CASE REPORT

Fluoroscopy-guided thrombolysis of mechanical mitral valve thrombosis in a young female with antiphospholipid antibody syndrome

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Accepted 1 April 2015

SUMMARY

Prosthetic valve thrombosis (PVT) is a rare but potentially fatal complication of mechanical valve prosthesis. The differential diagnoses for prosthetic valve obstruction includes pannus formation, prosthetic valve dehiscence, prosthetic valve endocarditis, chordae entrapment, patient-prosthesis mismatch and primary device failure. Establishing a diagnosis requires an understanding of prosthetic valve haemodynamics and careful correlation of clinical and imaging findings. Definitive therapy must be individualised based on various patient-specific factors. We present a case of mechanical mitral PVT in a young woman with antiphospholipid antibody syndrome, and outline the diagnostic and therapeutic approach utilised for successful treatment. The success and complication rates of various therapeutic strategies are also discussed, and highlight the need for individualised decision-making rather than a one-size-fits-all approach to PVT.

BACKGROUND

Prosthetic valve thrombosis (PVT) is a rare but potentially fatal complication of mechanical valve prosthesis. The incidence of obstructive PVT ranges from 0.1 to 5.7% per patient-year.¹ Therapeutic options include valve surgery, which carries a high risk of mortality, and fibrinolysis, which may lead to haemorrhage or embolisation. Therefore, management is often not straightforward and requires consideration of the risks and benefits of each treatment option, a multidisciplinary approach to treatment and shared decision-making with patients.

CASE PRESENTATION

A 40-year-old woman presented with symptoms of chest tightness and shortness of breath of several days duration, becoming intolerable over the past day. Her medical history included diabetes mellitus, hypertension, chronic kidney disease stage III, antiphospholipid antibody syndrome (APLAS) with left eye blindness due to central retinal artery occlusion and severe mitral valve regurgitation due to rheumatic heart disease. Of note, the patient had undergone mitral valve replacement with a St Jude bi-leaflet mechanical valve 3 weeks prior to presentation. She denied any palpitations, syncope or swelling in the legs. On arrival, she appeared anxious. Her blood pressure was 100/60 mm Hg, heart rate was 106 bpm, respiratory rate was 26/min, oxygen saturation 95% on 4 L nasal cannula and she was afebrile. Jugular venous distension

3 cm above the clavicle along the mid clavicular line was noted. She did not have oedema on her extremities. There was no lower extremity oedema. Cardiovascular examination revealed muffled heart sounds, no definitive valve click and a 3/6 systolic murmur at apex. On lung examination, there was decreased air entry in both lung bases with crackles bilaterally. The rest of her physical examination was unremarkable.

INVESTIGATIONS

Pertinent laboratory tests included normal complete blood cell count, renal function and electrolyte levels. NT-Pro brain natriuretic peptide level was elevated at 15 200 and international normalized ratio was subtherapeutic at 1.7. Cardiac biomarkers were non-elevated. ECG showed sinus tachycardia. Chest roentgenogram showed redistribution of pulmonary vasculature and interstitial oedema. Transthoracic echocardiogram (TTE) revealed normal global left ventricular systolic function, with an elevated gradient across the prosthetic mitral valve (mean gradient 24 mm Hg, peak gradient 34 mm Hg), reduced effective orifice area of 0.8 cm² by continuity equation, elevated Doppler velocity index (DVI) of 2.5 and no significant mitral regurgitation ([figure 1](#)). The patient subsequently underwent mitral valve fluoroscopy, which showed restricted opening of the anterior leaflet and normal opening of the posterior leaflet of the mechanical prosthesis ([video 1](#)). For further elucidation of her prosthetic valve dysfunction, a transoesophageal echocardiogram was obtained, showing a mean gradient of 26 mm Hg and peak gradient of 49 mm Hg ([video 2](#)) across the mechanical mitral valve prosthesis. Restricted opening of anterior leaflet was confirmed and a 0.8 cm² density suggestive of a thrombus was demonstrated between the anterior leaflet and the sewing ring.

DIFFERENTIAL DIAGNOSIS

The differential diagnoses for prosthetic valve obstruction includes pannus formation, prosthetic valve dehiscence, prosthetic valve endocarditis, chordae entrapment, patient-prosthesis mismatch, primary device failure and mechanical valve thrombosis.

TREATMENT

The patient was admitted to the hospital with a diagnosis of heart failure and volume overload resulting from prosthetic mitral valve obstruction

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To cite: Ikram S, Pant S, Hussain Z, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2015-210146

Figure 1 Transthoracic echocardiogram (TTE) at presentation showed normal global left ventricular function, elevated gradient across the prosthetic mitral valve (mean gradient: 24 mm Hg and peak gradient: 34 mm Hg), reduced effective orifice area of 0.8 cm² by continuity equation, elevated Doppler velocity index (DVI) 2.5 and no significant mitral regurgitation.

secondary to mechanical valve thrombosis. She was treated initially with supplemental oxygen, diuretics and therapeutic heparin as well as aspirin. A multidisciplinary discussion between cardiothoracic surgery, interventional cardiology, general cardiology and the patient, weighed the risks of benefits of various therapeutic strategies. Re-do open heart surgery was deemed extremely high risk by the cardiothoracic surgery team due to unacceptable surgical mortality within 1 month after the first sternotomy, owing to inflammation and a hostile chest. Contraindications to thrombolytic therapy were reviewed. Review of the literature revealed several therapeutic strategies for administration of fibrinolytic therapy with tissue plasminogen activator (tPA). A shared decision was reached to administer fibrinolytic therapy with tPA.

The patient was transferred to the intensive care unit for close monitoring. Based on the strategy identified in the literature, heparin was stopped and the activated partial thromboplastin time (aPTT) monitored closely. When the aPTT dropped below 50, tPA 25 mg infusion was administered over a 6 h period. Heparin drip was restarted following the infusion without any

Video 1 Transoesophageal echocardiogram at presentation showed mean gradient of 26 mm Hg and max gradient of 49 mm Hg. There was restricted opening of anterior leaflet and a 0.8cm² density suggestive of a thrombus, which was present between the anterior leaflet and the sewing ring.

Video 2 Mitral valve fluoroscopy in RAO (right anterior oblique) cranial projection at presentation showed restricted opening of the anterior leaflet of the mechanical valve and normal opening of the posterior leaflet.

bolus. Repeat TTE and fluoroscopy were carried out following the tPA infusion. The decision on repeat dosing was based on the results. The patient received the same regimen on four consecutive days. On day four, physical examination demonstrated a crisp mechanical click. TTE on day 4 showed a normal trans-mitral gradient of 5.6 mm Hg, and fluoroscopy showed normal opening and closing angle of both the leaflets (video 3). No embolic phenomenon was observed.

OUTCOME AND FOLLOW-UP

Following successful thrombolysis of the PVT, the patient was therapeutically anticoagulated with heparin, warfarin was restarted and dose-adjusted to achieve a new INR goal of 3.5–4.5.

Video 3 Mitral valve fluoroscopy at day 4 of therapy. Normal opening and closing angles of both the mitral leaflets, a significant change from her presentation fluoroscopic finding.

The patient was also started on aspirin 81 mg daily. Haematology was consulted to assess the status of the antiphospholipid syndrome and all the serological markers were found to be stable. The patient was discharged home and was found to be doing well at 1-month follow-up.

DISCUSSION

Mechanical valve thrombosis is a relatively rare but potentially fatal complication of mechanical valve replacement. Development of a thrombus is usually dependent on factors such as valve design, valve material (more common in mechanical versus bioprosthetic valves), location (mitral >aortic position) and subtherapeutic anticoagulation.² Presence of comorbidities such as atrial fibrillation, hypercoagulable state, or severe left ventricular dysfunction increase the risk of thrombus formation.³ Symptoms are often acute to subacute in onset and may include dyspnoea, cough or overt congestive heart failure.⁴ TTE is often the first test required for establishing the diagnosis. For a mechanical mitral PVT, the TTE findings to suggest obstruction include an increased transmitral gradient, increase in DVI, decrease in effective orifice area and a prolonged pressure half time. The differential diagnoses for prosthetic valve obstruction includes pannus formation, prosthetic valve dehiscence, prosthetic valve endocarditis, chordae entrapment, patient-prosthesis mismatch, primary device failure and PVT. TEE is helpful in the further assessment of prosthetic valve haemodynamics and in identifying the aetiology of prosthetic valve obstruction. Another useful diagnostic modality is fluoroscopy, where the opening and closing angles of mechanical valve leaflets can be assessed directly with appropriate cine angiographic images.

In our patient, the recent history of valve replacement, hypercoagulable disorder (APLA syndrome) and the subtherapeutic INR at presentation, clinically suggested PVT as the most probable diagnosis. This was further confirmed with TEE and mitral valve fluoroscopy, where the restricted opening angle of mechanical mitral prosthesis was well visualised. As far as definitive treatment is concerned, the 2014 ACC/AHA guidelines recommend emergency surgery for all patients with New York Heart Association (NYHA) III–IV symptoms or, alternatively, a mobile or large (>0.8 cm²) clot burden.⁵ Although the surgical option offers the best success rate, two major downsides of such a strategy in this patient were that: (1) surgery is associated with complications including in-hospital mortality ranging from 4.5% for patients with NYHA I–III symptoms to 17.5% for those with NYHA IV symptoms,⁵ (2) the type of valve selection in this patient was tricky as the patient would be at substantial risk for recurrent thrombosis if a mechanical valve was chosen (due to the patient's underlying thrombophilic disorder) or she would likely require repeat surgery in her lifetime if a bioprosthetic valve was chosen (due to limited lifespan of this type of valve).

An alternative strategy was hence selected for this patient, which involved the use of fibrinolytic agents. While the bleeding risk (including life-threatening bleeding such as intracranial haemorrhage) and risk of embolisation limits the use of fibrinolytic therapy to a small subset of patients with right-sided thrombosis or small left-sided thrombosis, the interest in this approach has been renewed by recent publication of the TROIA trial.⁶ In this prospective, single-centre study of patients with PVT who were not surgical candidates, 'low dose, slow infusion' of tPA repeated daily up to 6 days was associated with no major

bleeding, lowest rate of complications and equal efficacy as compared to the traditional higher dose regimens. Four consecutive days of infusion were required for successful thrombolysis in our case. Our patient did not have bleeding complications. Although serial TEE is the best modality to assess the success of fibrinolytic therapy, in a non-intubated patient, mitral valve fluoroscopy and TTE are more feasible tools as they can be repeated on a daily basis. The 2014 ACC/AHA valvular heart disease guidelines recommend a new INR goal of 3.5–4.5 and low dose aspirin in patients with PVT, both of which were implemented in our patient.

In conclusion, PVT is a complication of mechanical valves associated with high morbidity and mortality. Each therapeutic option for PVT carries significant risk and hence an individualised approach is necessary. The novel approach of 'low dose, slow infusion' tPA utilised by Ozkan *et al*,⁶ although not yet studied in large multicentre trials, is an alternative fibrinolytic strategy with a reported success rate equivalent to high dose tPA, but with fewer thrombotic or bleeding complications. This strategy was used successfully in our patient with APLAS and PVT occurring within 1 month of mitral valve replacement surgery.

Learning points

- ▶ A high index of suspicion is necessary for prosthetic valve thrombosis in recipients of prosthetic valves who have had valves placed recently, and who present with symptoms of congestive heart failure.
- ▶ Low dose and slow infusion of fibrinolytics may be a safe yet efficacious approach to prosthetic valve thrombosis.
- ▶ A higher INR goal may be considered for recipients of prosthetic valves who have a concomitant hypercoagulable disorder, especially if they fail anticoagulant therapy.

Contributors SI was involved in the concept, design, manuscript editing. SP was involved in the manuscript writing, concept. ZH was involved in the manuscript writing, referencing. LB was involved in the literature review, manuscript editing.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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