Received: 5 August 2022 | Accepted: 6 September 2022

DOI: 10.1002/ccd.30411

CASE REPORT

WILEY

Alcohol septal ablation for left ventricular outflow tract obstruction in cardiac amyloidosis: New indication for an established therapy

Lauren E. Fanta MD[1] | Steven M. Ewer MD[2] | Giorgio Gimelli MD[2] | Nicole M. Reilly MD[2]

[1]Department of Internal Medicine, University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin, USA

[2]Department of Medicine, Division of Cardiovascular Medicine, University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin, USA

Correspondence
Lauren E. Fanta, MD, Department of Internal Medicine, University of Wisconsin School of Medicine and Public Health, 600 Highland Ave, Madison, WI 53792, USA.
Email: lfanta@uwhealth.org

Abstract

Cardiac amyloidosis can occasionally demonstrate an atypical pattern of infiltration, causing asymmetric septal thickening and a left ventricular outflow tract (LVOT) gradient with systolic anterior motion (SAM) of the mitral valve resembling obstructive hypertrophic cardiomyopathy. We present a case of a 70-year-old man with cardiac light-chain amyloidosis and LVOT obstruction successfully treated with alcohol septal ablation (ASA). Following the procedure, he reported significant improvement in his heart failure symptoms as well as improvement in LVOT gradient and SAM of the mitral valve. This case demonstrates that ASA is a technically feasible and effective procedure for relieving LVOT obstruction in cardiac amyloidosis and can be considered as a treatment option in patients whose symptoms are refractory to medical therapy.

KEYWORDS
alcohol septal ablation, cardiac amyloidosis

1 | INTRODUCTION

Cardiac amyloidosis is a condition in which abnormal amyloid fibril proteins are deposited in the myocardium. These deposits compress cardiomyocytes, leading to myocardial dysfunction through both stiffenings of the extracellular space and direct myocyte damage. The most common forms of amyloid that affect the heart are immunoglobulin-derived light chains (AL) and transthyretin (TTR). Typically, the cardiac deposits in AL amyloidosis are diffuse peri-cellular, endocardial, arterial and/or arteriolar.[1] Occasionally, however, patients with cardiac amyloidosis demonstrate an atypical pattern of infiltration with asymmetric septal thickening and a left ventricular outflow tract (LVOT) gradient with systolic anterior motion (SAM) of the mitral valve that resembles obstructive hypertrophic cardiomyopathy (HCM).[2–4] It is unclear whether patients with cardiac amyloidosis and LVOT obstruction benefit from mechanical means of reducing the LVOT obstruction more commonly seen in obstructive HCM. We present a case of cardiac AL amyloidosis and LVOT obstruction successfully treated with alcohol septal ablation (ASA).

Abbreviations: ASA, alcohol septal ablation; ECG, Electrocardiogram; HCM, hypertrophic cardiomyopathy; LV, left ventricular; LVOT, left ventricular outflow tract; SAM, systolic anterior motion; TTE, transthoracic echocardiogram.

1.1 | Case report

A 70-year-old man with multiple myeloma, paroxysmal atrial fibrillation, and hypertension was transferred to this hospital for evaluation and management of acute decompensated heart failure. Six years prior, he was diagnosed with cardiac amyloidosis after presenting to his cardiologist with lower extremity edema, palpitations, and several episodes of presyncope. Electrocardiogram (ECG) at the time revealed low voltage QRS complexes, and transthoracic echocardiography (TTE) demonstrated normal left ventricular (LV) size and systolic function but marked thickening of the walls (19 mm at the septum, 17 mm in the basal inferolateral wall) in addition to a restrictive filling pattern consistent with severe diastolic dysfunction. Given his bone marrow biopsy-proven diagnosis of light chain multiple myeloma, the severe thickening of his LV walls in the absence of uncontrolled hypertension or other afterload stress, and the low voltages on his ECG, the decision was made to forgo cardiac biopsy as it was felt these findings were pathognomonic for cardiac amyloidosis. The patient was started on dexamethasone and lenalidomide, and his heart failure symptoms were managed with furosemide. He remained clinically stable for the next 5 years.

One year before admission, the patient again presented to his cardiologist with worsening heart failure symptoms as well as two episodes of syncope. Repeat TTE demonstrated persistent severe LV wall thickening up to 20 mm and new SAM of the mitral valve, mild mitral valve regurgitation, and LVOT obstruction with a peak gradient of 32 mmHg at rest and 50 mmHg with Valsalva. His medical management was intensified but invasive procedures deferred given the moderate gradients. Over the next several months, the patient continued to decline clinically with multiple admissions for acute decompensated heart failure. A repeat TTE 1 year later showed further progression of LV wall thickness up to 22 mm and worsening LVOT obstruction with a peak gradient of 70 mmHg (Figure 1). Given that his clinical decline and recurrent heart failure exacerbations correlated with progression of the LVOT obstruction, plans were made to proceed with an invasive treatment strategy. It was determined that an alcohol septal ablation was the most viable option, however, before this procedure could be scheduled, the patient was again admitted to an outside hospital for an acute decompensated heart failure exacerbation. There he experienced frequent hypotension associated with near-syncope and was no longer able to tolerate attempts at diuresis. He was subsequently transferred to our facility for ongoing heart failure treatment and to expedite the planned procedure.

On physical exam, he appeared in no acute distress. His heart rate was 98 beats per minute; blood pressure 89/55 mmHg; respiratory rate was 28 breaths per minute and oxygen saturation 94% on 2 L nasal cannula. Cardiac exam was notable for regular heart rate and rhythm, a 3/6 systolic murmur at the left lower sternal border without change with Valsalva, jugular venous distension, and 2+ pitting lower extremity swelling to the level of the mid-thighs bilaterally. The respiratory exam showed tachypnea without evidence of impending respiratory distress. Lungs were clear to auscultation bilaterally. The remainder of the physical exam was unremarkable.

Laboratory investigations were notable for normal electrolytes, acute on chronic kidney injury with initial creatinine 3.09 mg/dl from a baseline of 1.2–1.7 mg/dl (reference range 0.73–1.18 mg/dl), BUN 101 (reference range 9–20 mg/dl), and elevated BNP 4288 pg/ml (reference range 0–99 pg/ml). Initial hemoglobin 7.5 g/dl (reference range 13.6–17.2 g/dl) which quickly improved to 9.3 g/dl. ECG was notable for sinus tachycardia, left axis deviation, pseudo-infarct Q-waves in V3–V4, and low voltage QRS in the limb leads (Figure 2).

The patient was taken to the catheterization lab for percutaneous ASA. Preprocedure, a semipermanent pacemaker was placed. An EBU 3.5 guide catheter (Medtronic) was inserted into the left main coronary artery over a 0.35 J-tipped floppy wire (Medtronic). A 2 × 15 mm balloon was preloaded with a Cougar LS wire (Medtronic) and probed a second septal perforator which was small and did not opacify the bulkiest part of the septum when echo contrast was injected. The balloon was withdrawn and the third, more sizable septal perforator, was selected. At this level, contrast nicely opacified the bulkiest part of the septum. With the balloon

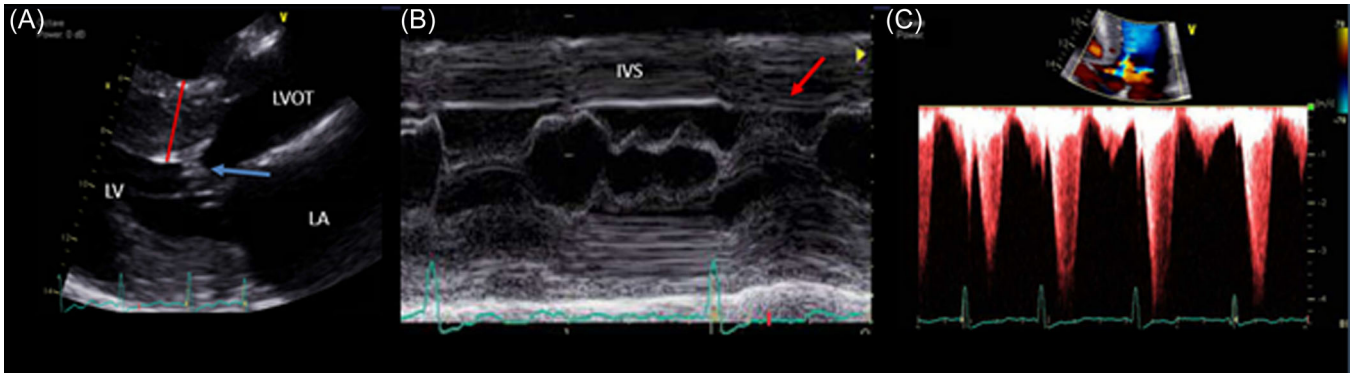

FIGURE 1 Transthoracic echocardiogram preprocedure. (A) Parasternal long-axis view depicts a markedly thickened interventricular septum (IVS) (red line) and systolic anterior motion of the mitral valve (blue arrow). (B) M-mode imaging in the parasternal long-axis view at the level of the mitral valve showing systolic anterior motion of the anterior mitral valve leaflet (arrow). (C) Continuous wave doppler through the left ventricular outflow tract (LVOT) showing a peak gradient of 70 mmHg. [Color figure can be viewed at wileyonlinelibrary.com]

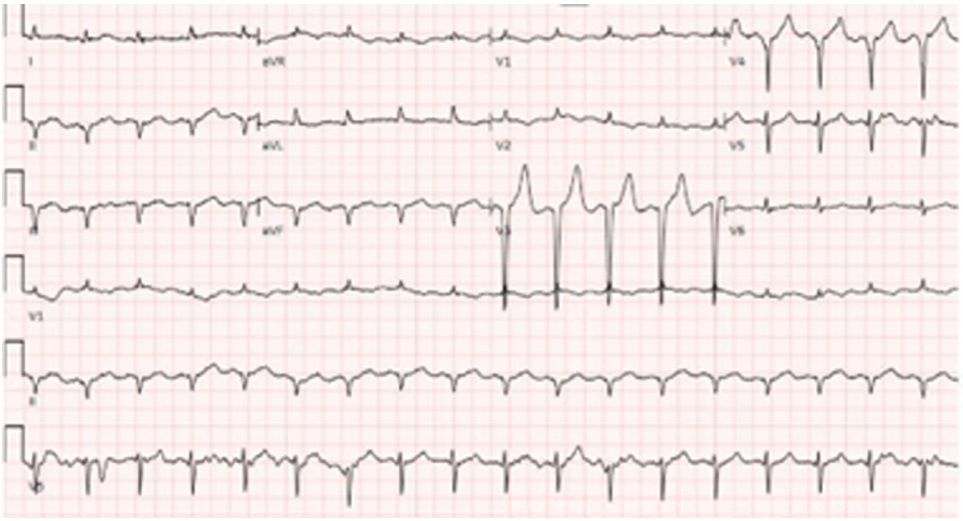

FIGURE 2 Electrocardiogram showing sinus tachycardia, left axis deviation, pseudo-infarct Q-waves V3–V4, low voltage QRS in limb leads. [Color figure can be viewed at wileyonlinelibrary.com]

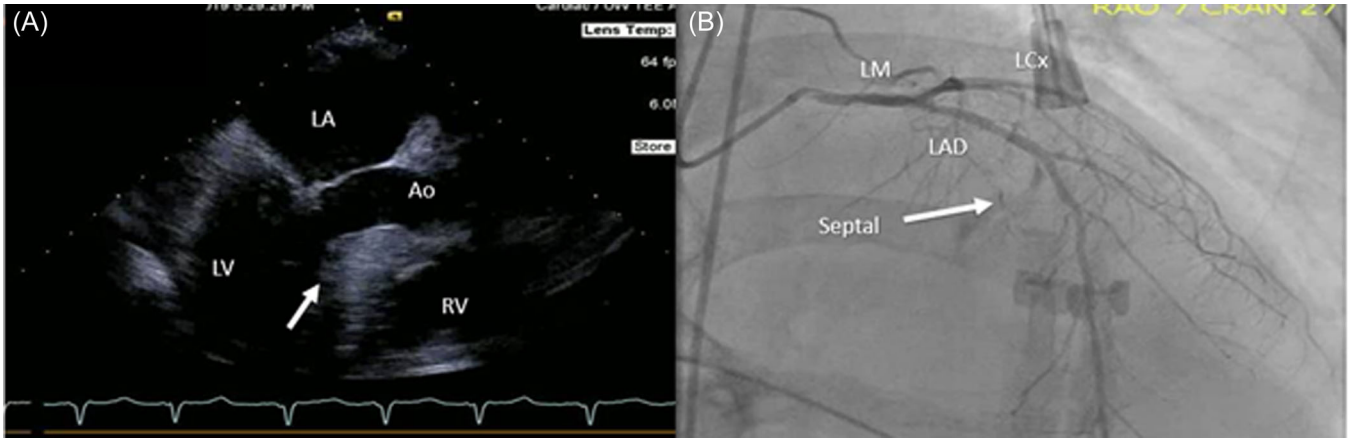

FIGURE 3 (A) Transesophageal echocardiogram intra-procedure, mid-esophageal long axis view. Injection of echocardiographic contrast into the target septal branch opacifies the basal part of the septum (arrow). (B) Left coronary angiography demonstrating absence of flow in the septal perforator after alcohol injection (arrow). LA, left atrium; LAD: left anterior descending artery; LCx: left circumflex artery; LV, left ventricle; RA, right atrium. [Color figure can be viewed at wileyonlinelibrary.com]

inflated at six atmospheres, 1.5 ml of ethanol was injected over 5 min. The balloon remained occlusive for 5 min, was flushed with saline, and then remained occlusive for an additional 3 min before deflating. Repeat angiography of the left anterior descending artery revealed complete occlusion of the vessel, and a transesophageal echocardiogram showed akinesis of the targeted portion of the septum (Figure 3). The LVOT was directly monitored during the outflow tract ablation. The peak LVOT gradient under general anesthesia with esmolol and phenylephrine infusions was 15 mmHg. Postablation, under similar hemodynamic conditions, the LVOT gradient decreased to 6 mmHg.

The patient reported significant improvement in dyspnea and near-syncope postprocedure. His semi-permanent pacemaker was removed 24 h after the ablation following interrogation demonstrating no pacing needs. Hospital course was complicated by spontaneous retroperitoneal hemorrhage and anuric acute kidney injury requiring dialysis. He was discharged home after a 2-week hospital course.

At 3-month follow-up, the patient reported significant improvement in his symptoms, especially dizziness. A limited TTE demonstrated an LVOT gradient of 20 mmHg which increased to 50 mmHg with Valsalva, and improvement in the SAM of the mitral valve. Two years after ASA, echocardiography continued to show only mild resting LVOT gradients (Figure 4).

2 | DISCUSSION

Cardiac amyloidosis typically presents with restrictive cardiomyopathy and diastolic dysfunction.[1] Diagnosis of cardiac AL amyloidosis is of particular importance, as left untreated, results in

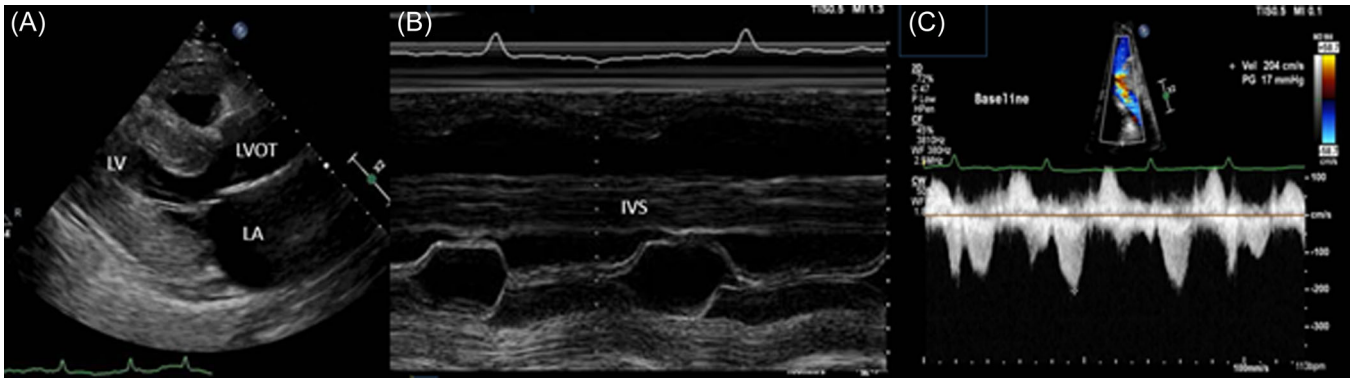

FIGURE 4 Transthoracic echocardiogram postprocedure. (A) Parasternal long-axis view showing reduced IVS thickening and resolution of systolic anterior motion of the anterior mitral valve leaflet. (B) M-mode imaging in the parasternal long-axis view demonstrating no systolic anterior motion of the mitral valve. (C) Continuous wave doppler through the LVOT showing a peak gradient of 17 mmHg. IVS, interventricular septum; LA, left atrium; LV, left ventricle; LVOT, left ventricular outflow tract. [Color figure can be viewed at wileyonlinelibrary.com]

a median survival of 6 months when heart failure symptoms are present.[1–3] Rarely, patients with cardiac amyloidosis have isolated wall thickening and evidence of LVOT obstruction, with a reported prevalence of LVOT obstructive physiology in 4% of patients with cardiac AL amyloidosis.[3] There is a lack of data regarding whether patients with cardiac amyloidosis and LVOT obstruction benefit from the invasive treatment strategies used in obstructive HCM. Because patients with cardiac amyloidosis often have restrictive physiology in addition to obstruction, there is a possibility that relieving the obstruction could fail to result in symptomatic improvement. In addition, the multiorgan involvement frequently seen in amyloidosis is associated with increased morbidity and can limit invasive treatment options.[3] Septal reduction therapy is the treatment of choice for symptomatic obstructive HCM refractory to medical therapy. The 2020 AHA/ACC Guideline for Hypertrophic Cardiomyopathy give a class 1B recommendation for surgical myectomy in symptomatic patients with obstructive HCM who have associated cardiac disease requiring surgical treatment, and a class 1C recommendation to pursue ASA in patients with contraindications to surgery.[5] ASA involves the injection of alcohol into the septal perforator coronary arteries creating a small, controlled myocardial infarction. Due to the lack of feasibility of randomized controlled trials, comparison of ASA and myectomy is predominantly observational, and it is unclear who is best served by ASA.[6] Myectomy is preferred in patients with concomitant primary valvular disease, multiple levels of obstruction, and other structural heart diseases, but is limited by the higher operative risk of sternotomy and inability to tolerate cardiopulmonary bypass. Conversely, ASA requires appropriate coronary anatomy and may be less effective with high resting gradients (>100 mmHg) and extreme septal thickness (>30 mm).[5]

In a large meta-analysis published in 2016, Singh et al found that ASA and myectomy were equally effective at resolving the symptoms of obstructive HCM with no difference in long-term all cause and cardiac mortality, despite the fact that patients in the ASA group were significantly older. The authors did find that 30-day mortality was higher in the myectomy group in nearly 70% of studies, however, this finding was not significant in the formal analysis.[7] Overall, myectomy has demonstrated mortality of <1% and clinical success >90–95%, and ASA has procedural mortality of <1% at experienced centers.[5] ASA was associated with higher device implantation postprocedure due to heart block, which can be reduced by injecting lower alcohol amounts into the septal perforators.[7] ASA is also associated with a greater need for repeat intervention because of residual obstruction, with repeat ASA or myectomy reported in 7–20% of patients post-ASA.[5] Finally, the authors of this manuscript hypothesize that an additional limitation of ASA in the setting of cardiac amyloidosis is that one may expect a less than usual decrease in septal thickness after the procedure, since the amyloid deposition is extracellular.

3 | CONCLUSION

This case demonstrates proof of concept that ASA is technically feasible and can be effective in relieving LVOT obstruction in cardiac amyloidosis. To our knowledge, this is the first report of LVOT obstruction from cardiac amyloidosis successfully treated with ASA with associated improvement in symptoms and quality of life. Although there are current guidelines for the use of ASA in obstructive HCM, more data is needed to support routine use in cardiac amyloidosis with LVOT obstructive physiology. This case suggests that ASA can be considered as a viable treatment option in patients with cardiac amyloidosis and LVOT obstruction with symptoms refractory to medical therapy.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

This material is the authors' own original work, which has not been previously published elsewhere. The paper reflects the authors' own research and analysis in a truthful and complete manner.

ORCID

Lauren E. Fanta http://orcid.org/0000-0003-3854-0865

REFERENCES

1. Falk RH, Alexander KM, Liao R, Dorbala S. AL (light-chain) cardiac amyloidosis: A review of diagnosis and therapy. *J Am Coll Cardiol*. 2016;68(12):1323-1341.
2. Sattar Y, Ruiz Maya T, Zafrullah F, Patel NB, Latchana S. Diagnosis and management of a cardiac amyloidosis case mimicking hypertrophic cardiomyopathy. *Cureus*. 2018;10(12):e3749.
3. Dinwoodey DL, Skinner M, Maron MS, Davidoff R, Ruberg FL. Light-chain amyloidosis with echocardiographic features of hypertrophic cardiomyopathy. *Am J Cardiol*. 2008;101(5):674-676.
4. Murphy RT, Ratliff NB, Lever HM, Kapadia SR. Use of percutaneous transluminal septal myocardial ablation for relief of outflow tract obstruction in cardiac amyloidosis: a novel therapeutic target. *Catheter Cardiovasc Interv*. 2006;68(4):637-641.
5. Ommen SR, Mital S, Burke MA, et al. 2020 AHA/ACC guideline for the diagnosis and treatment of patients with hypertrophic cardiomyopathy: executive summary: A report of the American College of Cardiology/American heart association joint committee on clinical practice guidelines. *J Am Coll Cardiol*. 2020;76(25):3022-3055.
6. Geske JB, Ommen SR, Gersh BJ. Hypertrophic cardiomyopathy: clinical update. *JACC Heart Fail*. 2018;6(5):364-375.
7. Singh K, Qutub M, Carson K, Hibbert B, Glover C. A meta analysis of current status of alcohol septal ablation and surgical myectomy for obstructive hypertrophic cardiomyopathy. *Catheter Cardiovasc Interv*. 2016;88(1):107-115.

How to cite this article: Fanta LE, Ewer SM, Gimelli G, Reilly NM. Alcohol septal ablation for left ventricular outflow tract obstruction in cardiac amyloidosis: New indication for an established therapy. *Catheter Cardiovasc Interv*. 2022;100:910-914. doi:10.1002/ccd.30411