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LETTER TO THE EDITOR

Management of prosthetic valve thrombosis complicated by ischemic stroke in pregnancy

Tratamento da trombose de prótese valvular complicada por acidente vascular cerebral isquémico na gravidez

To the Editor,

We have recently read with great interest the article by Morgado et al. entitled ''A pregnant woman with a prosthetic mechanical valve''.[1] The authors reported the management of a pregnant patient with a mechanical prosthetic valve in mitral position complicated by acute ischemic stroke (AIS). We congratulate the authors for achieving a successful management in such a high-risk patient for prosthetic valve thrombosis (PVT). However, we believe that the anticoagulation therapy and management of stroke proposed by the authors during pregnancy requires further discussion.

Mechanical prosthetic heart valves are highly thrombogenic and increase the risk of thrombosis by up to 10% in the procoagulant condition of pregnancy.[2] The most devastating complication is AIS (such as in this case report) caused by thromboembolism, which can occur in up to 6% of cases for left-sided PVT.[2–5] The first six hours after AIS are crucial for the decision whether to institute thrombolytic therapy (TT) and it is important to obtain an early diagnosis and exclude bleeding by computed tomography. Based on evidence from case reports, the American Heart Association/American Stroke Association recommend administering tissue-type plasminogen activator (t-PA) in pregnant patients with AIS when the anticipated benefits of functional improvements outweigh the anticipated risks of bleeding, although the recommendation class is low, and the level of evidence is poor (class IIb, level C).[6] Considering this recommendation, due to the similar incidence of complications between pregnant and nonpregnant cohorts, and as alteplase is unlikely to cross the placenta, treatment should not be withheld due to pregnancy alone. We have previously reported that low-dose, slow infusion of t-PA with repeated doses as needed is an effective therapy with an excellent thrombolytic success rate for the treatment of PVT in pregnant women and that TT should be considered first-line therapy in pregnant patients with PVT.[2] Although the recommended dose of tPA according to the stroke guidelines is 0.9 mg/kg (maximum dose 90 mg) for 60 min for AIS according to current guidelines, with 10% of the dose given as bolus for 1 min, we used lower doses for safety reasons. The high success rate may be due to early diagnosis and fresh nature of the thrombus.[4] Faster TT regimens may induce new AIS in patients with concomitant PVT.[7]

In this case report, the authors refer to the patient's ''sudden ischemic stroke'' at the first medical contact. In addition, they emphasized that ''fibrinolysis was also considered inappropriate because of recent stroke, ongoing anticoagulation and pregnancy'' in the article. The most important point in such cases is the elapsed time from the onset of stroke at admission. Since unfractionated heparin and pregnancy do not constitute an absolute contraindication for TT, if patients are admitted within six hours of AIS, TT would be considered as an appropriate option for such cases.

There are several alternative therapies for anticoagulation in pregnant women with mechanical heart valves, however all options have pros and cons for the mother and the fetus. The first trimester has a special importance due to undesirable effects of anticoagulants on the organogenesis of the fetus. A warfarin dose >5 mg/day in the first trimester has been associated with various embryopathies, but on the other hand anticoagulation with unfractionated heparin (UFH) or low molecular weight heparin (LMWH) carries risks of PVT and other related complications.[8,9] The European Society of Cardiology/European Association for Cardiothoracic Surgery guidelines on the management of cardiovascular diseases during pregnancy recommend that continuation of warfarin should be considered during the first trimester if the warfarin dose required for therapeutic anticoagulation is <5 mg/day (class IIa, level C). Discontinuation of oral anticoagulation between weeks 6 and 12 and replacement by adjusted-dose UFH (partial thromboplastin time $\geq 2\times$ control; applied as intravenous infusion) or LMWH twice daily (with dose adjustment according to weight and target anti-Xa level of 0.8-1.2 U/ml) should be considered in patients who require a warfarin dose of >5 mg/day (class IIa, level C). Moreover, LMWH is not recommended when weekly anti-Xa level monitoring and dose adjustment are not available (class III, level C).[10] In the case reported by Morgado et al., LMWH was preferred as anticoagulation therapy during pregnancy, but the authors did not provide detailed information about anti-Xa follow-up.

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Real-time three-dimensional transesophageal echocardiography (RT-3D TEE) emerged as an important clinical tool in the assessment of PVT more than 10 years ago. RT-3D TEE has higher spatial resolution compared with two-dimensional (2D) imaging, resulting in images with unparalleled anatomic detail. The detection of non-obstructive PVT can be challenging, particularly when Doppler parameters are within normal limits and clinical findings are subtle. Hence, non-obstructive PVT may be missed with 2D imaging. Briefly, diagnostic accuracy for detecting PVT was improved after introduction of RT-3D TEE, especially for valves in the mitral position.[11] The authors stated that the patient was assessed by transthoracic echocardiography (TTE) for PVT when admitted for the second time. For the reasons described above, 2D imaging may be insufficient in the diagnosis of PVT. In this case, mechanical heart valves should be thoroughly assessed with TEE (including RT-3D) prior to percutaneous intervention for AIS.

The percentage of time in therapeutic range (TTR) provides a useful and reliable measure of the quality of anticoagulation management. Increased TTR is associated with a lower risk of thromboembolic events and bleeding in patients using vitamin K antagonists (VKAs). This parameter is a major determinant of the efficacy and safety of VKAs, with maximum benefits evident when the TTR is above 70%.[12] In the present case report, data on the patient's TTR after the first trimester of pregnancy could be important regarding thromboembolic complications.

Conflicts of interest

The authors have no conflicts of interest to declare.

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