Case Report

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Arrhythmic Mitral Valve Prolapse with Features of Mitral Annular Disjunction and Myocardial Tissue Changes as Assessed with Cardiac Magnetic Resonance

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Abstract

Background: Mitral valve prolapse (MVP) is a rare disorder linked to abrupt cardiac mortality and malignant ventricular arrhythmias. Beyond conventional prognostic indicators, risk stratification may have a promising function in MVP patients, as cardiac magnetic resonance imaging (CMR) can identify tissue alterations in these patients.

Case Illustration: A 36-year-old female with palpitation, dyspnea on exertion, and an episode of near syncope had multifocal premature ventricular complex (PVC) with right bundle branch block pattern. Bileaflet MVP with multifocal benign infrequent PVC from posteromedial papillary muscle was diagnosed in this patient based on echocardiography and holter monitoring. Mitral annular disjunction (MAD), mitral regurgitation (MR), and tricuspid regurgitation (TR) were also noticed. CMR examination confirmed moderate MR due to AML-PML prolapse with MAD at PML (P1, P2, P3), moderate TR due to anterior tricuspid leaflet prolapse, myocardial inflammation, and myocardial fibrosis.

Conclusion: CMR has the ability to visualize myocardial inflammation and fibrosis that contribute as arrhythmia substrates in mitral valve prolapse.

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Keywords: *arrhythmic mitral valve prolapse, mitral annulus disjunction, endomyocardial fibrosis*.

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Introduction

One of the most common causes of chronic primary mitral regurgitation is mitral valve prolapse (MVP). Although it typically manifests as a benign illness, sudden cardiac death (SCD) and malignant ventricular arrhythmias (VA) are occasionally linked to it.[1] Bileaflet MVP and elevated risk of arrhythmias have been associated with papillary muscle fibrosis, mitral annulus disjunction (MAD), and MVP. When assessed echocardiographically in the parasternal or apical long-axis views, MVP is defined as the superior displacement of any portion of the mitral leaflet beyond the mitral annulus, measured at a distance of ≥2 mm.[2]

MVP has a prevalence of 1-3% in the general population. In a large study of Olmsted County patients, those with asymptomatic MVP had a 10-year cardiovascular morbidity and overall mortality of 30% and 19%, respectively.[3-4] Arrhythmic MVP is a condition in which MVP causes arrhythmia disturbance.[5] The incidence of arrhythmic MVP in general population is still not known clearly. The estimated occurrence of SCD in patients with MVP is low, about 16-41 per 10000 per year (0.2% to 0.4% per year).[1] Savage et al. reported incidence of premature ventricular complex (PVC) in MVP, as evaluated by holter monitoring, varies from 49-85% in adult population. With 8 years of follow-up, about 17% of patients required an ICD or VT ablation in a study of MVP patients referred to a tertiary center. This low SCD risk number but relatively high prevalence of MVP put a significant population at risk of SCD.[4]

There is currently no established protocol to reduce the risk of SCD in individuals with arrhythmogenic MVP. Cardiac magnetic resonance (CMR) can validate the degree of prolapse, annular disjunction, and regurgitation as well as identify myocardial abnormalities in MVP patients. Non-invasive CMR is a useful tool for SCD risk classification in addition to conventional prognostic indicators.

Case Illustration

A 36-year-old female came with a complaint of palpitation for six months. She also had an episode of near syncope and dyspnea on exertion with moderate to heavy intensity of activities. She has a brother with an implantable cardiac defibrillator (ICD); however, we couldn't obtain any further information regarding his arrhythmia. Her heart rate was irregular with a frequency of 90-97 beats per minute at rest. Other physical examinations were unremarkable. Electrocardiography (ECG) showed sinus rhythm with a QRS rate of 75-85 beats per minute, normal axis, normal P wave, normal PR interval, and normal QRS duration, no ST elevation or depression, and multifocal premature ventricular complex (PVC) with right bundle branch block (RBBB)

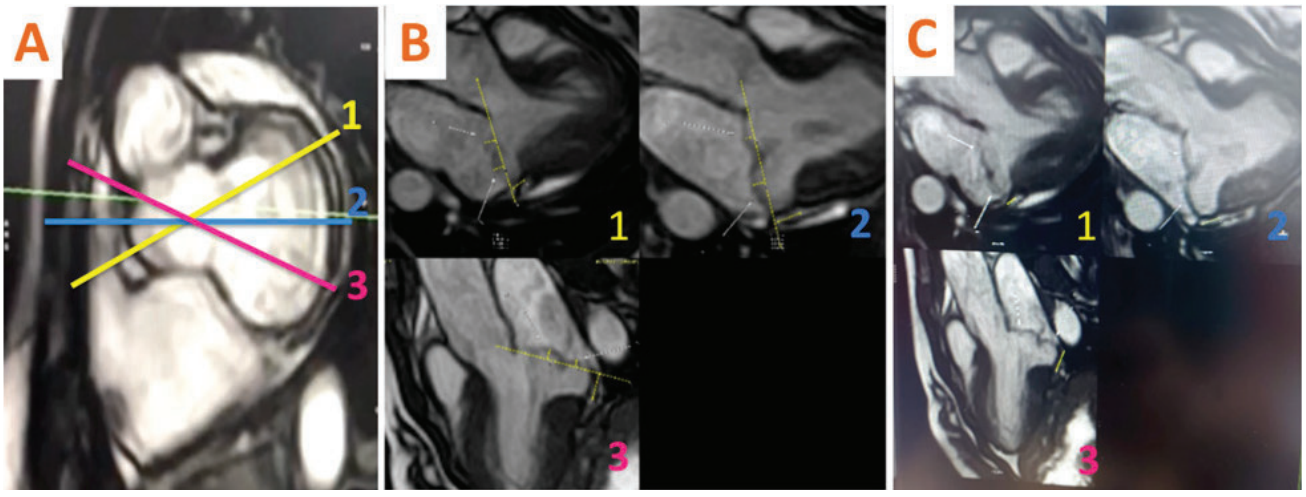

Figure 1. A. Planning for viewing mitral leaflets: A1-P1 (1), A2-P2 (2), A3-P3 (3). B. Mitral valve prolapse at A1-P1, A2-P2, and A3-P3. C. Mitral annular disjunction at P1 with length of 6 mm, at P2 with length of 9 mm, and at P3 with length of 13 mm

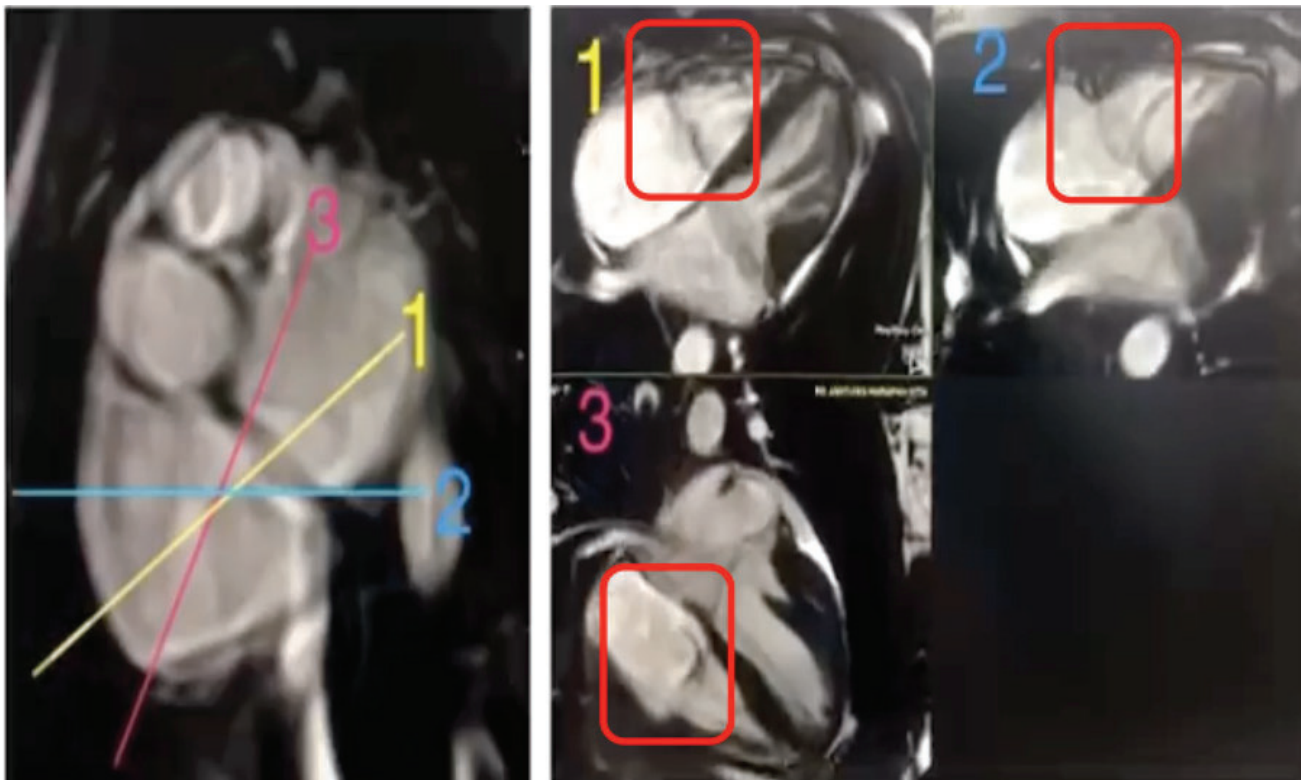

Figure 2. Planning for viewing mitral leaflets: anterior-septal (1 and 2), inferior-septal (3). Anterior tricuspid valve prolapse was noticed without tricuspid annular disjunction

pattern. Holter ECG examination showed sinus rhythm, good atrioventricular conduction, good chronotropic competence, multifocal benign infrequent PVC (4%) predominantly from posteromedial papillary muscle (PPM), and two episodes of non-sustained ventricular tachycardia (nsVT). Echocardiography showed mild mitral regurgitation due to anterior mitral leaflet (AML) A2 and posterior mitral leaflet (PML) P2 prolapse, due to degenerative, with mitral annular disjunction (MAD) of 11 mm, mild tricuspid regurgitation with low probability of pulmonary hypertension, good left ventricular ejection fraction (LVEF 61%), and good right ventricular function (TAPSE 31 mm) with global normokinetic and eccentric left ventricular hypertrophy. Laboratory findings were unremarkable.

CMR examination showed increased LV volume with mildly reduced LV systolic function (LVEF 54%) and mild hypokinetic at basal-apicoseptal, mid anterior; normal LV mass and wall thickness; normal right ventricular (RV) volume with normal RV systolic function (RVEF 69%) and global normokinetic RV; increased LA volume; moderate MR (regurgitant volume of 31 mL, regurgitant fraction 30%) with anterior mitral leaflet (AML) and posterior mitral leaflet (PML) prolapse and mitral annular disjunction at PML (6 mm at P1, 9 mm at P2, 13 mm at P3) as shown in **Figure 1**; moderate TR with anterior tricuspid leaflet prolapse without tricuspid annular disjunction as shown in **Figure 2**; myocardial inflammation at basal-mid anterior and basal anterolateral (**Figure 3**); increased T2 relaxation time at basal inferolateral (86 ms), mid inferolateral (78 ms), and mid septal (60 ms); subepicardial-intramyocardial late gadolinium enhancement (LGE) as non-ischemic myocardial fibrosis predominantly at basal-mid inferolateral, basal-mid inferior, apicolateral, and also at basal anterolateral and basal anteroseptal LV with fibrosis volume of 14% as shown in **Figure 4**; and rest hypoperfusion at basal-mid inferoseptal, basal-mid inferior, basal-mid inferolateral.

Patient was diagnosed with infrequent PVC predominant from posteromedial papillary muscle and MVP involving AML and PML. The patient was observed clinically to determine the timing of the appropriate intervention for arrhythmia. The patient

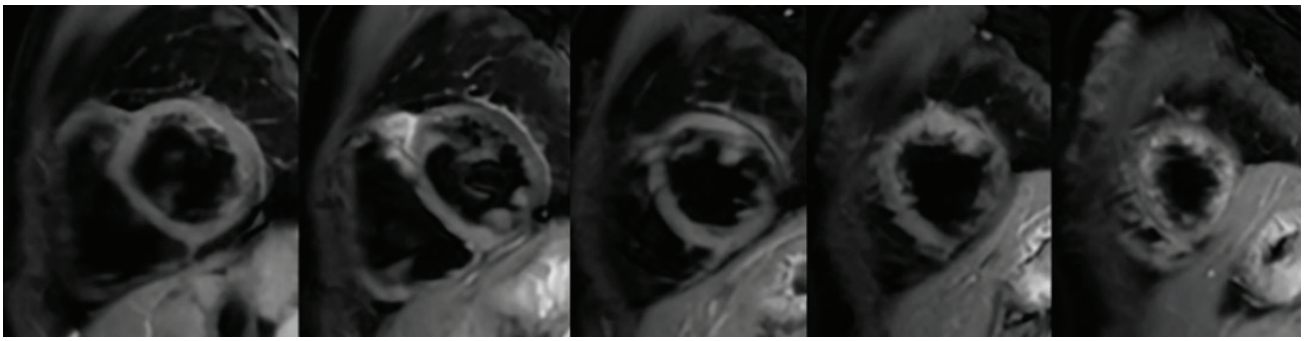

Figure 3. Myocardial edema at basal-mid anterior and basal anterolateral LV from T2w images.

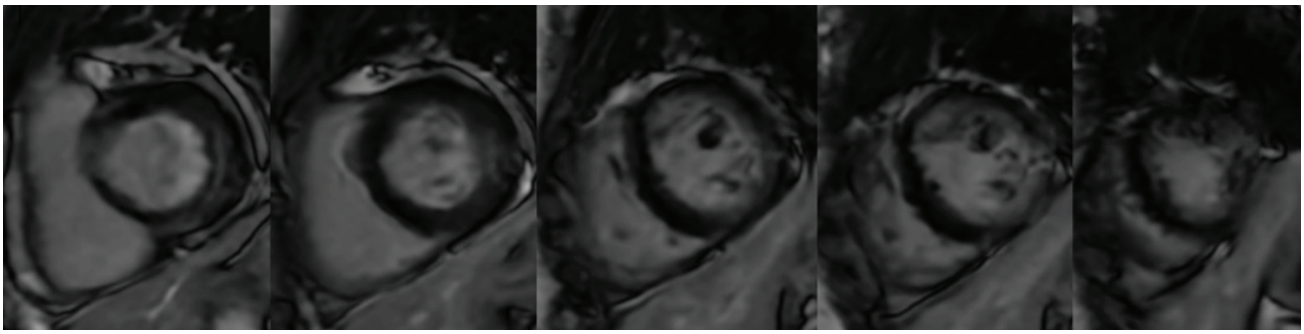

Figure 4. Late gadolinium enhancement at basal-mid inferolateral, basal-mid inferior, apicolateral, basal anterolateral, and basal anteroseptal LV

was prescribed bisoprolol 1x2.5 mg, amiodarone 3x200 mg, and candesartan 1x4 mg.

Discussion

This patient had symptomatic infrequent PVC due to mitral valve prolapse, diagnosed by Holter electrocardiography and echocardiography. Risk stratification was done with CMR. Examination revealed moderate MR with AML-PML prolapse. CMR is considered a robust noninvasive technique that can provide comprehensive assessment of the MV. The added value of CMR lies in its accurate estimation of LV volumes and function, as well as multiparametric tissue characterization, which is important for risk stratification.[6]

CMR has the ability to quantitatively assess regurgitant volume and regurgitant fraction accurately using data of LV stroke volume from 3D-LV volumetry and the aortic forward flow from the aortic phase-contrast image. CMR examination of our patient showed regurgitant volume of 31 mL and regurgitant fraction of 29.5%. Based on this data, MR is classified as moderate in primary MR.[6]

In Holter and CMR examinations, we obtained consistent findings. Holter revealed PVC predominant from the posteromedial papillary muscle, aligned with the fibrosis finding of LGE on CMR at basal-mid inferolateral and basal-mid inferior. Mitral valve prolapse causes abnormal papillary muscle tension and abnormal myocardium wall stress on the basal and inferolateral LV. Prolonged stress eventually leads to fibrosis, as illustrated by the patient's CMR. CMR can produce high-resolution cine images with customized slices for regions of interest. CMR examination of our patient showed prolapse A1-P1, A2-P2, and A3-P3 mitral leaflets with mitral annular disjunction. The severity of MAD correlates with the occurrence of VA. MAD > 8.5 mm is a strong predictor of VA.4,7 MAD in our patient was 6.4 mm at P1, 9.5 mm at P2, 13.1 mm at P3. CMR is a powerful technique to assess cardiac structure, function, AND myocardial fibrosis. LGE

is most commonly observed in the basal inferolateral wall and papillary muscle and less commonly in the myocardium adjacent to papillary muscles or other locations. Arrhythmic MVP is more strongly associated with LGE than non-arrhythmic MVP, with a relative risk of 4.38 (p=0.001) in meta-analysis. Areas of LGE correlate with histologic scars in pathologic specimens from patients who suffered SCD and correlate with the origins of ventricular arrhythmias identified during electrophysiologic studies.[8,9] CMR examination in our patient showed subendocardial-intramyocardial LGE predominantly at basal-mid inferolateral, apicolateral, and basal-mid inferior.

Currently, the development of cardiac fibrosis (a substrate for arrhythmias) in conjunction with a trigger for arrhythmias represents the current understanding of arrhythmogenesis in MVP. Leaflet prolapse, an MVP anatomical defect, results in excessive wall stress on the neighboring basal and inferolateral myocardium as well as inappropriate strain on the papillary muscles. Prolonged mechanical stress cause localized ischemia or inflammation, which can progress to fibrosis. For sustained ventricular arrhythmias (VA), a trigger is usually required in addition to the substrate. Purkinje tissue involvement and aberrant mechanical stretching are two important hypotheses for triggers. Papillary muscle traction locally extends the ventricular functional refractory period in animal studies. Papillary muscle arrhythmias can be induced or maintained locally by changes in the refractory time because of the aberrant mechanics of prolapsing leaflets in MVP. Moreover, Purkinje fibers arborize the inferior/inferolateral myocardium and the region next to the papillary muscle. These could also contribute to VA in individuals with MVP.[4]

The basic recommendations for arrhythmia, valvular abnormality, and heart failure are generally followed in the treatment of patients with MVP who have significant valve heart disease and arrhythmias. Relatively little information exists about the effectiveness of antiarrhythmic medications for ventricular arrhythmias, particularly in relation to MVP. Medical therapy is frequently the first course of treatment due to its relative safety. Depending on the severity of mitral regurgitation, there may be surgical indications for mitral valve repair when MVP is present. In patients with MVP, catheter ablation is usually carried out for recurrent ICD discharges that are not responsive to antiarrhythmic medication therapy, persistent ventricular fibrillation/tachycardia (including PVC-triggered), or frequent symptomatic ventricular ectopy.[5]

Even though MVP is generally considered a benign illness, there is a wide range of outcomes, and its complications are well-recognized, including mitral regurgitation, atrial fibrillation, congestive heart failure, endocarditis, and stroke. There have been reports of both sudden cardiac death (SCD) and ventricular arrhythmias. A young woman with a mid-systolic click during auscultation, bileaflet mitral valve involvement, T-wave abnormalities on inferior leads, and polymorphic or right bundle branch block type ventricular arrhythmias on ECG is typically at risk of SCD. This study provides unambiguous evidence of an electrical instability substrate in MVP, manifesting as myocardial scarring affecting the papillary muscles and the basal inferior-inferolateral LV free wall beneath the posterior leaflet, which is consistent with the location of RBBB-type ventricular arrhythmias. The clinical aspect of the study confirmed the LV myocardial fibrosis observed histologically in SCD patients, finding signs of late gadolinium enhancement (LGE) on cardiovascular magnetic resonance (CMR) imaging in arrhythmic patients with MVP.[5]

When patients have MVP and complicated ventricular arrhythmias, CMR can identify LGE in LV, which closely resembles the histological characteristics seen in SCD patients. The morphology of arrhythmias and electrophysiological investigations show that the basal inferior-inferolateral wall is the most frequent location of PVC in patients with MVP.

Conclusion

The arrhythmogenesis in MVP involves myocardial inflammation and fibrosis due to the abnormal papillary muscle tension and abnormal myocardium wall stress. CMR can locate the myocardial inflammation and fibrosis as substrates for arrhythmia in MVP.

List of Abbreviations

AML	Anterior Mitral Leaflet
CMR	Cardiovascular Magnetic Resonance

ICD	Implantable Cardiac Defibrillator
LGE	Late Gadolinium Enhancement
LV	Left Ventricular
MVP	Mitral Valve Prolapse
MAD	Mitral Annular Disjunction
nsVT	Non-Sustained Ventricular Tachycardia
PML	Posterior Mitral Leaflet
PPM	Posteromedial Papillary Muscle
PVC	Premature Centricular Complex
RV	Right Ventricular
sudden	

References

1. Haugaa KH, Aabel EW, Tani T, Konda T, Kitai T, Ota M, et al. Varied Extent of Mitral Annular Disjunction Among Cases With Different Phenotypes of Mitral Valve Prolapse. *JACC Cardiovasc Imaging*. 2021;3:1251-1257.
2. Dejgaard LA, Skjølsvik ET, Lie ØH, Ribe M, Stokke MK, Hegbom F, Scheirlynck ES, Gjertsen E, Andresen K, Helle-Valle TM, Hopp E, Edvardsen T, Haugaa KH. The Mitral Annulus Disjunction Arrhythmic Syndrome. *J Am Coll Cardiol*. 2018;72:1600-1609.
3. Freed LA, Benjamin EJ, Levy D, Larson MG, Evans JC, Fuller DL, Lehman B, Levine RA. Mitral valve prolapse in the general population: The benign nature of echocardiographic features in the Framingham Heart Study. *J Am Coll Cardiol*. 2002;40:1298-1304.
4. Chakrabarti AK, Bogun F, Liang JJ. Arrhythmic Mitral Valve Prolapse and Mitral Annular Disjunction: Clinical Features, Pathophysiology, Risk Stratification, and Management. *J Cardiovasc Dev Dis*. 2022;9.
5. Basso C, Perazzolo Marra M, Rizzo S, De Lazzari M, Giorgi B, Cipriani A, Frigo AC, Rigato I, Migliore F, Pilichou K, Bertaglia E, Cacciavillani L, Bauce B, Corrado D, Thiene G, Iliceto S. Arrhythmic Mitral Valve Prolapse and Sudden Cardiac Death. *Circulation*. 2015;132:556-566.
6. Garg P, Swift AJ, Zhong L, Carlhäll CJ, Ebbers T, Westenberg J, Hope MD, Bucciarelli-Ducci C, Bax JJ, Myerson SG. Assessment of mitral valve regurgitation by cardiovascular magnetic resonance imaging. *Nat Rev Cardiol*. 2020;17:298-312.
7. Carmo P, Andrade MJ, Aguiar C, Rodrigues R, Gouveia R, Silva JA. Mitral annular disjunction in myxomatous mitral valve disease: a relevant abnormality recognizable by transthoracic echocardiography. *Cardiovasc Ultrasound*. 2010;8:53.
8. Kitkungvan D, Nabi F, Kim RJ, Bonow RO, Khan MA, Xu J, Little SH, Quinones MA, Lawrie GM, Zoghbi WA, Shah DJ. Myocardial Fibrosis in Patients With Primary Mitral Regurgitation With and Without Prolapse. *J Am Coll Cardiol*. 2018;72:823-834.
9. Oliveri F, Kakargias F, Panday P, Arcia Franchini AP, Iskander B, Anwer F, Hamid P. Arrhythmic mitral valve prolapse: Diagnostic parameters for high-risk patients: A systematic review and meta-analysis. *Pacing Clin Electrophysiol PACE*. 2021;44:1746-1755.