Case Report

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TANAFFOS

Treatment of Recurrent Prosthetic Mitral Valve Thrombosis with Reteplase: A Report of Four Cases

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Thrombosis is a life threatening complications of prosthetic mitral valves and is associated with high morbidity and mortality. Even in presence of systemic anticoagulation prosthetic valve thrombosis has an incidence of 0.5% to 8%. Recurrent prosthetic valve thrombosis and the resulting thrombotic occlusion require re-establishment of blood flow across the valve. While surgical repair is considered the classic first line treatment option for prosthetic valve thrombosis, intravenous thrombolysis has emerged as an acceptable alternative for the first episode of prosthetic valve thrombosis. Due to the limitation of using streptokinase in recurrent thrombotic events, fibrin-specific tissue plasminogen activators have been successfully utilized to treat cases of recurrent prosthetic valve thrombosis. In this case-series, we have reported four cases of recurrent prosthetic valve thrombosis that were successfully treated with Reteplase at our hospital.

Key words: Prosthetic mitral valve, Complications, Antithrombotic therapy, Reteplase

INTRODUCTION

Prosthetic mitral valves have been widely used over the past decades (1). However, their use is accompanied by serious life-threatening complications such as thrombosis to endocarditis (2, 3). Prosthetic valve thrombosis has an incidence of 0.5% to 8% despite using systemic anticoagulation therapy, and is associated with high morbidity and mortality (3-5). Recurrent prosthetic valve thrombosis and the resulting thrombotic occlusion are uncommon yet life-threatening conditions and require immediate re-establishment of adequate blood flow across the valve (6, 7). While surgery is considered the classic first line treatment for prosthetic valve thrombosis intravenous thrombolysis has emerged as an acceptable treatment option for the first episode of prosthetic valve thrombosis (7-10). Due to the limitation of using streptokinase in recurrent thrombotic events, fibrin-specific tissue plasminogen activators have been successfully utilized to treat recurrent cases of prosthetic valve thrombosis (11). Herein, we report four cases of recurrent prosthetic valve thrombosis that were successfully treated with reteplase at our hospital.

CASE 1

A 46-year old woman with a history of prosthetic mitral valve replacement (St. Jude Medical) and aortic valve repair due to rheumatic heart disease three years ago presented with dyspnea (functional class III). Decreased artificial valve sounds were noted on physical examination. The patient was on systemic anticoagulation therapy with coumadin and had an INR of 1.6.

Transthoracic (TTE) and transesophageal echocardiography (TEE) were notable for normal left ventricular size and function, a bileaflet mechanical prosthetic mitral valve with fixation of one of the leaflets and severely increased transvalvular gradient due to entrapped clot within the prosthesis (mean pressure gradient (MPG) 25 mm Hg, pressure half time (PHT) 297 msec). The patient underwent surgical thrombectomy, which was successful, with improvement of echocardiographic indices (MPG=5.5 mm Hg, PHT=65 msec) and was subsequently discharged home in a stable condition.

Eight months later, the patient presented again with dyspnea and had an INR of 2. Echocardiographic evaluation revealed valvular dysfunction (MPG=8 mm Hg, PHT=120 msec). As the patient refused surgery she was treated with streptokinase for 48 hours. However, since she only had a partial response to streptokinase, she was switched over to reteplase, which is a fibrin specific agent. The patient responded successfully to this treatment and the valvular motion and gradient improved afterwards (MPG= 5 mm Hg, PHT=52 msec). The patient was discharged home in a stable condition and has remained symptom free for 21 months.

CASE 2

A 54-year-old woman with severe mitral stenosis underwent mitral valve replacement (St. Jude Medical). Two months later, the patient presented with dyspnea and chest discomfort. Reduced heart sounds were noticed on physical exam and she was found to have an INR of 1.9. Transesophageal echocardiography showed a mechanical bileaflet mitral valve with fixed medial leaflet (MPG=14 mm Hg, PHT=240 msec). She underwent thrombolysis with intravenous streptokinase and her valvular function became normal within 3 days. The patient was discharged home on oral anticoagulation therapy with coumadin. However, she was admitted 4 months later with dyspnea and functional class IV heart failure, as well as hypotension and was found to have an INR of 2.1. Transesophageal echocardiography revealed reduced leaflet motion (MPG=6 mm Hg, PHT=170 msec). The patient was treated with reteplase and valvular motion was normalized afterwards (MPG=3.2 mm Hg, PHT= 92 msec). The patient was discharged in a stable condition. She was readmitted after 4 months with severe dyspnea and had an INR of. At this time, TEE showed fixed medial mitral valve leaflet due to entrapped thrombus (MPG=6.5, PHT= 105 msec). The patient was treated again with reteplase and had normal echocardiographic indices at discharge. The patient has remained symptom free for the past 13 months.

CASE 3

A 32 year-old woman with pas medical history of systemic lupus erythematosus and Libman-Sacks vegetation underwent mitral valve replacement due to severe mitral regurgitation (St. Jude Medical). Her medications included azathioprine, chloroquine, prednisolone, and warfarin. Three years later, she presented with dyspnea functional class III and decreased valve sounds and had an INR of 1.1. Transesophageal echocardiography was significant for bileaflet mechanical prosthesis with increased gradient and fixed medial leaflet in closed position and a clot was observed (MPG=30 mm Hg, PHT=150 msec). Echocardiographic findings were subsequently confirmed with fluoroscopy. The patient was successfully treated with reteplase and the valvular motion improved on follow-up TEE (MPG=7 mm Hg, PHT=100 msec). The patient has been symptom free for the last 18 months.

CASE 4

A 49-year-old man with a past medical history of smoking and diabetes mellitus underwent mitral valve replacement two years ago and was maintained on coumadin therapy. His coumadin was held for two weeks in anticipation of a dental procedures. He presented with pleuritic chest pain and progressive dyspnea and had an INR of 1. Transesophageal echocardiography showed bileaflet mechanical mitral valve prosthesis with

significantly increased transvalvular gradient and a fixed medial leaflet and an entrapped clot within the prosthesis (MPG=20 mm Hg, PHT=355 msec). The tip of the left atrial appendage was filled with an organized clot (15×9 mm). The patient refused surgery and was treated with reteplase with subsequent normalization of valvular motion (MPG=5 mm Hg, PHT=92 msec). Repeat TEE was also notable for a residual mobile mass on the valve while the clot in the left atrial appendage had completely resolved. The patient underwent high dose anticoagulant therapy and was discharged in a stable condition. The patient has remained symptom free for the past 2 months.

DISCUSSION

The management of patients suspicious for left-sided prosthetic valve thrombosis begins with TTE in order to assess the degree of hemodynamic instability and follow the resolution of valve dysfunction (12, 13). If the presence of a thrombus is confirmed, TEE can help to measure thrombus size and asses valvular motion (13, 14). Current guidelines recommend emergency surgical repair for patients with left-sided prosthetic valve thrombosis in association with New York Heart Association (NYHA) class III-IV symptoms or mobile/large thrombi (>0.8 mm) (1). However, fibrinolytic therapy is recommended if the thrombus is less than 14 days old, the patient has NYHA class I-II symptoms, or a small thrombus (<0.8 cm2). Fibrinolytic therapy has been shown to be successful in over 80% of the cases of prosthetic valve thrombosis (15). Nevertheless, this treatment is associated with complications such as major bleeding, cerebrovascular accidents, cardiovascular mortality, as well as increased risk of recurrent thrombosis compared to surgical repair (15, 16). Recurrent prosthetic valve thrombosis has been reported to occur in 11% to 18% of the patients (15, 16) and is associated with poor response to treatment (17). Therefore choosing the appropriate antifibrinolytic is of utmost value to reduce the risk of recurrent thrombosis.

Streptokinase has been widely used as the first-line thrombolytic agent for a long time. However, it has the potential of serious allergic reaction.. In order to prevent this hypersensitivity reaction, the next course of treatment with streptokinase should be postponed for at least after 6 months from the initial treatment. Therefore, in cases with recurrent thrombotic events, utilization of other thrombolytic agents seems necessary.

Reteplase is a third generation thrombolytic agent and is a recombinant human tissue plasminogen activator (18). Reteplase is widely used in occlusive thrombotic disorders such as myocardial infarction (19). Long half-life, lack of need for weight based dose adjustment, bolus injection instead of infusion, rapid onset of action, and lower rates of serious complications such as bleeding and fibrinogen depletion have made it an ideal thrombolytic agent (20). While there are multiple reports of using plasminogen activators to treat recurrent prosthetic valve thrombosis, evidence for using reteplase to treat this condition remains sparse. In a single case-series of patients treated with reteplase for recurrent prosthetic mitral valve thrombosis successful re-establishment of blood flow across the valve and normalization of the mean gradient was achieved in all patients without significant complications (21). In another case report, tenecteplase was successfully used to treat second and third episodes of recurrent prosthetic valve thrombosis (22). The authors concluded that tenecteplase is a good alternative for thrombolytic therapy for recurrent prosthetic valve thrombosis.

Here we report four patients with recurrent prosthetic mitral valve thrombosis who were successfully treated with reteplase. Rapid response to treatment was an advantage of reteplase that was observed in these cases. Moreover, we observed no complications or unwanted side effects in these patients.

In summary, we believe that reteplase is an appropriate therapeutic option for treating patients with recurrent prosthetic mitral valve thrombosis. However, clear guidelines for dosing and duration of therapy in order to reach maximum therapeutic effect need to be investigated in future studies.

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