Thromboembolism in a Patient With a Mechanical Mitral Valve During Anticoagulation With Dabigatran Eteixilate

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Recently, several new anticoagulants have been used instead of warfarin for preventing thromboembolism. In the RE-LY (Randomized Evaluation of Long-Term Anticoagulation Therapy) trial, the direct thrombin inhibitor dabigatran etexilate was as effective and safe as dose-adjusted warfarin for prevention of stroke in high-risk patients with atrial fibrillation. However, the safety and efficacy of thromboprophylaxis after mechanical valve replacement is uncertain. We report a 57-year-old man with a mechanical heart valve who experienced acute upper limb thromboembolism during dabigatran intake. Dabigatran might be inadequate for thromboprophylaxis after mechanical valve replacement.


Several new anticoagulants are being used instead of warfarin. In the RE-LY (Randomized Evaluation of Long-Term Anticoagulation Therapy) trial, the direct thrombin inhibitor dabigatran etexilate was as effective and safe as warfarin for prevention of stroke in high-risk patients with atrial fibrillation [1]. However, the safety and efficacy of thromboprophylaxis after mechanical valve replacement is unclear.

In this report we describe a patient who underwent mechanical mitral valve replacement and experienced acute upper limb thromboembolism while receiving anticoagulation with the direct thrombin antagonist dabigatran etexilate.

A 57-year-old Japanese man with congenitally corrected transposition of the great arteries (ccTGA) was transferred to our department from a clinic because of right upper limb numbness persisting 10 days. He had a 31-mm St. Jude bileaflet mechanical mitral valve replacement that was implanted for severe regurgitation of the anatomic tricuspid valve (systemic atrioventricular valve) in October 1993. After operation, he underwent anticoagulation with warfarin, with an accurate target prothrombin international normalized ratio. His anatomic right ventricle (RV; systemic ventricle) displayed severely depressed global systolic function, and his ejection fraction was 35%. He also had paroxysmal atrial fibrillation after operation, but it was well controlled with amiodarone.

One day in May 2011, the patient chose to stop warfarin and start dabigatran 150 mg twice daily because he had longed to eat natto, which has interactions with warfarin. Ten days later, the symptom appeared and he was transferred to our department from the clinic. He said he had taken his medication regularly at the expected times.

On admission, he was in sinus rhythm at 60 bpm, with blood pressure 98/60 mm Hg. Laboratory test results showed the following: normal hemoglobin value at 14.6 g/dL, platelet count at 25.6 × 10^9/mm^3, and creatinine level at 0.68 mg/dL, with a slightly increased aspartate transaminase level at 40 IU/L and alanine transaminase level at 56 IU/L. A coagulation screen performed about 8 hours after the last dose was consistent with activated partial thromboplastin time of 33.1 seconds, prothrombin international normalized ratio of 0.86, antithrombin III of 129%, and D-dimer levels of 1.2 μg/mL. Admission computed tomography showed right axillary artery occlusion besides a typical ccTGA anomaly with atrioventricular and ventricular-arterial discordance but without intracardiac thrombus.

An urgent thromboembolectomy was performed from the right brachial artery approach, and a 10 × 30 mm thrombus was removed. On transesophageal echocardiography performed the next day, there was no thrombus in cardiac chambers or on the mechanical valve, but there was a smoke-like echo in the right atrium.

Eventually he was discharged home after dabigatran was discontinued and warfarin was restarted. He remained well during 20 months of follow-up without cardiac thrombus or a thromboembolic event.

Comment

Warfarin reduces the risk of stroke and death in patients with mechanical heart valves but increases the risk of hemorrhage, and it is difficult to use because of its interactions with food and drugs.

Dabigatran is a potent direct competitive inhibitor of thrombin. Compared with warfarin, dabigatran is easier to use because it has no interactions with food or drugs and does not require blood monitoring. After publication of the RE-LY trial, dabigatran was widely used for patients with atrial fibrillation. However, for patients with mechanical valves, the safety and the efficacy for preventing thrombosis is still unclear.

Some authors reported the effectiveness of dabigatran in thromboprophylaxis of mechanical heart valves in vitro [2–4]. Maegdefessel and colleagues [2] reported that dabigatran was as effective as unfractionated heparin and...
low-molecular-weight heparin in preventing thrombus formation on mechanical heart valves in an vitro model. McKellar and associates [3] reported that dabigatran prevented valve thrombus and platelet deposition on St. Jude mechanical valves in a porcine heterotopic model. However, in these 2 reports, dabigatran could not completely prevent valve thrombosis. Actually, Stewart and colleagues [5] described a patient with a St. Jude aortic valve replacement who experienced valve thrombosis and an embolic stroke when undergoing anticoagulation with dabigatran. Price and associates [6] reported 2 patients with mechanical heart valves, 1 in the aortic position and the other in the mitral position, who had been switched from warfarin to dabigatran, leading to thrombosis of their prosthetic valves. They required valve replacement, although they recovered without any complications.

In our patient, multiple factors might have contributed to the thrombus formation. First, his prosthetic valve was placed in the mitral position, which is more thrombogenic than the aortic position. Second, his cardiac function was so bad that the ejection fraction of the systemic ventricle was 35%. Third, the fact that his systemic ventricle was the morphologically RV played a role. Among cTGA patients, it is known that thrombus is sometimes formed in the RV/systemic ventricle because of its prominent trabeculae. Fourth, he had a history of paroxysmal atrial fibrillation.

Considering the fact that he had never experienced a thromboembolic event during warfarin use although he had these risks of thrombus formation, dabigatran might not be effective in preventing thrombosis in patients with mechanical heart valve replacements. Actually, Toeg and coworkers [7] warned that off-label use of dabigatran leads to catastrophic complications and jeopardizes patient care. Further study is required to ascertain whether dabigatran has the capacity for thrombophylaxis in the patient who has undergone mechanical valve replacement.

References