ESC European Heart Journal - Case Reports (2026) **10**, ytag348
https://doi.org/10.1093/ehjcr/ytag348

CASE REPORT
Inherited cardiac conditions/cardiomyopathies

Cardiogenic shock and atrial fibrillation after mavacamten dose escalation in obstructive hypertrophic cardiomyopathy: a case report

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Received 22 December 2025; revised 23 March 2026; accepted 30 April 2026; online publish-ahead-of-print 11 May 2026

Background Mavacamten is a first-in-class cardiac myosin inhibitor (CMI) that reduces left ventricular outflow tract (LVOT) obstruction in patients with symptomatic obstructive hypertrophic cardiomyopathy (HCM). However, excessive myosin inhibition may cause significant systolic dysfunction and rarely requires intensive care.

Case summary A 40-year-old woman with obstructive HCM presented with dyspnoea and palpitations. Mavacamten 5 mg daily improved symptoms after an inadequate response to β-blocker therapy, although significant LVOT obstruction persisted. Following dose escalation to 10 mg daily, her condition rapidly deteriorated, and she developed cardiogenic shock with severe biventricular systolic dysfunction and atrial fibrillation (AF) with a rapid ventricular response. Further history revealed recent alcohol consumption before the symptom exacerbation. She was admitted to the intensive care unit, mavacamten was discontinued, and intravenous amiodarone was initiated. Given the persistent haemodynamic instability and recent anticoagulation interruption, transoesophageal echocardiography was performed, identifying a large left atrial thrombus and precluding cardioversion. With therapeutic anticoagulation, rate control, and supportive care, sinus rhythm was spontaneously restored, and the left ventricular ejection fraction recovered to 50% within 5 days. At follow-up, systolic function had fully normalised. Low-dose mavacamten and β-blocker therapy were cautiously reintroduced, with reinforced counselling on alcohol abstinence and anticoagulation adherence. The patient remains clinically stable without recurrent ventricular dysfunction.

Discussion This case highlights that acute biventricular dysfunction may occur abruptly after CMI dose escalation, particularly when complicated by AF. Early recognition, prompt drug discontinuation, careful monitoring, and comprehensive patient education are essential for the safe clinical use of CMIs.

Keywords Hypertrophic cardiomyopathy • Cardiac myosin inhibitor • Heart failure • Atrial fibrillation • Case report

ESC curriculum 2.2 Echocardiography • 6.5 Cardiomyopathy • 6.4 Acute heart failure

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Handling Editor: Emmanouil Androulakis
Peer-reviewers: Enrico Bonni; Elvis J Amao-Ruiz; Tijn Julian Pieter Heeringa
Compliance Editor: Deepti Ranganathan

Learning points

- Mavacamten dose escalation may precipitate acute systolic dysfunction and cardiogenic shock in obstructive hypertrophic cardiomyopathy.
- Atrial fibrillation in hypertrophic cardiomyopathy requires strict anticoagulation; if adherence is uncertain, transoesophageal echocardiography should be performed before cardioversion due to rapid thrombus formation.

Introduction

Hypertrophic cardiomyopathy (HCM) is characterised by hypercontractility and left ventricular outflow tract (LVOT) obstruction.[1,2] Mavacamten, a cardiac myosin inhibitor (CMI), has emerged as an effective treatment for symptomatic obstructive HCM refractory to β-blocker therapy.[3] However, excessive myosin inhibition may reduce left ventricular ejection fraction (LVEF), necessitating careful surveillance.[4] This report describes a patient with obstructive HCM who developed cardiogenic shock with acute biventricular dysfunction and atrial fibrillation (AF) during mavacamten therapy.

Summary figure

January 2025	• Diagnosis of gene mutation-positive obstructive hypertrophic cardiomyopathy. • Treatment with a β-blocker (bisoprolol 5 mg/day) was initiated.
March 2025	• Mavacamten 5 mg/day was initiated because of persistent dyspnoea and significant left ventricular outflow tract (LVOT) obstruction.
June 2025	• Clinical symptoms and NT-proBNP level improved; however, haemodynamically significant LVOT obstruction persisted. • The dose of mavacamten was up-titrated to 10 mg/day.
August 2025	• The patient was admitted with palpitations, dyspnoea, and oedema. • Cardiogenic shock with severe biventricular dysfunction and atrial fibrillation with rapid ventricular response was identified. • Transoesophageal echocardiography revealed a large left atrial thrombus, which precluded electrical cardioversion. • Mavacamten was discontinued, and sinus rhythm and haemodynamic stability were restored after 5 days.
September 2025	• Complete recovery of biventricular systolic function was documented. • Lower-dose mavacamten (5 mg/day) was cautiously reintroduced in combination with bisoprolol 3.75 mg/day. • The patient was counselled on strict alcohol abstinence.
December 2025	• At an outpatient clinic visit, the patient remained clinically stable on the same medical regimen. • She reported no dyspnoea during daily activities, and the LVOT gradient remained < 30 mmHg even with provocation.

Case presentation

A 40-year-old woman with class III obesity (height 157 cm, weight 135 kg, body mass index 54.7 kg/m^2) presented with chest discomfort and palpitations. Electrocardiography showed AF with rapid ventricular response (RVR); N-terminal pro-B-type natriuretic peptide (NT-proBNP) was elevated at 2856 pg/mL. Transthoracic echocardiography (TTE) revealed asymmetric left ventricular hypertrophy (basal septum 24.0 mm vs. posterior wall 15.5 mm) and significant LVOT obstruction (62 mmHg at rest, 73 mmHg with Valsalva). She was unaware of an HCM diagnosis. Anticoagulation therapy with edoxaban and intravenous amiodarone was initiated, and sinus rhythm was restored the following day.

After 2 months on bisoprolol 5 mg/day, she remained in sinus rhythm; however, symptoms, elevated NT-proBNP (1649 pg/mL), and LVOT obstruction (84 mmHg at rest, 122 mmHg with Valsalva) persisted, with preserved LVEF (63%) (*Figure 1* and Supplementary material online, *Video S1*). Severe exertional dyspnoea precluded physical exercise, and despite strict dietary restrictions, meaningful weight reduction could not be achieved. During further evaluation, she reported that her father had died suddenly at a young age from a presumed cardiac event, raising the possibility of familial HCM. Genetic testing subsequently identified a pathogenic troponin I type 3 (*TNNI3*) variant, confirming HCM. Although her siblings were reportedly asymptomatic, familial screening was recommended to evaluate for silent disease; however, they were unable to visit our institution owing to personal and geographical constraints. Cardiac magnetic resonance imaging was deferred due to financial constraints and obesity-related technical concerns. As disopyramide was not locally approved or reimbursed for obstructive HCM at the time of treatment, mavacamten 5 mg/day was initiated. After 3 months, symptoms improved to NYHA class II, NT-proBNP declined to 682 pg/mL, and LVOT obstruction decreased but remained significant (50 mmHg at rest, 69 mmHg with Valsalva), with an LVEF of 59%. Mavacamten dosage was increased to 10 mg/day.

Two months later, she developed dizziness, dyspnoea, and oedema and was admitted to the intensive care unit with hypotension (84/51 mmHg) and AF with RVR (142 b.p.m.). She had continued mavacamten despite worsening symptoms over the preceding week, but discontinued anticoagulation therapy because of bruising and reported regular alcohol use for stress relief. Transthoracic echocardiography showed severe biventricular

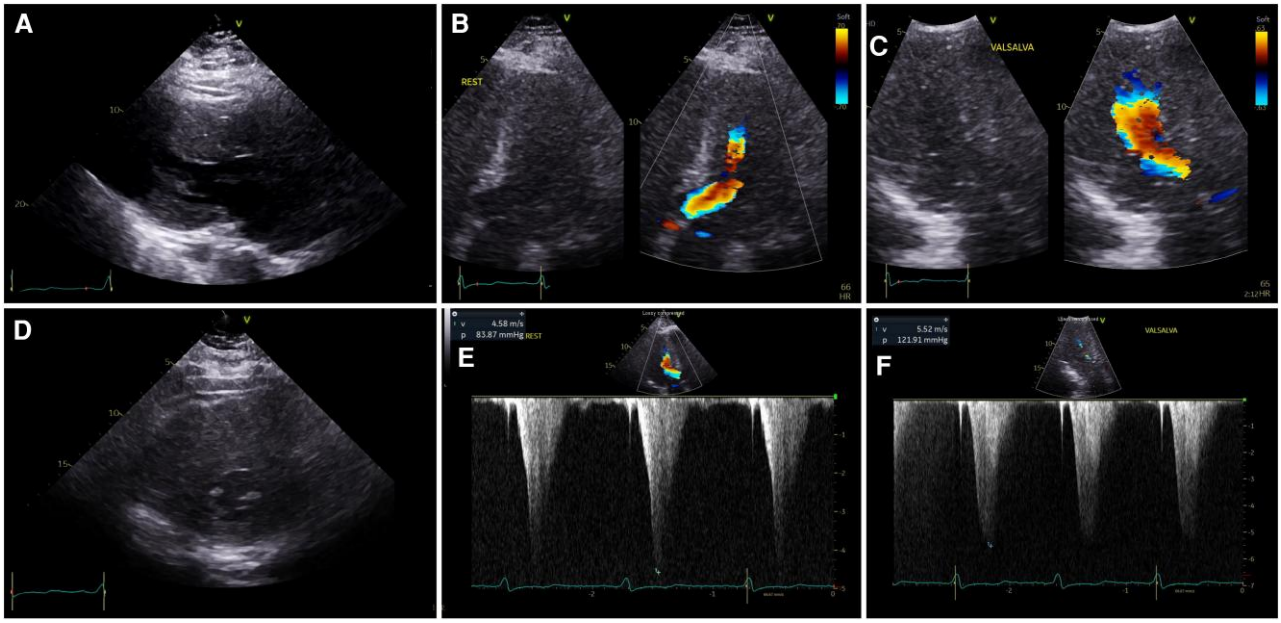

Figure 1 Baseline echocardiographic findings before mavacamten initiation. (*A*) Parasternal long-axis view showing asymmetric septal hypertrophy. (*B*, *C*) Apical views with colour Doppler at rest and during Valsalva manoeuvre demonstrating turbulent LVOT flow. (*D*) Parasternal short-axis view showing marked asymmetric septal hypertrophy and systolic cavitary obliteration. (*E*, *F*) Continuous-wave Doppler demonstrating a resting LVOT gradient of 84 mmHg and an increased gradient of 122 mmHg during a Valsalva manoeuvre. LVOT, left ventricular outflow tract.

dysfunction (LVEF, 28%; right ventricular S', 4.7 cm/s; *Figure 2* and Supplementary material online, *Video S2*). NT-proBNP rose to 2852 pg/mL. Despite continued intravenous amiodarone, AF with RVR and hypotension persisted, accompanied by NYHA class IV dyspnoea. Despite considering mechanical circulatory support, a stable lactate level and the absence of progressive hypotension allowed for conservative management. Because of ongoing haemodynamic instability and recent interruption of anticoagulation, transoesophageal echocardiography (TOE) was performed before cardioversion and revealed a large left atrial thrombus, precluding electrical cardioversion (*Figure 3* and Supplementary material online, *Video S3*). Mavacamten was withdrawn, and treatment included fluid support and therapeutic anticoagulation. By Day 5, sinus rhythm was restored, and LVEF recovered to 50%, with haemodynamic stabilisation. After a further 48 h of stability, she was discharged on bisoprolol 3.75 mg/day with strict counselling on alcohol abstinence.

One month later, biventricular function had normalised (LVEF 65%; right ventricular S' 13.0 cm/s), and LVOT obstruction was noted (15 mmHg at rest, 54 mmHg with Valsalva). Mavacamten 5 mg daily was cautiously reintroduced. Subsequently, provoked LVOT gradients remained < 30 mmHg, LVEF was 56%, and NT-proBNP was 615 pg/mL (*Figure 4* and Supplementary material online, *Video S4*). She currently reports no dyspnoea during daily activities.

Discussion

This case provides important lessons for safe CMI administration in clinical settings.

First, cardiogenic shock developed shortly after dose escalation, suggesting that myosin inhibition may extend beyond isolated left ventricular impairment, particularly in the presence of additional aggravating factors such as tachyarrhythmia or alcohol use. Nonetheless, CMI-induced systolic dysfunction is generally reversible after drug discontinuation.[4,5] In normal metabolisers, mavacamten has an elimination half-life of 6–9 days, with washout expected within 4 weeks.[6] In this case, recovery began 5 days after withdrawal, supporting reversible myocardial depression rather than structural injury. Given reports of severe cases requiring prolonged extracorporeal membrane oxygenation,[7,8] patients with systolic dysfunction should be monitored for at least 7–10 days after drug discontinuation.

Second, this case illustrates the complex interaction between AF and CMI. Atrial fibrillation is highly prevalent (>25%) in HCM.[9] However, the temporal relationship between AF onset and ventricular dysfunction in this case could not be definitively established, and specific predictors of AF during CMI therapy remain uncertain. In EXPLORER-HCM, AF incidence was similar between mavacamten and placebo groups (2% vs. 3%, respectively).[4] Nevertheless, AF in this setting requires prompt recognition and careful management. Hypertrophic cardiomyopathy is an independent risk factor for thromboembolism, and guidelines recommend anticoagulation for patients with HCM and AF.[3,10] In this patient, interruption of anticoagulation for 1 week, together with AF with RVR and acute systolic dysfunction, led to rapid left atrial thrombus formation. Because intracardiac thrombi may develop quickly under impaired haemodynamic conditions, TOE should be performed before cardioversion when anticoagulation adherence is uncertain. In this case, TOE-guided deferral of cardioversion averted a potentially catastrophic embolic event.

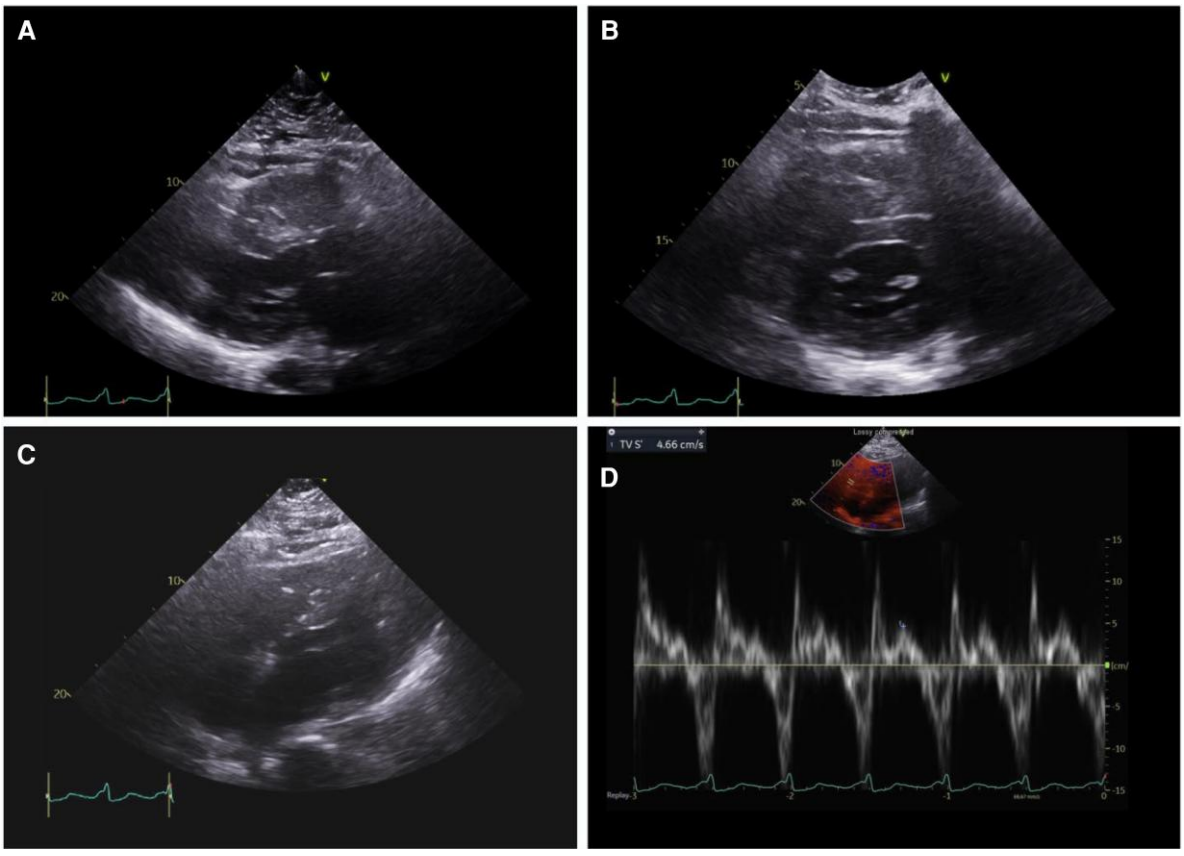

Figure 2 Echocardiography at the time of intensive care unit admission. (*A*, *B*) Parasternal views showing markedly depressed systolic function of both ventricles. (*C*) RV-focused view demonstrating hypokinesia of the RV free wall with reduced annular excursion. (*D*) Tissue Doppler showing reduced tricuspid annular systolic velocity (*S′* 4.7 cm/s). RV, right ventricle.

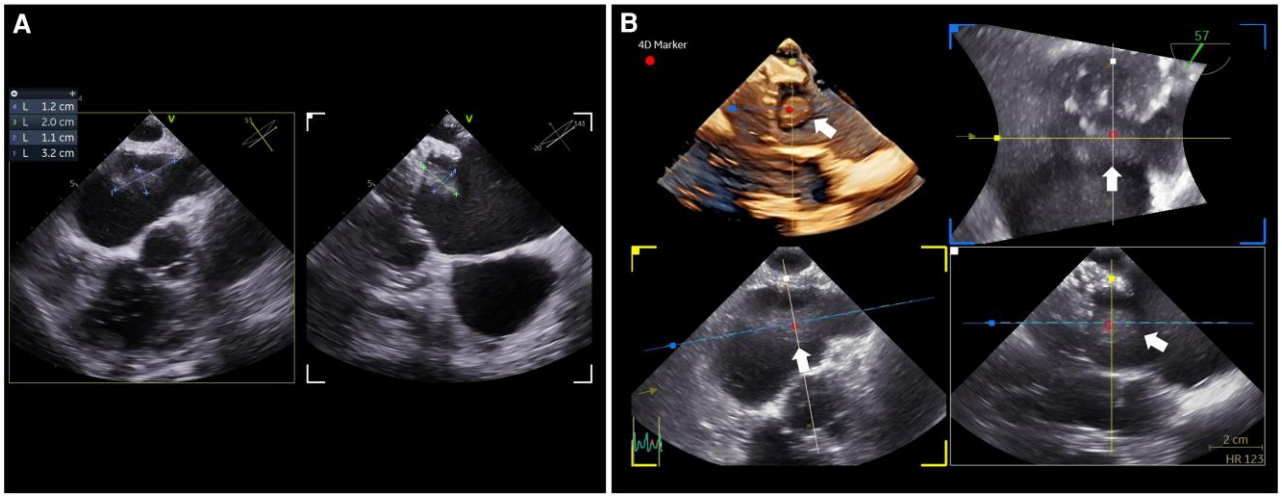

Figure 3 Transoesophageal echocardiography for the evaluation of an intracardiac thrombus. (*A*) Biplane views identifying an echogenic mass (1.2 × 2.0 and 1.1 × 3.2 cm in orthogonal planes) consistent with left atrial thrombus. (*B*) Three-dimensional multiplanar reconstruction image demonstrating the thrombus attachment site on the posterolateral wall of the left atrium near the left atrial appendage orifice; the precise location is confirmed by a 4D marker (white arrow).

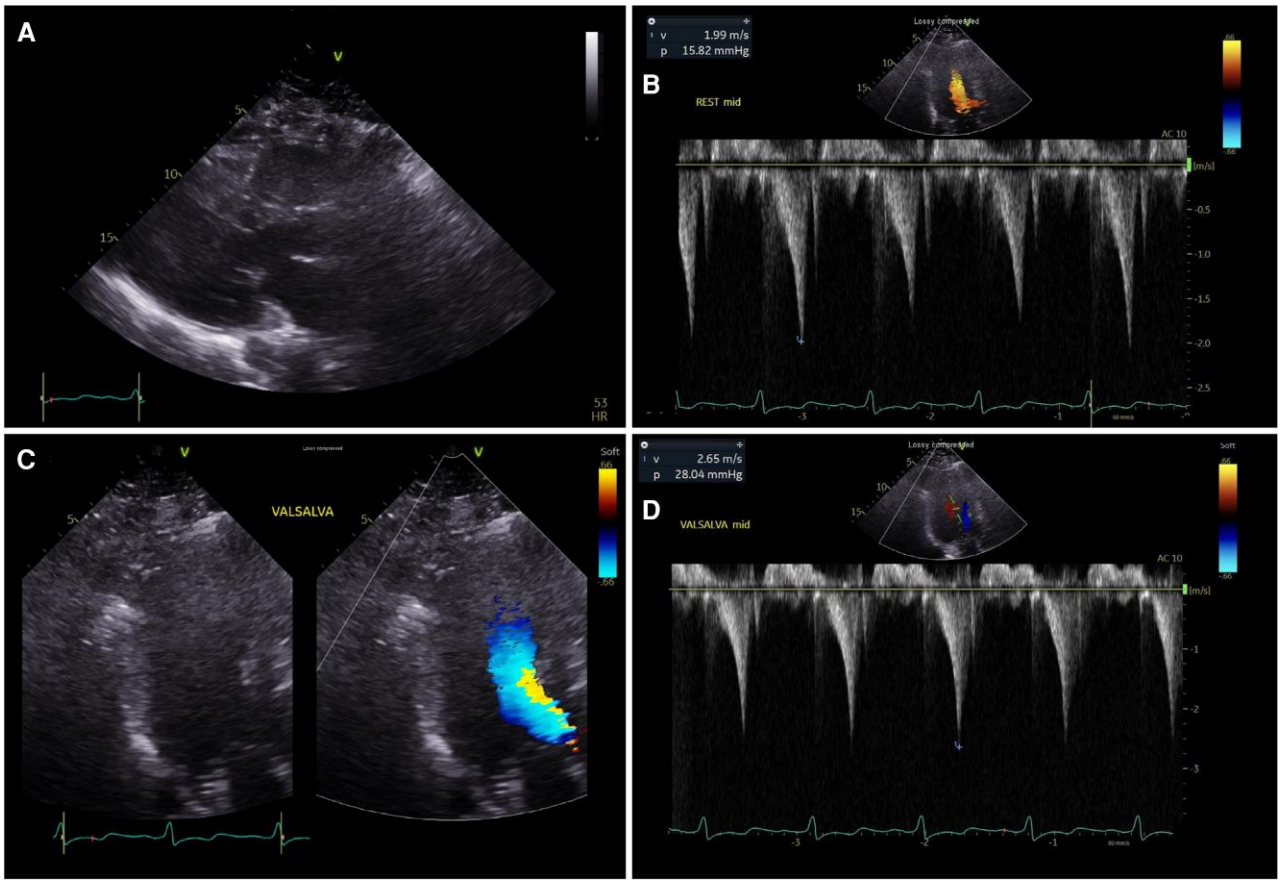

Figure 4 Follow-up echocardiography after re-initiation of lower-dose mavacamten. (*A*) Parasternal view showing preserved biventricular systolic function on mavacamten 5 mg and bisoprolol 3.75 mg. (*B*) Resting left ventricular outflow tract gradient measured of 16 mmHg. (*C*) Apical view showing reduced systolic cavitary obliteration with decreased left ventricular outflow tract flow acceleration on colour Doppler. (*D*) Provoked left ventricular outflow tract gradient of 28 mmHg during Valsalva manoeuvre, demonstrating the absence of haemodynamically significant obstruction. LVOT, left ventricular outflow tract.

Third, cautious re-initiation of low-dose CMI may be feasible following recovery from systolic dysfunction in accordance with the prescribing protocol. While surgical myectomy remains an established option for refractory obstructive HCM, recent guidelines support shared decision-making between pharmacological and surgical options.[3,10] Following the adverse event, surgical myectomy was explicitly discussed with the patient; however, she declined owing to concerns regarding perioperative risk. Dose-reduced re-initiation under close echocardiographic surveillance successfully controlled symptoms without further adverse events.

Fourth, this case highlights comprehensive patient education and pharmacogenetic screening. Although upfront CYP2C19 genotyping is not mandated by local regulatory guidelines and was not performed, East Asians notably have a significantly higher prevalence of the poor metaboliser phenotype compared to European populations (11.9% vs. 2.1%).[11] Therefore, CYP2C19 genotyping should be considered if adverse events occur even at the 5 mg dose. However, because our patient tolerated the initial 5 mg dose for 3 months without adverse events, standard up-titration to 10 mg was pursued. Subsequently, the acute pathophysiological effects of alcohol consumption, including vasodilation, reduced preload, and exacerbation of LVOT obstruction, and its known association with provocation of atrial fibrillation, likely acted synergistically with the potentially elevated mavacamten exposure from the recent dose escalation to precipitate cardiogenic shock.[12,13] Given the half-life of mavacamten and the absence of an antidote, delayed discontinuation may prolong myocardial depression. Therefore, patient education should emphasise strict alcohol abstinence, prompt reporting of worsening symptoms, and early clinical review if heart failure symptoms deteriorate. Following recovery, mavacamten was successfully reintroduced at a reduced dose, and LVOT obstruction remained well-controlled through reinforced patient education and lifestyle modification.

Thus, CMIs are promising treatment agents for obstructive HCM; however, their safe use requires meticulous monitoring, strict anticoagulation adherence, comprehensive patient education, and multidisciplinary care.

Lead author biography

Woo Jae Jeong, MD, earned his medical degree from Inje University and is currently completing residency and fellowship training in cardiology at Ilsan Paik Hospital. His clinical interests focus on developing broad expertise as a general cardiologist.

Supplementary material

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

Author contributions

Woo Jae Jeong [Writing—original draft (lead)], Sung Eun Kim [Data curation (lead)], Sung Woo Cho [Supervision (lead)], June Namgung [Supervision (equal)], and Kyu-Yong Ko [Conceptualization, Writing—review & editing (lead)]

Acknowledgements

The authors thank all the healthcare professionals involved in the patient's care.

Consent: The authors confirm that written informed consent for submission and publication of this case report, including images and associated text, was obtained from the patient in compliance with COPE guidelines.

Conflict of interest. None declared.

Funding

None declared.

Data availability

The data underlying this article are available in the article and its online supplementary materials.

Ethical approval

This study was approved by the Institutional Review Board of Inje University Ilsan Paik Hospital (no. 2025-11-007).

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