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CASE REPORT
Other

Severe mitral regurgitation from Libman–Sacks endocarditis treated with MitraClip: a case report

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Background Systemic lupus erythematosus (SLE) valvulopathy can manifest as a spectrum of pathologies and treatment of severe valvular dysfunction thus far has been surgical. However, surgery in patients with SLE is frequently associated with high morbidity and mortality due to the presence of significant co-morbidities.

Case summary We report the case of a 41-year-old woman with SLE and anti-phospholipid syndrome with extensive co-morbidities including lupus nephritis, pancytopaenia, cerebrovascular accident, and severe airway obstruction from ipsilateral lung collapse and bronchiectasis. She had severe mitral regurgitation (MR) from Libman–Sacks endocarditis and in recent months developed heart failure with progressive exertional dyspnoea from New York Heart Association (NYHA) functional Class from New York Heart Association (NYHA) functional class II to III. In addition, there was progressive left ventricular dilatation and reduction in left ventricular ejection fraction. In view of the high surgical risk, she underwent transcatheter edge-to-edge repair (TEER) of the mitral valve with the MitraClip system. At 1-month follow-up, she was back to NYHA functional Class II with mild MR.

Discussion Our case demonstrates that in select patient with suitable anatomy, TEER is a potential treatment option for severe MR from SLE valvulopathy.

Keywords Mitral regurgitation • Systemic lupus erythematosus • Libman–Sacks endocarditis • MitraClip • Case report

Learning points

- To recognize the complexities in the management of systemic lupus erythematosus (SLE)-related valvular dysfunction due to the unique tissue pathology as well as clinically significant co-morbidities that frequently accompany SLE.
- To keep in mind the treatment option of transcatheter edge-to-edge repair for severe mitral regurgitation from SLE valvulopathy in appropriate patients who are at prohibitive or high surgical risk.

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Introduction

Valvular involvement in systemic lupus erythematosus (SLE) can manifest as a spectrum of pathologies: leaflet thickening, vegetations, valvular regurgitation, and stenosis.[1,2] Thus far, treatment of severe valvular dysfunction has been surgical.[3] However, due to the systemic nature of SLE and hence the presence of multiple co-morbidities, surgery is frequently associated with high mortality and morbidity.[4] We report the case of a patient with SLE and severe mitral regurgitation (MR) from Libman–Sacks endocarditis that was successfully treated with transcatheter edge-to-edge repair (TEER) technique using the MitraClip system.

Timeline

23 years before procedure	Diagnosis of systemic lupus erythematosus and anti-phospholipid syndrome at age 18, complicated by Libman–Sacks endocarditis of the mitral valve, lupus nephritis, pancytopaenia, and cerebrovascular accident
6 months before procedure	Worsening exertional dyspnoea [New York Heart Association (NYHA) Class III] from severe mitral regurgitation (MR) with progressive left ventricular dilatation and reduction in left ventricular ejection fraction
Procedure	MitraClip procedure (2 NTW clips) with reduction of MR to mild–moderate
1 month after procedure	Back to NYHA Class II with mild MR

Case presentation

A 41-year-old Asian female, who was diagnosed with SLE at the age of 18, and anti-phospholipid syndrome (APS) with complications including lupus nephritis, pancytopaenia, and cerebrovascular accident, was referred for TEER for treatment of severe MR. Her SLE was clinically quiescent and she was on Hydroxychloroquine 200 mg once daily and Prednisolone 5 mg once daily. Her co-morbidities included deep vein thrombosis on Rivaroxaban, epilepsy on sodium valproate, and chronic right pleural effusion with ipsilateral lung collapse and bronchiectasis. This resulted in very severe airway obstructive pattern on spirometry as evident by FEV1/FVC (forced expiratory volume in 1 second / forced vital capacity) ratio below lower limit of normal and FEV1 at 29% of predicted value. She was diagnosed with Libman–Sacks endocarditis of the mitral valve at the time of SLE diagnosis, but was stable at New York Heart Association (NYHA) functional Class II. However, 6 months prior, she reported progressive exertional dyspnoea to NYHA functional Class III. Furosemide 40 mg once daily was started and this had to be up-titrated to 40 mg twice daily. Physical examination showed a pulse rate of 65 beats per minute, blood pressure of 90/67 mmHg, respiratory rate of 14 per minute, and 95% oxygen saturation on room air. Auscultation revealed a pansystolic murmur over the apex and reduces breath sounds over the right lower one-third of the chest. There was mild bipedal pitting oedema. She was afebrile and had no signs of infection. Her most recent complete blood count showed normal haemoglobin (12.5 g/dL), total white blood cell count (9.45×10^9/L), and mild thrombocytopaenia (120×10^9/L). Her renal function had been stable at Stage 3a with a creatinine clearance of 58 mL/min.

Transthoracic echocardiogram showed severe left ventricle (LV) dilatation (end-diastolic diameter of 65 mm and end-systolic diameter of 44 mm) with mildly impaired LV systolic function (LV ejection fraction 53%), in the setting of severe MR. Transoesophageal echocardiogram (TOE) showed thickened mitral valve leaflets with irregular-shaped, hyperechoic nodularities of varying sizes on both the anterior and posterior leaflet tips, consistent with healed Libman–Sacks endocarditis (*Figure 1A–C* and *Videos 1–3*). Although slightly restricted, the posterior mitral valve leaflet had a length of 11.2 mm. The mitral annulus was dilated (43 mm), with a mitral valve area of 4.2 cm^2 [by three-dimensional (3D) planimetry] and a trans-mitral mean pressure gradient of 1 mmHg. There was severe MR with two MR jets, located medially at A3/P3, and centrally at A2/P2 (*Figure 1D and E* and Supplementary material online, *Video S1*). The largest MR jet's effective regurgitant orifice area was 0.47 cm^2 by proximal isovelocity surface area and the regurgitant volume was 66 mL. Three-dimensional vena contracta area (VCA) from the summation of the two largest jets was 0.70 cm^2 (0.48 and 0.22 cm^2). Pulmonary vein systolic flow reversal was present (*Figure 1F*). The other valves were morphologically normal. Computed tomography scan showed minor coronary artery disease.

Her unique and complex case was discussed in our multidisciplinary heart team. Her Society of Thoracic Surgeons (STS) score was 4.46% for mortality and 25.21% for mortality and morbidity, while her EuroSCORE II was 1.63%. Although not considered high in terms of mortality risk, the heart team felt that the scores did not truly reflect the high surgical risk in her case based on the extensive co-morbidities. Transcatheter edge-to-edge repair was a potential treatment option but there was an absence of data on its use in Libman–Sacks endocarditis and hence uncertainty in long-term outcomes. In addition, there was a risk of leaflet tear. This was discussed extensively with the patient as well as the risk of emergency surgery in the event of leaflet tear or in the future if MR recurred. She and the team eventually decided to proceed with TEER.

Transcatheter edge-to-edge repair was performed using the MitraClip G4 system. The first NTW clip was deployed medially at A3/P3 with reduction of MR to 3+ lateral to the clip. A second NTW clip was deployed centrally at A2/P2 with reduction of MR to 1–2+ (*Figure 2A and B* and Supplementary material online, *Video S2*). Mitral regurgitation 3D VCA was reduced from 0.70 to 0.13 cm^2 (*Table 1*). Final trans-mitral mean pressure gradient was 3 mmHg with pulmonary vein flow showing systolic predominance (*Figure 2C*). Mitral valve area by 3D planimetry was 2.66 cm^2 from the summation of both orifices (*Figure 2D*).

She reported well and was back to NYHA functional Class II at 1 month. Transthoracic echocardiogram showed stable clips and the MR remained mild (*Figure 3* and Supplementary material online, *Video*

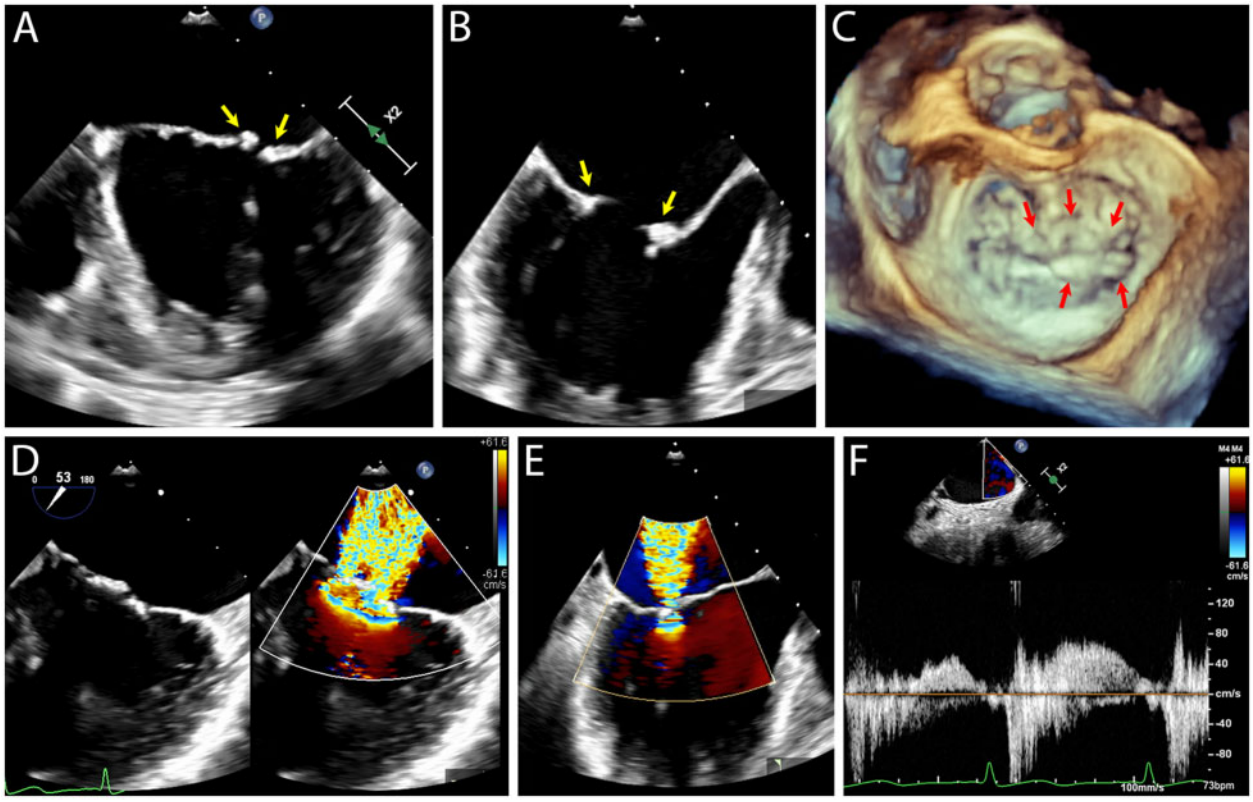
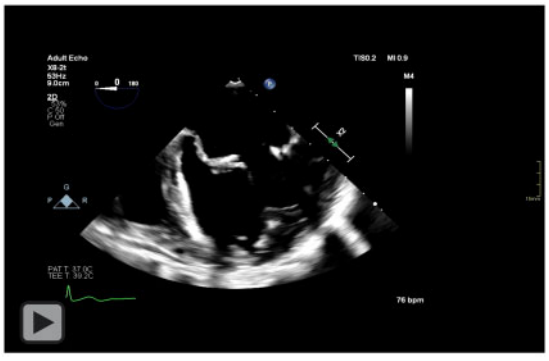
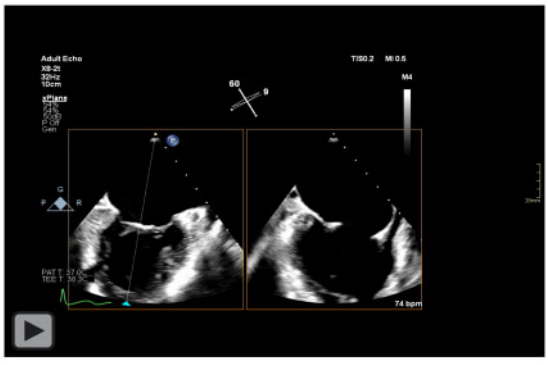


Figure 1 Transoesophageal echocardiogram images showing (*A* and *B*) thickened mitral valve leaflets with irregular-shaped, hyperechoic, nodular lesions located on both leaflet tips (yellow arrows), consistent with healed Libman–Sacks endocarditis. (*C*) Three-dimensional view showing multiple irregular-shaped nodularities of different sizes on both leaflet tips (red arrows), predominantly at A2/P2 and A3/P3 regions. (*D* and *E*) Severe mitral regurgitation from two mitral regurgitation jets, located medially at A3/P3, and centrally at A2/P2. (*F*) Pulmonary vein systolic flow reversal.



Video 1 Transoesophageal echocardiogram mid-oesophageal four-chamber view showing thickened mitral valve leaflets and irregular-shaped, hyperechoic, nodular lesions located on both leaflet tips, consistent with healed Libman–Sacks endocarditis.



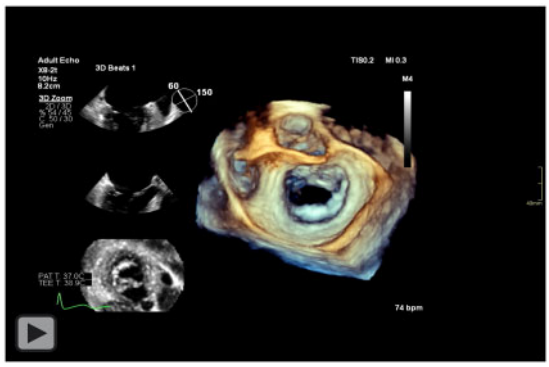
Video 2 Transoesophageal echocardiogram inter-commissural and left ventricular outflow tract views showing thickened mitral valve leaflets and similar Libman–Sacks vegetations on the mitral valve leaflets.

S3). The trans-mitral mean pressure gradient stayed at 3 mmHg. In addition, there was a reduction in mitral annulus diameter from 43 mm before MitraClip to 37 mm, as well as LV end-diastolic diameter from 65 to 52 mm (*Table 1*).

Discussion

Systemic lupus erythematosus can involve all components of the heart including the pericardium, myocardium, valves, conduction

system, as well as the coronary arteries.[5] Valvular involvement is a common cardiac manifestation and presents as a spectrum of pathologies.[1,2] The classic lesion is that of sterile verrucous vegetations, termed 'Libman–Sacks' endocarditis, first described in 1924 by Libman and Sacks,[6] which is best appreciated on TOE,[7] typically affecting the mitral valve. Although mostly asymptomatic, it may lead to significant complications such as severe valvular dysfunction, infective endocarditis, and embolic cerebrovascular events.[8–10] Leaflet thickening, however, is the most frequent valvular pathology encountered.[2] Thus far, the treatment of severe valvular dysfunction from SLE has been surgical.[3] To the best of our best knowledge, this is the first case of severe MR from Libman–Sacks endocarditis to be treated percutaneously with the MitraClip system.



Video 3 Three-dimensional transoesophageal echocardiogram view showing multiple nodularities of varying sizes on both mitral valve leaflets.

In patients with severe MR, mitral valve repair is preferred over replacement if a successful and durable repair is possible. For SLE valvulopathy, repair may not be possible in the presence of extensive structural damage. In addition, even after a successful mitral valve repair, further insults on the valve may continue due to the underlying autoimmune process, rendering the need for a repeat intervention.[11] If mitral valve replacement is anticipated, metallic prosthesis may be preferred given the patient's relatively young age. Nonetheless, the surgical risk for patients with SLE is frequently high[4] due to commonly associated systemic manifestations such as renal failure, cytopaenias, and respiratory disease, as well

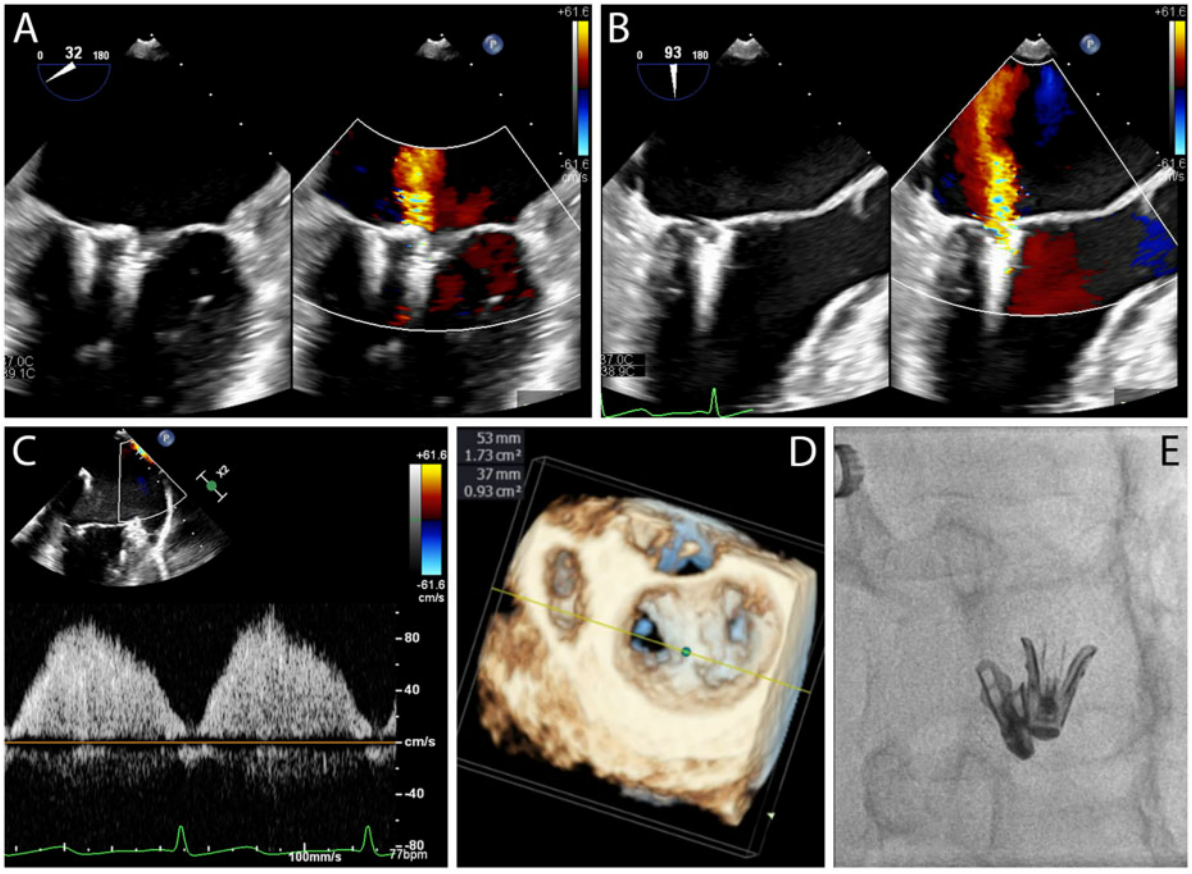


Figure 2 Transoesophageal echocardiogram images showing (*A*) first MitraClip (NTW) implanted medially at A3/P3 and second MitraClip (NTW) implanted centrally at A2P2 with (*B*) reduction of mitral regurgitation to 1–2+. (*C*) Pulmonary venous flow showing systolic predominance. (*D*) Mitral valve area was 2.66 cm^2 from the summation of both orifices with a trans-mitral mean gradient of 3 mmHg. (*E*) Fluoroscopic images showing two NTW MitraClips with wider distance between the clip arms and grippers due to more tissue grasped between them.

Table 1 Echocardiographic parameters before and after MitraClip

	Pre-MitraClip	Immediate post-MitraClip	1-Month post-MitraClip
MR severity	4+	1–2+	1+
MR 3D vena contracta area (cm^2)	0.7	0.13	NA
Trans-mitral mean pressure gradient (mmHg)	1	3	3
Mitral annulus diameter (mm)	43	42	37
LV ejection fraction (%)	53	45	55
LV end-diastolic diameter (mm)	65	55	52
LV end-systolic diameter (mm)	44	43	40
Pulmonary artery systolic pressure (mmHg)	35	36	32

3D, three-dimensional; LV, left ventricle; MR, mitral regurgitation; NA, not available.

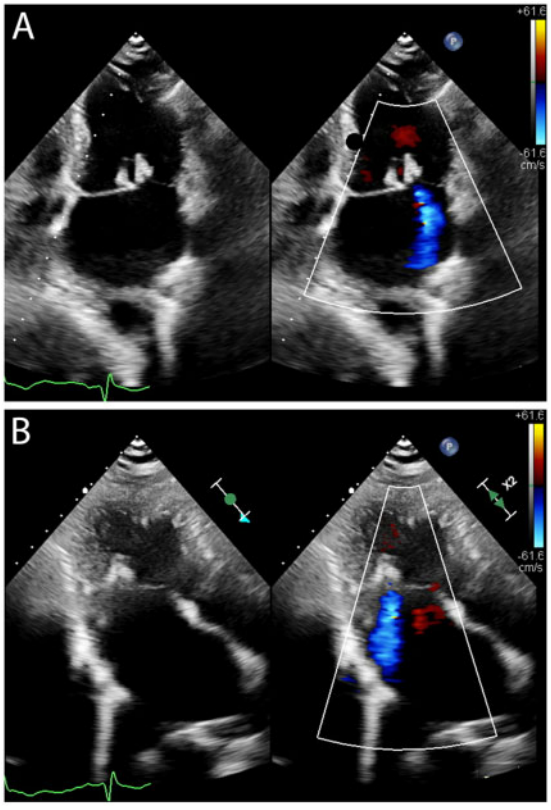


Figure 3 (*A* and *B*) Transthoracic echocardiogram images showing stable clips with mild mitral regurgitation 1 month after MitraClip implantation.

as the use of immunosuppressants, which remain as challenges during the post-operative phase. The association of SLE valvulopathy with APS further increases the surgical morbidity and mortality, especially in term of cerebrovascular events.[12] With the rapid advancement in the field of structural valve interventions, percutaneous option, if available and feasible, is an attractive option in this high-risk group. In patients with SLE who are at increased risk for open heart surgery, percutaneous valve intervention such as TEER can potentially serve as a bridge to future valve surgery, during which systemic disease can be further optimized and controlled.

There was an initial concern that the tissue quality in SLE valvulopathy may be suboptimal for TEER, with the risk of leaflet tear during grasping. However, the pathophysiology of Libman–Sacks endocarditis is believed to be the result of valvular endothelial injury from circulating immune complexes and cytokines, which causes inflammation and deposition of fibrin and platelet thrombi.[13] It may progress to a different stage—a healed form, consisting of dense fibrous and scar tissue, especially with the use of corticosteroids and increased duration of disease.[1,14] We postulate that the thickened and fibrotic valve may surprisingly allow for the gripper frictional elements to anchor itself and achieve a secure grasp. This is in contrast to the friable tissue, seen in active infective endocarditis, which is contraindicated for MitraClip therapy. It is hence reasonable to consider TEER in the late-stage or healed form of Libman–Sacks endocarditis but not advisable in the early inflammatory stage. In fact, the Libman–Sacks vegetations and thickened valve result in more tissue being grasped between the clip arms and the grippers, as evidenced by the wider distance between the clip arms and the grippers even after full closure (*Figure 2E*). It is thus important to ensure adequate tightening of the clip arms to achieve a secure grasp before clip deployment. Another concern is the development of progressive mitral stenosis (MS) which was reported in a patient with SLE and MR that was treated with the MitraClip system.[15] She developed severe MS 28 months after the procedure together with increasing doses of corticosteroid therapy for worsening SLE. Thickening of the tissue bridge from mitral valve inflammation and fibrosis was postulated as the reason. Hence regardless of a percutaneous or surgical approach to valve repair, it is critical to achieve good and sustained control of SLE disease activity. In addition, careful long-term follow-up is required.

Conclusion

In select patient with suitable anatomy, TEER is a potential treatment option for severe MR from SLE valvulopathy. However, it is important to recognize in the absence of long-term data, surgery should be considered as the preferred option, and a surgical bail-out should always be prepared if a TEER procedure is attempted in this uncommon clinical entity.

Lead author biography

Wong Ningyan graduated with the Bachelor of Medicine and Bachelor of Surgery Degree from the National University of Singapore Yong Loo Lin School of Medicine. He completed both his Internal Medicine Residency and Cardiology Senior Residency in SingHealth and obtained the following degrees—Membership of the Royal Colleges of Physicians (UK) Internal Medicine and Master of Medicine (Internal Medicine) Singapore. He is currently a Consultant as well as an Interventionist with National Heart Centre Singapore.

Supplementary material

Supplementary material is available at *European Heart Journal - Case Reports* online.

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

Consent: The authors confirm that written consent for submission and publication of this case report including images and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: Y.K.K. is a speaker, consultant, and proctor for Abbott Vascular (MitraClip) and reports receiving honoraria from Abbott Vascular. W.N. reports receiving honoraria from Abbott Vascular. All other authors declared no conflict of interest.

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