in decision making, such as thrombolysis, anticoagulation, and surgery. Moreover, TEE provides direct

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imaging of the thrombus in the body or the appendage of the left atrium which usually cannot to be detected with TTE. The presence of a left atrial thrombus is accepted as a contraindication for thrombolysis and should be ruled out by TEE before TT. The reduction of thrombus burden and need for additional TT sessions can be evaluated only by TEE [4].

In conclusion, it is reasonable to continue with warfarin therapy throughout pregnancy if the required dose before pregnancy is low (<5 mg/day). TT with low-dose and slow infusion of tPA should be the first-line therapy for pregnant PVT patients unless contraindicated. Serial TEE guidance should complement TTE in every step of the management algorithm in patients undergoing TT for PVT.

Conflict of interest

All of the authors have no conflict of interest.

Disclosure

We have nothing to declare.

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References

[1] Komatsu T, Motoki H, Kimura K, Saigusa T, Ebisawa S, Yokokawa Y, et al. A case of thrombolytic therapy with recombinant tissue plasminogen activator for mechanical valve thrombosis at 9 weeks of pregnancy in a Japanese woman. J Cardiol Cases 2018;19:15–8.
[2] Güner A, Bayam E, Kalkan S, Gündüz S, Özkan M. Is the use of low molecular weight heparin a rational choice during pregnancy in patients with a mechanical heart valve: a report of three cases. Turk Kardiyol Dern Ars 2019;47:63–8.
[3] Regitz-Zagrosek V, Roos-Hesselink JW, Bauersachs J, Blomström-Lundqvist C, Cífková R, De Bonis M, et al. ESC guidelines for the management of cardiovascular diseases during pregnancy. Eur Heart J 2018;39:3165–241.
[4] Özkan M, Cakal B, Karakoyun S, Gürsoy OM, Çevik C, Kalçk M, et al. Thrombolytic therapy for the treatment of prosthetic heart valve thrombosis in pregnancy with low-dose, slow infusion of tissue-type plasminogen activator. Circulation 2013;128:532–40.
[5] Gürsoy MO, Kalçk M, Yesin M, Karakoyun S, Bayam E, Gündüz S, et al. A global perspective on mechanical prosthetic heart valve thrombosis: diagnostic and therapeutic challenges. Anatol J Cardiol 2016;16:980–9.

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