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CASE REPORT

Recurrent valve obstruction in a patient with a pure carbon bileaflet metallic mitral valve: a case report

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Background Despite overcoming the morbidity from severe native valve disease, prosthetic metallic valve replacement is not without its inherent morbidity, in particular from prosthetic valve thrombosis (PVT). The contemporary pure carbon bileaflet metallic valve confers reduced thrombogenicity.

Case Summary We describe the case of a 45-year-old woman with a pure carbon bileaflet metallic mitral valve replacement (27/29 mm On-X) 6 months previously for severe rheumatic mitral stenosis, who presented with a rapid onset of dyspnoea, paroxysmal nocturnal dyspnoea, and haemoptysis. This was preceded by an interruption in therapeutic anticoagulation. On admission the patient was in cardiogenic shock. Transthoracic and transoesophageal (TOE) echocardiograms revealed increased transmitral gradients with disc hypomobility, suggestive of PVT, unexpected given the favourable safety profile of the On-X valve. Fluoroscopy confirmed the findings. The patient was thrombolysed successfully with alteplase, with restoration of normal transmitral gradients. A target international normalized ratio of 3.5–4.5 was chosen, in addition to aspirin 75 mg, to minimize thrombotic sequalae. Repeat TOE 6 weeks later revealed disc hypomobilty with a large adherent clot. Due to the high risks from thrombolysis, emergency redo-mitral bioprosthetic valve surgery was performed, to negate the need for long-term anticoagulation.

Discussion Subtherapeutic anticoagulation and the rapid development of dyspnoea, should prompt the clinician to suspect PVT. Thorough clinical examination and immediate bedside echocardiography are critical for assessing prosthetic valve patients in cardiogenic shock. The treatment of PVT is complex, with considerable risks to the patient, irrespective of the strategy (thrombolysis/emergency valve replacement), necessitating the expertise of cardiologists and cardiac surgeons.

Keywords Prosthetic valve thrombosis • Mitral valve • Thrombolysis • Echocardiography • Case report

Learning points

- Prosthetic valve thrombosis (PVT) is a life-threatening condition, made even rarer due to the contemporary pure carbon bileaflet metallic valve, owing to its smoother surface and improved haemodynamics.
- History of subtherapeutic anticoagulation, rapid onset of symptom and short time interval from surgery, raises the clinical suspicion of PVT.
- Transoesophageal echocardiogram and cine-fluoroscopy offer complementary information in determining disc mobility.
- Thrombolysis is an effective treatment but carries risks of bleeding and peripheral systemic thromboembolism.
- Recurrent thrombosis should prompt the clinician to investigate for other rare causes of hypercoagulability.

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Introduction

Despite overcoming the morbidity associated with severe native valve disease, prosthetic metallic valve replacement is not without its inherent morbidity, in particular from prosthetic valve thrombosis (PVT).

Although rare, with an incidence of 0.2–6% per patient-year, PVT remains a serious and potentially fatal complication.[1,2] This is strongly influenced by various interacting factors such as prosthetic valve location, type of prosthesis, presence of low cardiac state, and the adequacy of anticoagulation.[3] Metallic mitral valve prostheses confer higher PVT risk compared with those in the aortic position, owing to lower flow rates. Furthermore, the type of prosthesis, in particular the out-dated caged ball valve conferred the highest PVT risk, compared with the bileaflet or tilting disc valves.[3] Technological advances in valve design, composition and improved haemodynamics have led to favourable safety profiles.[4,5]

Herein, we describe a rare case of PVT presenting with cardiogenic shock, on a background of the contemporary On-X valve, which confers a favourable thrombogenicity profile. It highlights the importance of thorough clinical examination and prompt use of echocardiography in differentiating potential causes in mechanical valve patients.

Timeline

6 months prior to presentation	Patient with severe rheumatic mitral stenosis undergoes mitral valve replacement with 27/29 mm On-X valve
14 days prior to presentation	Subtherapeutic international normalized ratio (INR) of 1.8
10 days prior to presentation	Patient experiences dyspnoea and reduced exercise tolerance
Day 1	Patient presented with cardiogenic shock. INR 6.1. Transthoracic echocardiography showed severe mitral stenosis. Treated with IV furosemide and low dose GTN infusion. Warfarin withheld and IV unfractionated heparin commenced once INR <3.5
Day 3	Transoesophageal echocardiogram (TOE) confirmed the antero-lateral disc to be fixed with no flow across the disc and the postero-medial disc to have restricted movement, with a mean transmitral gradient of 22 mmHg
Day 4	Patient thrombolysed with Alteplase
Day 5	Normalization of transmitral gradient
Day 10	Patient discharged with higher target INR 3.5–4.5 and aspirin
6 weeks after presentation	TOE revealed disc hypomobilty with a large adherent clot. Patient was admitted immediately back to cardiac care unit (CCU)
7 days after TOE	Patient underwent emergency redo-mitral bioprosthetic valve surgery
10 weeks after redo surgery	Patient was followed-up with cardiac surgeons and made good recovery without any complications

Case summary

A 45-year-old woman was admitted to directly to our cardiology department, with a 10-day history of dyspnoea, reduced exercise tolerance, paroxysmal nocturnal dyspnoea, and haemoptysis, whilst on vacation abroad. She had a background of pure carbon bileaflet metallic mitral valve (27/29 mm On X) for severe rheumatic mitral stenosis, operated on 6 months previously, with no other comorbidities or prior history of thrombosis. Her medication comprised only of warfarin and bisoprolol 2.5 mg once daily.

Her trip was abandoned prematurely due to a deterioration in her symptoms. Prior to her trip her international normalized ratio (INR) was subtherapeutic at 1.8.

Clinical examination revealed a normal jugular venous pulse (JVP), soft mechanical first heart sound, widespread bilateral pulmonary crepitations, with no peripheral oedema. Her blood pressure was 91/56 mmHg with a heart rate of 85 b.p.m. Clinical impression was acute left ventricular failure secondary to valve obstruction.

Her electrocardiogram showed sinus rhythm. Arterial blood gas sampling revealed a type 1 respiratory failure with partial pressures of oxygen of 7.9 kPa (NR >10.5 kPa) and carbon dioxide of 4.1 kPa (NR 4.5–6.0 kPa) on room air. Her chest radiograph confirmed pulmonary oedema. Blood tests were unremarkable except for an INR of 6.1 (target INR 2–3) and D Dimer of 0.48 μg/mL (NR <0.50 μg/mL). Bedside transthoracic echocardiography showed restricted metallic mitral disc mobility with a mean transmitral gradient of 25 mmHg, indicating severe mitral stenosis with preserved left ventricular function (*Figure 1*). Fluoroscopy was performed to further delineate the disc motion, which revealed severely reduced mobility. An urgent transoesophageal echocardiogram (TOE) confirmed the antero-lateral disc to be fixed with no flow across the disc and the postero-medial disc to have restricted movement, with a mean transmitral gradient of 22 mmHg (*Figure 2*). Three-dimensional (3D) TOE of the prosthetic mitral valve was performed for better visualization and to distinguish between thrombus and pannus (*Figure 3*). Three-dimensional TOE demonstrated the antero-lateral disc to be fixed with surrounding thrombus.

She was commenced on diuretics and a low dose of GTN infusion for pulmonary venodilatation. Her warfarin was withheld and she was commenced on intravenous (IV) unfractionated heparin once her INR was below 3.5.

Urgent cardiac surgical review was sought. After close discussion between the cardiologists, cardiac surgeons and the patient, it was decided that further surgery on the valve carried an excess mortality risk. Thrombolysis was therefore offered to the patient. On Day 4 of admission, following written informed consent, a bolus of 10 mg of alteplase was administered followed by 80 mg infusion over 3 h. IV unfractionated heparin was re-instituted following completion of thrombolysis. Within 24 h of the infusion the metallic first heart sound became audible. Repeat transthoracic echocardiogram revealed normalization of mean transmitral gradients of 3 mmHg (*Figure 4*). Fluoroscopy showed normalization of one of the discs with improved mobility of the other disc. The patient was discharged with a higher therapeutic INR range of 3.5–4.5 and aspirin 75 mg, with weekly INR monitoring.

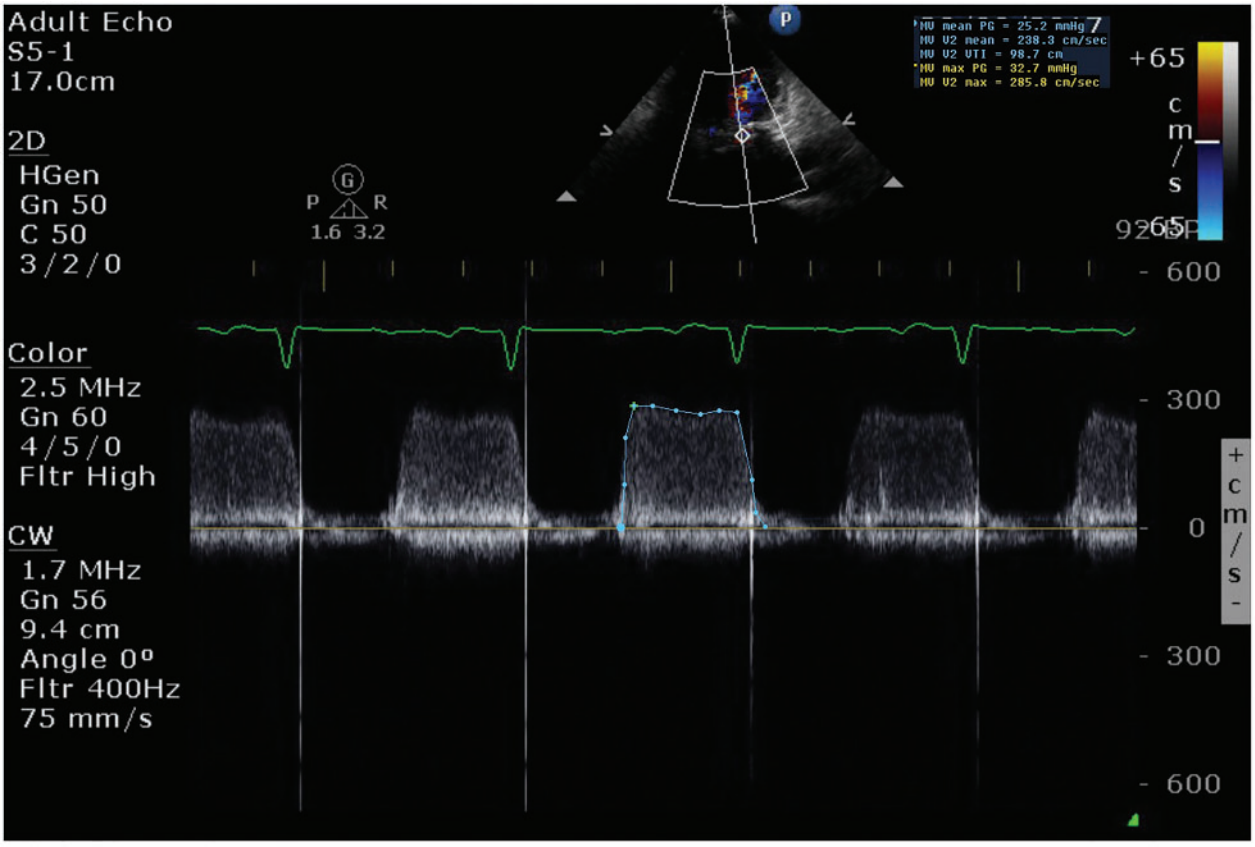

Figure 1 Continuous wave Doppler through the mitral valve on admission (transthoracic echocardiogram), showing a raised mean transmitral gradient of 25 mmHg.

Unfortunately, despite being asymptomatic, her repeat TOE 6 weeks post-thrombolysis, revealed an elevated mean transmitral gradient of 10 mmHg with an immobile antero-lateral disc and a mobile postero-medial disc (*Figure 5*). A mobile 10 mm × 7 mm structure was attached to the postero-medial disc causing intermittent severe mitral stenosis. It transpired that despite the patient's best efforts, her INR on one occasion dropped below two. The patient was admitted immediately back to coronary care unit, further thrombolysis was considered, but the risk of peripheral embolization from the large thrombus was deemed too high. Emergency valve replacement with a bioprosthetic valve was chosen as the best strategy, to avoid further morbidity from prosthetic valve thrombosis and negate the need for anticoagulation. Seven days after the TOE, the patient underwent redo mitral valve surgery. She made a good recovery without any complications and was followed up with the cardiac surgeons 10 weeks later.

In view of recurrent thrombosis, the patient was tested for rare causes of hypercoagulability. The JAK-2 (V617F) mutation is linked with the myeloproliferative neoplasias, polycythaemia rubra vera and essential thrombocythemia, both of which confer increased arterial and venous thrombotic risk, tested negative in this patient. In addition, anti-cardiolipin antibody and IgM and IgG β2-glycoprotein I antibodies, specific for antiphospholipid syndrome, also tested negative in this patient.

Discussion

The prospect of prosthetic valve thrombosis is a feared complication, due to its significant impact on mortality. This patient presented with symptoms of acute left ventricular failure due to left side valve obstruction from mitral valve thrombosis. In this case, a history of subtherapeutic anticoagulation, the subsequent rapid development of symptoms and the short time interval from surgery, strongly supported prosthetic valve thrombosis.[6]

Unexpectedly, this prosthetic valve thrombosis occurred in a patient with the contemporary On-X valve, which has a favourable safety profile.[4] It has a flared inlet which reduces flow turbulence and a long exit point which aligns flow, both of which contribute to better haemodynamics across the valve.[5] Furthermore, the pure pyrolytic carbon design confers a smoother surface reducing thrombogenicity. A study by Chambers *et al.*[4] revealed that in 407 patients with On-X mitral valve, only two cases (0.1% per patient-year) developed valve thrombosis, over a mean follow-up of 5 years. A previous study by Williams *et al.*,[7] reported that in a poorly anticoagulated population of 242 patients with the On-X mitral valve, only one case (0.2%

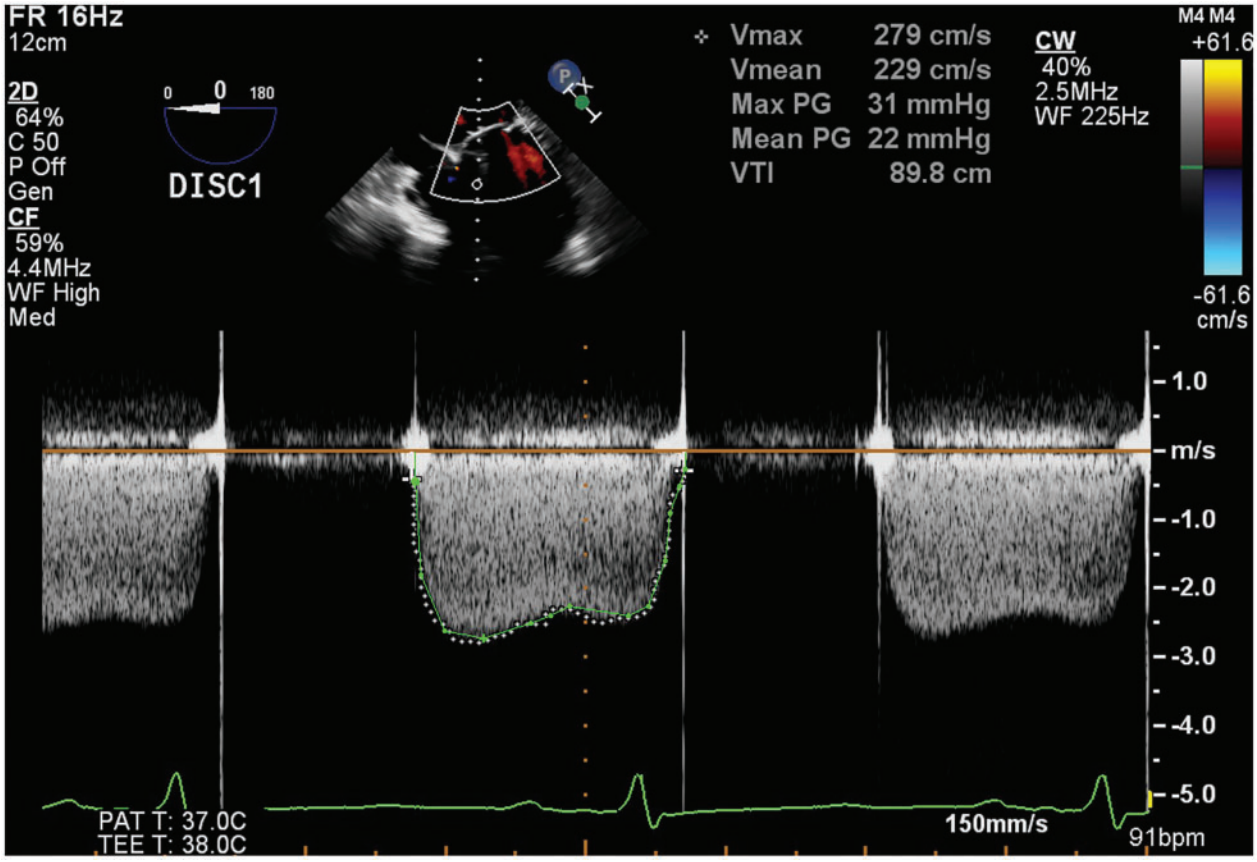

Figure 2 Continuous wave Doppler through the mitral valve (transoesophageal echocardiogram), showing a raised mean transmitral gradient of 22 mmHg.

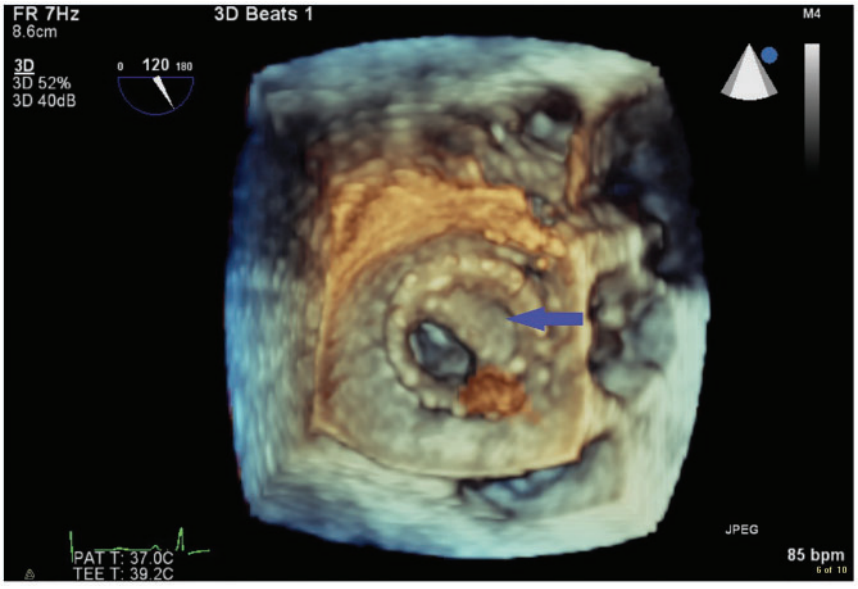

Figure 3 Still frame of three-dimensional rendered image from transoesophageal echocardiogram of the mitral valve. Arrow indicates the fixed antero-lateral disc of the mitral valve.

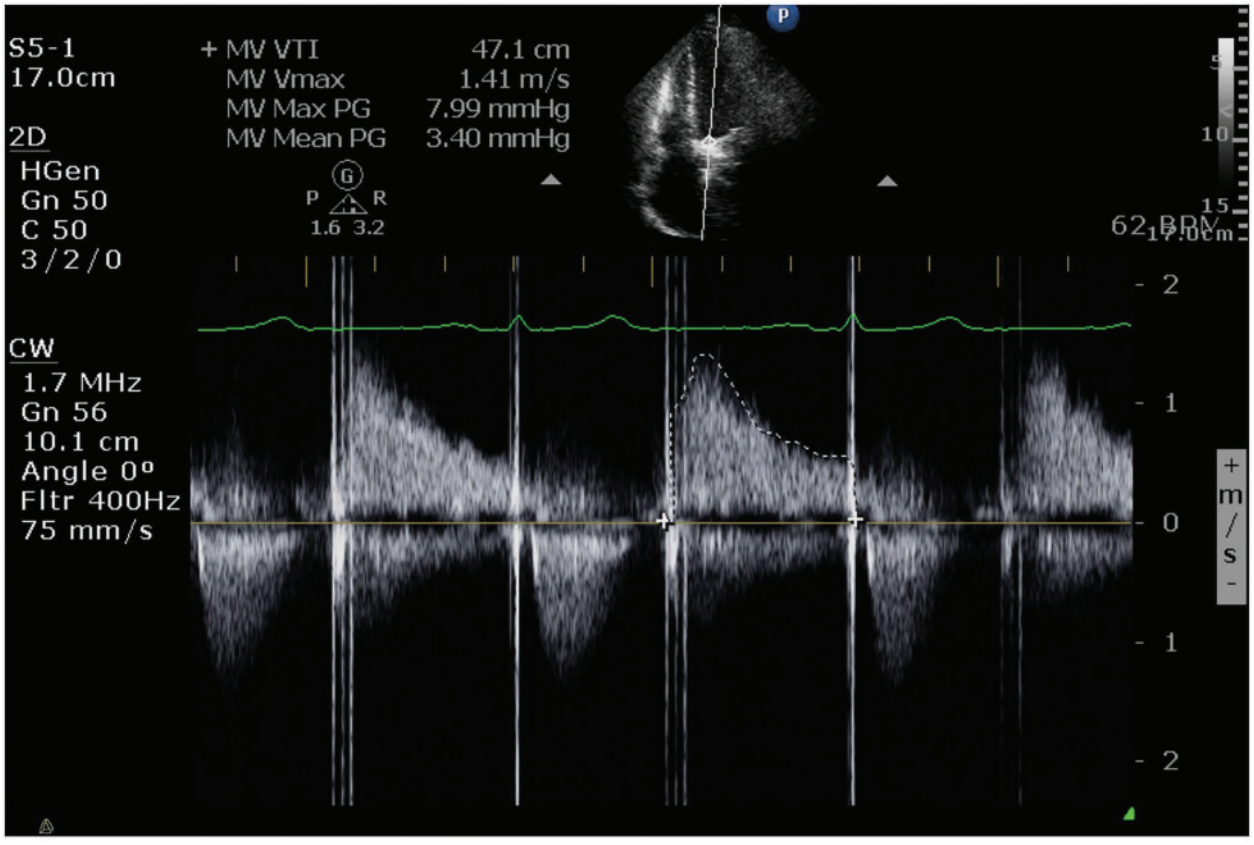

Figure 4 Continuous wave Doppler through the mitral valve (transthoracic echocardiogram) post-thrombolysis, showing normalization with a mean transmitral gradient of 3.4 mmHg.

patient-year) developed valve thrombosis. This emphasises the true rarity of such a case presentation. Bedside transthoracic echocardiography was performed in this patient. The demonstration of an elevated mean transmitral Doppler gradient confirmed valve obstruction. TOE offers better visualization of the valve and enabled the distinction between thrombus and pannus; the later tends to occur around the sewing ring, develops over a period longer than 6 months post-surgery and has a more insidious symptom onset. A study by Barbetseas *et al.*[6] reported that valve hypomobility was observed in all patients with PVT compared with 60% in those with pannus. Furthermore, the 3D functionality conferred by TOE was particularly useful. Cine-fluoroscopy has a valuable role in determining leaflet mobility, with a very high negative predictive value of 91% compared with 78% for TOE as shown by Montorsi *et al.*[8]

The management of such patients necessitates the expertise of both cardiologists and cardiac surgeons in agreeing the best treatment strategy for the patient. The surgical risk from reoperation can be up to 30%, which for this case on initial presentation was deemed too high.[9] Thrombolysis has been shown to be a feasible strategy especially in cases of cardiogenic shock with New York Heart Association (NYHA) 4 (4). However, thrombolysis is not without its inherent risks, with systemic embolism occurring in 10%, re-thrombosis in 20% and mortality risk in 10%.[10,11] The improvement in patient symptoms and transmitral gradient, despite restricted disc mobility on fluoroscopy, prompted the adoption of a higher target INR and aspirin. A study by Laffort *et al.*[12] showed that patients on both aspirin and oral anticoagulants had lower incidence of non-obstructive periprosthetic valve thrombi compared with those on oral anticoagulation alone. Further admission with recurrent valve thrombosis led to the decision for replacement of the valve with a bioprosthetic valve, to negate the risk of future valve thrombosis.

In patients with recurrent thrombosis, attention should be given to the possibility of an underlying pro-thrombotic state. This may be influenced by an underlying myeloproliferative neoplasia, which are strongly associated with thrombosis in unusual sites (cerebral, hepatic). This patient tested negative for the JAK2 (V617F) mutation, which is present in 97% of patients with polycythaemia rubra vera and 60% of patients with essential thrombocythemia.[13] A potential systemic condition contributing to a prothrombotic milieu is anti-phospholipid syndrome. This is characterized by a history of recurrent miscarriages, arterial and venous thrombosis of unusual sites, livedo reticularis and the presence of lupus anticoagulant, anticardiolipin and anti-β2 glycoprotein I antibodies.[14] This patient had no history of recurrent foetal loss and tested negative for the auto-antibodies. In this case, the repeated interruption in therapeutic anticoagulation albeit brief was the strongest culprit for repeated PVT.

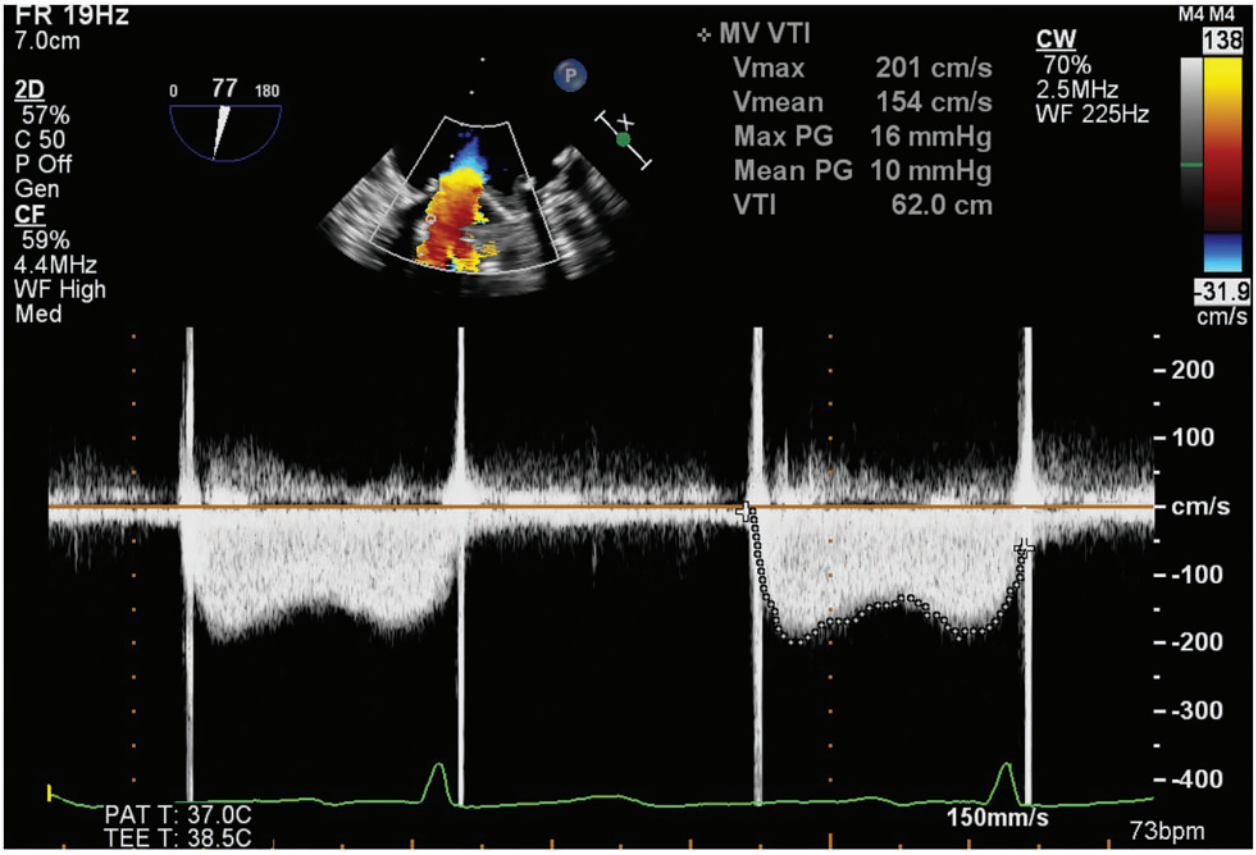

Figure 5 Continuous wave Doppler through the mitral valve (transoesophageal echocardiogram) 6 weeks post-thrombolysis, showing a raised mean transmitral gradient of 10 mmHg.

Conclusion

A history of subtherapeutic anticoagulation and the rapid development of dyspnoea, should prompt the clinician to suspect PVT. Thorough clinical examination and immediate bedside echocardiography are critical for assessing prosthetic valve patients in cardiogenic shock. The treatment of PVT is complex, with considerable risks to the patient, irrespective of the strategy (thrombolysis/emergency valve replacement), necessitating the expertise of cardiologists and cardiac surgeons.[15]

Consent: The author/s confirm that written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: none declared.

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