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SUDDEN CARDIAC ARREST AS FIRST MANIFESTATION OF MALIGNANT MITRAL VALVE PROLAPSE IN A YOUNG PATIENT: A CASE REPORT AND REVIEW OF THE LITERATURE

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ABSTRACT

Mitral valve prolapse (MVP) is a primary valvular disease of the mitral valve with a prevalence of 2.4% of the general population. Valve abnormalities range from simple fibroelastic deficiency of the leaflets to diffuse myxomatous degenerative changes. MVP is a usually a benign condition. However, the scattered reports of sudden cardiac death in patients with MVP in the absence of severe mitral insufficiency or coronary artery disease suggest the existence of a malignant phenotype of MVP. We report a case of a young female who survived life-threatening arrhythmias and cardiac arrest and was found to have characteristic features of the malignant phenotype of MVP and had an implantable cardioverter defibrillator as a secondary prevention.

KEYWORDS

Mitral valve prolapse, malignant phenotype, sudden cardiac death

LEARNING POINTS

- Malignant MVP may be associated with life-threatening arrhythmias and sudden cardiac death.
- MVP is not always a benign condition, and physicians should be aware of the diagnostic criteria for malignant MVP.
- Echocardiography and cardiac magnetic resonance are crucial diagnostic methods to detect signs suggestive of malignant MVP.

INTRODUCTION

Mitral valve prolapse (MVP) is the most frequent cause of primary mitral regurgitation in Western countries. The incidence of sudden cardiac death in patients with MVP is low. However, it is higher than in the general population, with an annual incidence of MVP-related sudden cardiac death (SCD) of <1%. A phenotype of MVP with certain features has been found to have potential risk factors for SCD. However, defining the subgroup of MVP patients who may be at increased risk of SCD remains a challenge. The malignant phenotype of MVP may include elongated, myxomatous bileaflet prolapse, electrocardiogram (ECG)

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changes, complex ventricular ectopy, echocardiographic characteristics like the "Pickelhaube sign" on Doppler tissue imaging, and mitral annulus disjunction (MAD) in addition to its association with myocardial fibrosis in the papillary muscles and inferobasal region of the left ventricle (LV) on cardiac magnetic resonance imaging (MRI).

CASE DESCRIPTION

A 28-year-old female presented to the emergency department (ED) with frequent episodes of palpitations and 2 episodes of pre-syncope for the last 3 months which had not been investigated. She had no past medical or family history of cardiac disease or sudden cardiac arrest. She was not on any traditional supplements/medications. In the ED, she was symptom-free. Her vital signs were normal. The clinical examination was unremarkable except for an apical late systolic murmur. Her ECG showed sinus rhythm with an inverted T wave in lead III and AVF. While the patient was connected to a cardiac monitor, she suddenly collapsed, and the monitor showed wide complex tachycardia that degenerated into ventricular fibrillation *(Fig. 1 and 2)*. The patient was successfully resuscitated and regained consciousness. ECG after resuscitation showed premature ventricular contraction with no new ischemic changes, no evidence of Brugada-type changes, prolonged QT, delta, or epsilon wave. Blood investigations indicated normal liver and renal function and ruled out infective and toxicological causes. Computed tomography coronary angiography showed normal origin of coronary arteries without stenosis. Transthoracic echocardiography declared bileaflet mitral valve prolapse (MVP) with moderate mitral regurgitation, mitral annulus disjunction (MAD) of 1 cm *(Fig. 3)*, normal LV size, and function with an ejection fraction of 65%. The tissue Doppler imaging of the lateral mitral annulus showed a prominent mid-systolic spike of 21 cm/sec suggestive of the Pickelhaube sign *(Fig. 4)*. The late gadolinium enhancement on cardiac MRI revealed inferior and inferolateral ventricular wall fibrosis with no evidence of inflammation or edema of the myocardium *(Fig. 5)*. The investigation of this young patient who survived a cardiac arrest showed no evidence of ischemia, cardiac inflammation, or infiltrative disease in addition to the absence of a high-risk ECG pattern. However, she had evidence of bileaflet MVP associated with MAD and Pickelhaube sign on tissue Doppler of lateral mitral annulus in addition to the fibrosis of inferior and inferolateral LV wall which is highly suggestive of malignant MVP that is associated with ventricular arrhythmias and sudden cardiac death. As a secondary prevention, an implantable cardioverter defibrillator (ICD) was inserted. Follow-up after 6 months showed only multiple frequent premature ventricular contractions with no episodes of ventricular tachycardia.

DISCUSSION

MVP is the most frequent cause of primary mitral regurgitation[1]. MVP is a frequent echocardiographic

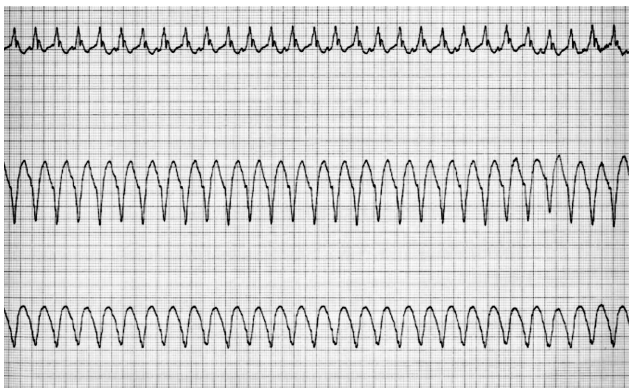

Figure 1. Ventricular arrhythmias recorded on electrocardiographic monitoring.

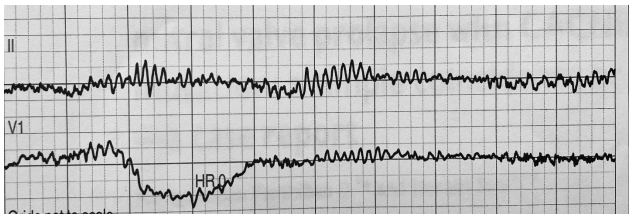

Figure 2. Ventricular fibrillation.

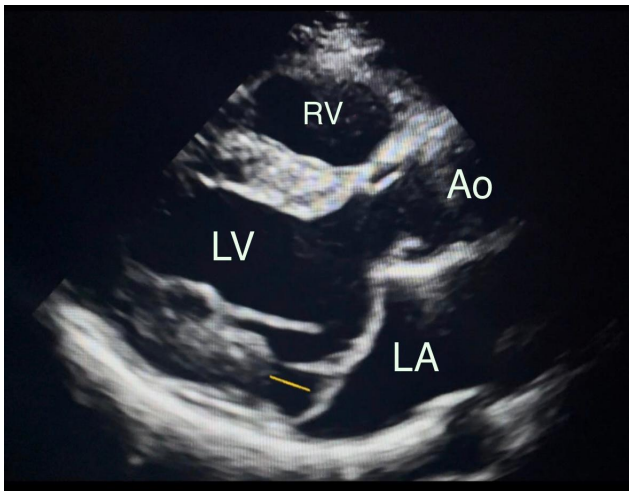

Figure 3. Transthoracic echocardiography, left parasternal view: Mitral annulus disjunction (yellow line) and bileaflet mitral valve prolapse. Abbreviations: LV, left ventricle; RV, right ventricle; LA, left atrium; Ao, aorta.

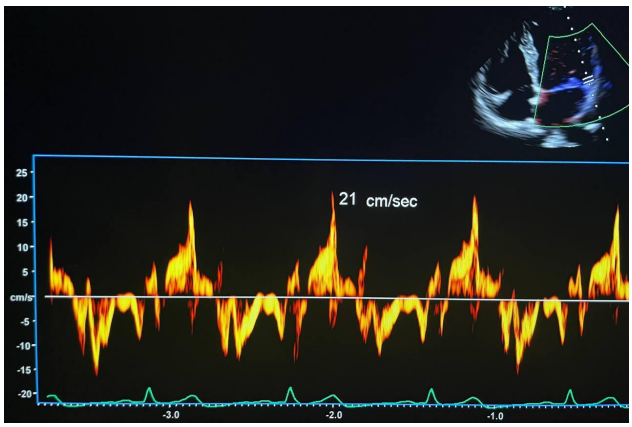

Figure 4. Tissue Doppler imaging of the lateral mitral annulus showed a prominent mid-systolic spike of 21 cm/sec suggestive of the Pickelhaube sign.

finding and is found in 2-3% of the general population[2]. It is defined as the superior displacement of the systolic mitral leaflet relative to the mitral annulus and adjacent leaflet portions. The risk of MVP-related SCD is underestimated. In individuals with MVP, the incidence of SCD is estimated to be 0.2%–0.4% per year[2]. A prospective study of Italian patients under the age of 35 found that MVP was the third most prevalent cause of cardiac arrest, after arrhythmogenic right ventricular dysplasia and coronary artery disease[3]. Although MVP is usually following a benign course, significant complications such as endocarditis and arrhythmias can be extremely troubling or even fatal[4]. A high-risk profile of MVP patients suggested by Han et al. includes being a female with a median age of 30, either physiological or psychological stress, frequent premature ventricular complexes, or ventricular arrhythmias on a Holtermonitor, and echocardiographic findings of bileaflet MVP with moderate mitral regurgitation[4]. A malignant phenotype of MVP associated with life-threatening ventricular arrhythmias even in the absence of hemodynamics compromise or significant mitral regurgitation (MR) had been noted in cumulative reports[5]. In MVP, the exact mechanism of arrhythmias is still not completely clear. Imaging modalities such as echocardiography with tissue Doppler and speckle-tracking echocardiography in addition to cardiac MRI can play a major role in understanding and exploring the mechanism of ventricular arrhythmias associated with the malignant phenotype of MVP[6]. Defining the subgroup of high-risk patients with MVP who may be at increased risk of ventricular arrhythmias and SCD remains a challenge since the prevalence of malignant MVP is modest relative to the overall large MVP population[7]. The clinical picture can be palpitations and syncope as preexistent symptoms in SCD victims. The potential risk factors of life-threatening arrhythmias and sudden cardiac death in patients with MVP should be evaluated carefully using ECG, echocardiographic findings including tissue Doppler and speckle-tracking, and late gadolinium enhancement on cardiac MRI.

Biphasic or inverted T-waves in the inferior leads of the 12-lead ECG are frequently observed in up to 83% of MVP cases with SCD[8]. However, this finding alone is not enough to identify patients at high-risk for arrhythmias. Premature ventricular contractions (PVCs) on Holter monitor are frequently seen in patients with MVP. However, PVCs alone, because of their high frequency in MVP in general, do not make a patient high risk.

Echocardiography is usually the initial imaging modality to evaluate MVP and can provide crucial information to detect high-risk patients with MVP. One of the features that may suggest malignant MVP is the myxomatous changes in the leaflets with morphological elongation and thickness which are usually associated with bileaflet prolapse[9]. The association of bileaflet MVP with several risk factors is more suggestive of patients with high risk as compared to the majority of benign bileaflet MVP. The association of the mitral regurgitation severity and ventricular arrhythmias

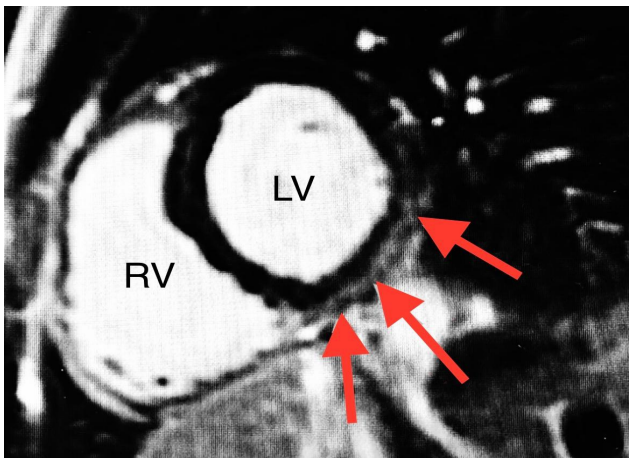

Figure 5. Late gadolinium enhancement of cardiac magnetic resonance imaging showed cardiac fibrosis on inferior and inferolateral wall of left ventricle (red arrows).
Abbreviations: RV, right ventricle; LV, left ventricle.

has been reported in patients with MVP due to chronic volume overload that may lead to the deterioration of the ventricular function which can serve as an arrhythmogenic substrate[10]. However, MVP-related SCD can occur with minimal mitral regurgitation as well[11]. An MVP-specific abnormal motion of the basal inferolateral wall, created by the interaction between the prolapsing leaflets, mitral annulus, papillary muscles, and myocardium, is called systolic curling motion. In other words, systolic curling motion mostly mirrored the excessive traction on the papillary muscles and the adjacent myocardium induced by prolapsed leaflets which can result in abnormal properties that manifest in ventricular arrhythmias[12]. This kind of systolic motion illustrates how mechanical traction plays a vital role in creating myocardial fibrosis in the papillary muscles and adjacent myocardium which can lead to ventricular ectopy and sudden cardiac arrest in MVP. A potential risk marker for malignant ventricular arrhythmias in patients with MVP is the Pickelhaube sign which is considered another form of abnormal prolapse-induced LV mechanics. Using pulse-wave tissue Doppler echocardiography, the lateral mitral annulus velocity can be measured and a spiked systolic high-velocity signal of the lateral mitral annulus ≥16 cm/s is considered significant and is known as the "Pickelhaube sign"[13]. Patients with this sign were found to have increased malignant ventricular arrhythmias and myocardial fibrosis on cardiac MRI. Another finding on echocardiography, namely, MAD, was found to have a link with life-threatening ventricular arrhythmias and SCD in patients with MVP[14]. Detection of fibrosis in the papillary muscles and inferobasal myocardium using cardiac MRI-late gadolinium enhancement in patients with MVP demonstrated a significant link with complex ventricular arrhythmias and SCD in several studies[15]. Basso et al. reported in 2015 an important observation from the Italian cardiac pathology registry where all 43 SCD victims with MVP had fibrosis of the papillary muscles whereas 88% of them had fibrosis in the inferobasal wall[16]. The combinations of several potential risk factors consequently

increase the risk of developing complex ventricular arrhythmias and SCD in patients with MVP. The subject of arrhythmias and SCD in patients with MVP can be viewed as the interaction between the presence of arrhythmogenic substrates that are now well recognized to be cardiac fibrosis and the mechanical triggers in the form of phasic traction that can trigger the substrates leading to ventricular electrical instability.

Therapeutic options have not been established yet. However, several therapeutic strategies are available. Medical strategy with beta-blockers may be considered as an ancillary therapy in malignant MVP. For patients with aborted SCD, an ICD can be utilized as secondary prevention[17] whereas only limited data is available regarding primary prevention and risk stratification. The benefit of mitral valve surgery as an option to reduce arrhythmias is likely limited in malignant MVP when fibrosis has already developed. Currently, there is no evidence base for guidelines for risk stratification or treatments.

The approach to MVP patients with a history of palpitation/syncope or asymptomatic patients with evidence of abnormal LV mechanics on echocardiography typically seen in patients with malignant MVP and myocardial fibrosis on cardiac MRI starts with prolonged ECG monitoring for arrhythmias. If sustained ventricular tachycardia or ventricular fibrillation is detected, then therapeutic measures similar to those for patients with sudden cardiac arrest should be considered. If monitoring shows frequent and/or complex ventricular ectopic activity, and there is echocardiographic evidence of abnormal papillary muscle or myocardial mechanics and/or myocardial fibrosis on cardiac MRI, then interventions can also be considered based on a higher predicted risk of malignant MVP.

CONCLUSIONS

Ventricular arrhythmias and cardiac arrest can be the first manifestation of malignant MVP. MVP is not always a benign condition, and physicians should be aware of the diagnostic criteria for malignant MVP.

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