Amyloidosis is a protein misfolding disorder characterized by aggregation and deposition of amyloid fibrils in tissues and organs disrupting architecture and function. Although this disorder often results in a restrictive cardiomyopathy with diffuse biventricular thickening, bialtral dilation, and conduction disease, clinically significant valvular heart disease is rarely described.

The MitraClip percutaneous edge-to-edge mitral valve repair is an important and effective treatment for patients with severe and symptomatic mitral regurgitation (MR). In patients at high risk for cardiac surgery, the MitraClip has shown excellent safety and durable results with 83% of patients demonstrating ≤2+ MR at 1-year and 87% of patients with New York Heart Association class I to II symptoms.1

We describe herein a patient with primary (AL) amyloidosis who suffered a ruptured mitral chord resulting in severe MR that was successfully treated using the MitraClip (Abbott Vascular, Minneapolis, MN) system. To our knowledge, this is the first reported case of degenerative MR related to cardiac amyloidosis that has been treated with a MitraClip.

Case Report

The patient is a 69-year-old man with a history of hypertension and hyperlipidemia. He presented one and half years before with worsening exertional dyspnea. Transthoracic echocardiography demonstrated severe biventricular hypertrophy, and bileaflet mitral valve thickening with mild prolapse (Figure 1; Movie I in the Data Supplement). Cardiac magnetic resonance imaging demonstrated diffuse right and left ventricular thickening with delayed enhancement suggestive of cardiac amyloidosis, and subsequent endomyocardial and bone marrow biopsies confirmed the diagnosis of light chain AL amyloidosis.

He underwent treatment for his systemic amyloidosis using bortezomib, cyclophosphamide, and dexamethasone. He demonstrated good response with normalization of his lambda light chains and reduction in N-terminal prohormone of brain natriuretic peptide. Unfortunately, he developed progressive and severely limiting shortness of breath (New York Heart Association class III–IV), and transesophageal echocardiography demonstrated posterior mitral leaflet prolapse and flail at the P2 segment (Figure 2A; Movie II in the Data Supplement) resulting in severe, anteriorly directed MR (Figure 2B; Movie II in the Data Supplement). He was considered extreme risk for surgical mitral valve repair given his recent chemotherapy, concerns about his overall prognosis, and likelihood of difficult rehabilitation from open-heart surgery because of progressive deconditioning in light of his limiting dyspnea. We, therefore, considered it reasonable to pursue percutaneous mitral valve repair using the MitraClip system.

He was brought to the hybrid operating room and the procedure performed via the right femoral vein under general endotracheal anesthesia and using biplane fluoroscopy and transesophageal echocardiography for guidance. One MitraClip was placed in the area of flail (Figure 3A; Movie III in the Data Supplement), with reduction in MR from 4+ to trivial (Figure 3B; Movie III in the Data Supplement). All sheaths were removed and the right femoral venous site closed by completion of the previously deployed Perclose preclosures (Abbott Vascular, Minneapolis, MN) using standard technique. The patient was extubated uneventfully before leaving the OR.

Acutely, the patient experienced a reduction in left atrial pressure from a mean of 24 to 18 mm Hg with v waves reduced from 38 to 26 mm Hg, with a corresponding increase in systolic blood pressure from 90 to 110 mm Hg. Transthoracic echocardiography more than 2 months later demonstrated a durable result of the procedure with trivial MR and peak/mean gradients of 8/4 mm Hg across the double-orifice mitral valve (Figure 4; Movie IV in the Data Supplement). At 6-month clinical follow-up, he remains almost free of exertional dyspnea with New York Heart Association class I to II symptoms.

Discussion

Treatment of AL amyloidosis consists of targeting the plasma cell dyscrasia with chemotherapy, and contemporary management has resulted in substantially improved survival over the past 2 decades. Nevertheless, cardiac involvement is a major cause of morbidity and mortality. For patients with cardiac amyloidosis, which most frequently presents as a restrictive cardiomyopathy because of amylod infiltration of the right and left ventricular myocardium, typical heart failure medications are not effective or indicated, and treatment is generally limited to diuretics for symptom relief. In selected cases, cardiac transplant may also be a viable treatment.
Amyloid may also deposit in the mitral valve apparatus causing thickening and stiffening of the valve and subvalvular apparatus, although significant regurgitation is rarely reported.² In patients with mitral valve involvement, tissue analysis demonstrates reduced elasticity of the valve.³ It is, therefore, possible that routine cardiac forces in the setting of stiffened mitral chords could result in chordal rupture, although only 1 case has been previously reported with the diagnosis of amyloid infiltration of the valve confirmed at the time of surgical valve repair and biopsy.⁴ These and other possible mechanisms of MR in cardiac amyloidosis are summarized in Figure 5.

From a technical standpoint, various factors can make MitraClip placement challenging. Secure grasping of the leaflets may prove difficult in situations of leaflet thickening >4 to 5 mm, substantial flail gap between the leaflets, and chordal shortening resulting in leaflet restriction/reduced coaptation. Furthermore, patients with annular/leaflet calcification that results in reduced mitral valve area may present a relative contraindication to clip placement because of further reduction in mitral valve area. We find that 3-dimensional transesophageal echocardiography assessment often proves helpful in understanding whether there is a prohibitive restriction to mitral valve opening. Another consideration is leaflet integrity, as various series have described detachment of the clip either because of leaflet tear or perforation of loss of leaflet-tip grasp.

In considering MitraClip therapy for our patient, we were initially apprehensive about the thickness of the mitral valve leaflets by transthoracic echocardiography, although this did not seem prohibitive on further evaluation with transesophageal echocardiography. We were also concerned about the leaflet integrity and the stability of clip placement given amyloid infiltration, although our patient has now demonstrated a stable and durable result beyond 6 months of follow-up. As in usual cases of degenerative MR, it may, therefore, be reasonable to consider MitraClip therapy for appropriately selected patients with severe primary MR in the setting of cardiac amyloidosis.

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Disclosures

None.

References


Figure 1. Transthoracic echocardiogram at initial visit demonstrated severe biventricular hypertrophy and thickening of the mitral valve leaflets (arrow). LV indicates left ventricle; and RV, right ventricle.
Figure 2. Transesophageal echocardiogram demonstrates (A) posterior leaflet prolapse (arrow) and chordal flail (arrowhead) resulting in (B) severe, anteriorly directed mitral regurgitation.

Figure 3. Procedural transesophageal echocardiogram. A, MitraClip positioned in the left atrium just above the mitral valve at the area of prolapse/flail (arrow). B, Trivial residual mitral regurgitation (arrow) after clip placement. LA indicates left atrium; and LV left ventricle.
Figure 4. Transthoracic echocardiogram at 2-month follow-up demonstrates stable MitraClip with trivial mitral regurgitation (arrow).

Figure 5. Potential mechanisms of mitral regurgitation (MR) in cardiac amyloidosis. A, Leaflet thickening due to amyloid deposition results in malcoaptation due to leaflet restriction or roughened leaflet edges. B, Reduced elasticity of the mitral chordae resulting in greater stress during systolic closing forces leads to broken chords and leaflet prolapse/flail. C, Dilated cardiomyopathy leads to apical MV tenting and typical functional MR. Reprinted with permission, Cleveland Clinic Center for Medical Art & Photography © 2016. All Rights Reserved.
First Reported Case of MitraClip Placement Due to Mitral Valve Flail in the Setting of Cardiac Amyloidosis
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**Video Legends:**

**Video 1.** Transthoracic echocardiogram at initial visit demonstrated Severe biventricular hypertrophy and thickening of the mitral valve leaflets.

**Video 2.** Transesophageal echocardiogram demonstrates (A) severe, anteriorly directed mitral regurgitation due to (B) posterior leaflet prolapse and chordal flail.

**Video 3.** Procedural transesophageal echocardiogram. (A) Trivial residual mitral regurgitation (arrow) after clip placement. (B) MitraClip positioned in the left atrium just above the mitral valve at the area of prolapse/flail.

**Video 4.** Transthoracic echocardiogram at 2-month follow-up demonstrates stable MitraClip with trivial mitral regurgitation.