Case Report

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Future CARDIOLOGY

How many clues make an evidence? An unusual case of aborted cardiac arrest due to mitral valve prolapse

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There is an increasing awareness on the association between mitral valve prolapse (MVP) and sudden cardiac death. Mitral annular disjunction (MAD) is a phenotypic risk feature that can help in risk stratification. We present a case of a 58-year-old woman who experienced an out-of-hospital cardiac arrest caused by ventricular fibrillation interrupted by a direct current-shock. No coronary lesions were documented. Echocardiogram showed myxomatous MVP. Nonsustained ventricular tachycardia have been registered during hospital stay. Interestingly, cardiac magnetic resonance revealed MAD and a late gadolinium enhancement area in inferior wall. Finally, a defibrillator has been implanted. For arrhythmic risk stratification of MVP with MAD, multimodality imaging is the diagnostic tool to find out the disease behind many cardiac arrests of unknown cause.

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Presentation of the case: setting/history patient details

We report an unusual case of a 58-year-old woman who experienced, in an out-of-hospital setting, a sudden cardiac arrest caused by ventricular fibrillation (VF). Cardiopulmonary resuscitation was promptly performed by the emergency team and VF interrupted after four shocks by external semiautomatic defibrillator. The patient had a known history of mild hypertension, a high burden of monomorphic isolated premature ventricular complex (PVC) in treatment with sotalol (80 mg/b.i.d) and a known mitral valve prolapse with moderate regurgitation and normal ejection fraction (no data on PVC morphology available). In the last few months, she was complaining about worsening of palpitations, but the 24 h ECG Holter monitoring performed in that occasion only showed rare supraventricular ectopic beats. No other symptoms were reported before the event.

Initial diagnosis/assessment

On admission at intensive care unit, she denied chest pain and/or dyspnea, serum electrolytes were in range and 12-leads ECG reported sinus rhythm, low QRS voltages in limb leads and negative T waves in inferior leads (Figure 1). Lab tests revealed a moderate increase of high-sensitivity troponin I, probably due to VF and multiple DC-shocks. Inflammatory markers were in normal range and she neglected any phlogistic episodes in the previous days. Anyway, early angiography was performed, but no critical coronary artery stenosis were found. Transthoracic echocardiogram documented a bileaflet myxomatous mitral valve prolapse (MVP) with moderate regurgitation characterized by mid-end systolic regurgitant jet; normal biventricular systolic function was detected (Figure 2).

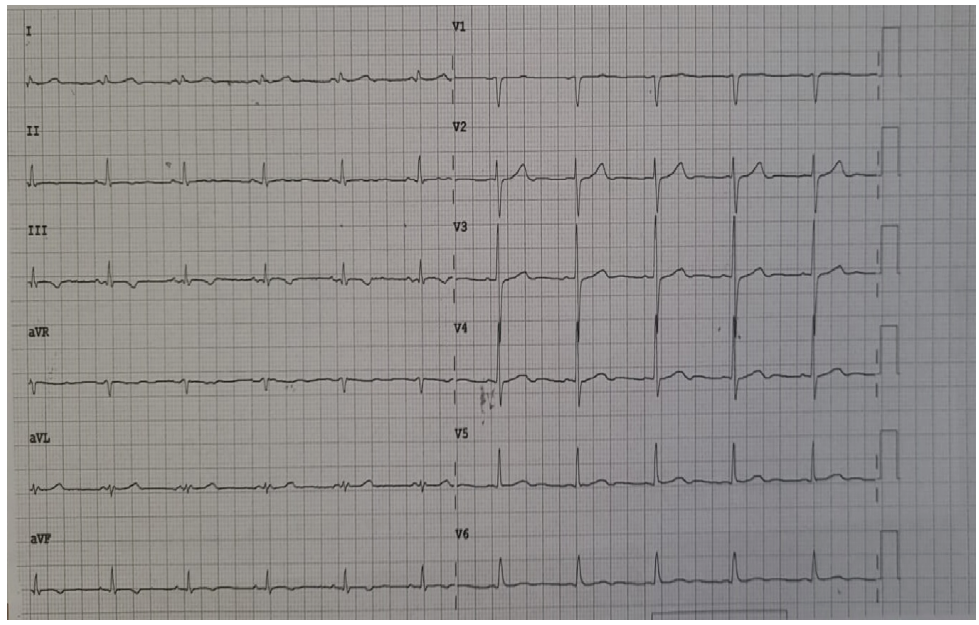

Figure 1. Basal 12-leads electrocardiogram. Sinus rhythm at 65/bpm, low QRS voltage in limb leads and negative T wave in inferior leads.

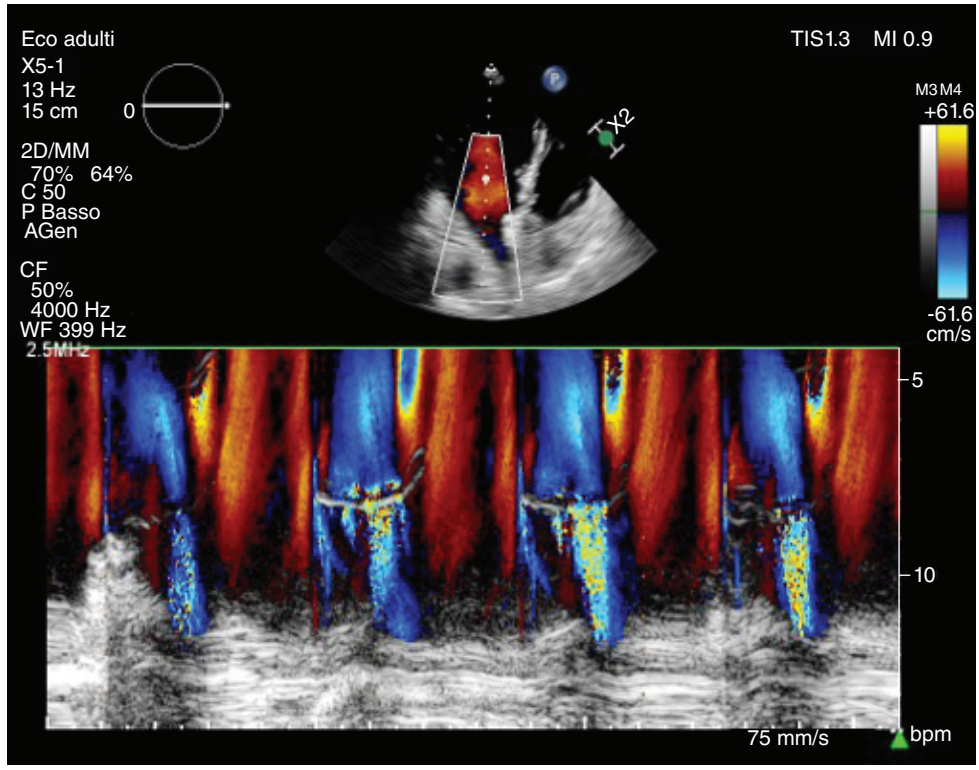

Figure 2. Two-dimensional transthoracic echocardiography. Parasternal long-axis view: color Doppler M-Mode frame shows an end-systolic regurgitation due to mitral bileaflet prolapse.

Frequent episodes of nonsustained ventricular tachycardia with right bundle branch block morphology and superior axis were registered at monitor.

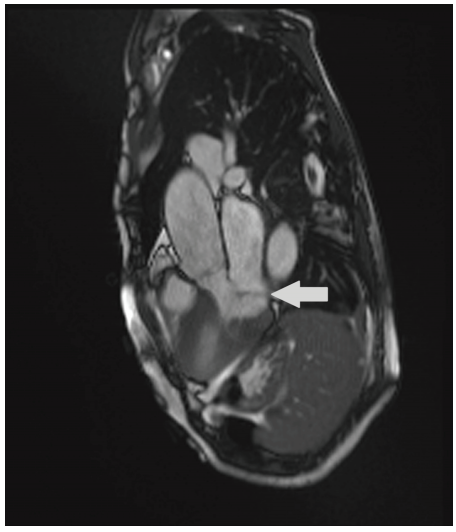

Figure 3. Cardiac magnetic resonance, steady-state free procession sequence. In this 3-chamber view mitral annular disjunction is clearly visible (white-filled arrow).

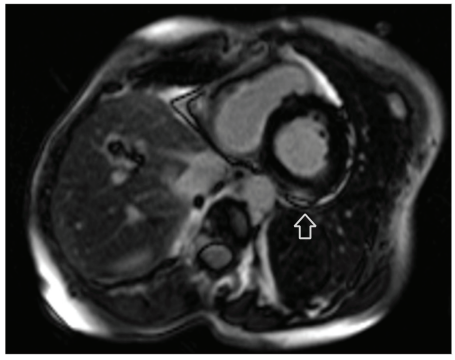

Figure 4. Cardiac magnetic resonance, contrast enhanced sequence. Nonischemic-late gadolinium enhancement (black and white arrow) could be seen in the inferobasal left ventricular wall in this short axis view.

Management & treatment

A myocardial infarction with nonobstructive coronary arteries (MINOCA) diagnosis was initially suspected [1]. Conversely, acute coronary syndrome was ruled out as well as cardiomyopathies. Myocarditis was clinically unlikely. To deeply investigate, cardiac magnetic resonance (CMR) imaging was performed after 2 days. CMR confirmed the normal biventricular volumes and systolic function, and, surprisingly, revealed the presence of mitral annular disjunction (MAD) (measuring 4 mm in three chamber view) with systolic curling of the posterior leaflet and moderate mitral regurgitation (Figure 3). No myocardial edema was found (normal T2 mapping) but interestingly there was a focal increase of T1 mapping values in inferior basal wall, and in the same area, a nonischemic pattern of late gadolinium enhancement (LGE) was described (Figure 4) [2]. The fundamental role of CMR exam in order to make diagnosis was clear. The presence of many clues (Barlow's disease together with negative inferior T waves, MAD with systolic curling, and inferior nonischemic LGE) built evidence: a diagnosis of aborted cardiac arrest due to malignant arrhythmic mitral valve prolapse with MAD and LGE was made [3]. Finally, a bicameral defibrillator (RESONATE™ EL ICD, Boston Scientific, MA, USA) was implanted for secondary prevention and the patient was discharged with bisoprolol 2.5 mg/daily. No events have happened so far and patient remained asymptomatic for palpitations.

Discussion & implications

Coronary artery disease represents the first diagnostic hypothesis of an arrhythmic cardiac arrest in patients with moderate-to-high cardiovascular risk factors [4]. Nondiagnostic angiogram, female sex and patient age (under 65 years old) led to high MINOCA suspicion [2]. Our patient had a known history of palpitation and high burden PVCs for which she took only medical therapy without further previous investigation of any possible cause. This clinical case focuses on the rare clinical onset with VF in a patient with Barlow's disease and MAD as the only 'evident cardiomyopathy'. Possible alternative diagnoses were easily excluded: no myocarditis 'red flags' (no symptoms of systemic inflammation, no increase of C reactive protein) and low Tako–Tsubo syndrome probability (because

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of the absence of some typical signs like ventricular disfunction with apical ballooning, prolonged QT interval, psychophysical stressors and low INTERTAK diagnostic score) [5]. Coronary vasospasm or microvascular disease were unlikely; but to exclude any possibility of ischemic origin, CMR was performed. Nowadays CMR is considered as a 'noninvasive histological analysis' because it is the only technique that can look deeply into the myocardial tissue giving a fundamental characterization of the type of damage occurred. In our case, CMR represented the last (but not the least) clue that focused attention on the real structural abnormality (the presence of MAD) that allowed us to make the correct diagnosis. MAD and a LGE with nonischemic pattern in a specific area (inferior wall) represented two sides of the same coin. Thus, as A Christie says: "*one coincidence is just a coincidence, two coincidences are a clue, three coincidences are a proof*", diagnosis of arrhythmic valve prolapse (AMVP) was made [2].

Mitral valve prolapse, with annulus disjunction and systolic curling of the ventricular wall, increase wall stress and progressively lead to a fibrotic substitution of the myocardial wall. This evolutive process increases the probability of malignant arrhythmias originating from the fibrotic areas in the inferolateral basal wall or into papillary muscles [3].

In this setting, CMR imaging turns out a promising tool for arrhythmic risk stratification: maybe it is time to consider MVP with LGE a novel form of 'scar-related' cardiomyopathy and, in this regard, as well as in other cardiomyopathies with a scar substrate, we have to pay attention to the administration of antiarrhythmic drugs because of their possible proarrhythmic effect in this subset of patients. Our patient, indeed, was taking a low dose of sotalol when she experienced sudden cardiac death (SCD).

The AMVP is a well-known phenomenon and a rare cause of SCD, but risk stratification of affected patients is still challenging. The association of AMVP and MAD is described in literature in different studies, but we still do not know if MAD itself could represent a proarrhythmic feature, in association with mitral valve prolapse or not. Only a recent Swedish study spoke about a 'mitral annular disjunction arrhythmic syndrome' indicating an independent role of MAD in causing SCD [6]. Noteworthy, literature does actually not exclude the possibility to consider mitral annular disjunction as a congenital malformation because in some cases it is found in young patients without mitral valve prolapse. This abnormal conformation could be progressive in time due to the shear stress onto the myocardial wall and it could have in itself arrhythmic consequences [3].

Screening for AMVP is challenging as well because of the lack of prospective outcome data and the lack of recommendations for rhythm monitoring in current valvular European guidelines [7]. Expert consensus suggest that MVP patient should be screened for SCD risk with accurate personal history, 12-leads ECG, Holter monitoring and detailed echocardiography [8] but, even if no pathological arrhythmic or echocardiographic findings are present, when the clinical suspicious of arrhythmia is strong (just like in our case report), we suggest to not stop. In this case there was an important clue suggesting an underling disease: abnormal 12 lead ECG. This simple and inexpensive exam must always carefully evaluated given its key role in suggesting the presence of some cardiomyopathy, especially the scar-related ones [9]. Performing CMR in order to find some risk features, like the presence of MAD and/or a nonischemic pattern of LGE in specific areas, could be very useful and make the difference. Its high sensitivity spatial resolution, higher than echocardiography, led us to find MAD, otherwise not visible. Moreover, the presence of some phenotypic risk features, like negative T waves in inferior leads, polymorphic nonsustained ventricular tachycardia (NSVT), MAD and LGE should suggest close follow-up or, in some cases, loop recorder implantation. PVCs type and morphology are important too: right bundle branch block with superior axis morphology originating from the inferolateral ventricular wall, short coupling (<300 ms) and fast NSVT (<250 ms coupling) require more attention as they are associated to high-risk arrhythmias profiles [4,10]. Furthermore, European Heart Rhythm Association (EHRA) experts consensus suggests to consider the option of an implantable cardioverter defibrillator (ICD) if there is an AMVP patient with history of unexplained syncope and NSVT, likely arising from the mitral apparatus [8]. But syncope, in this clinical setting, should already be considered a serious and advanced event (surrogate for aborted sudden cardiac death), as in other contexts (e.g., Brugada syndrome, long QT syndrome, etc.). Thus, the real bet for the future is to have the tools for a reliable risk stratification before syncope and give adequate primary prevention. Scores taking into account clinical and instrumental parameters – such as those set out above and over all the CMR data – could be helpful.

In our case we chose a bicameral ICD because of the patients turned out to be bradycardic at monitor but at the same time she needed beta-blocker administration for supraventricular and ventricular nonsustained tachycardias and her history of palpitation and PVCs.

Conclusion

This clinical case suggests that there is an impelling necessity to better screen and evaluate this category of 'misunderstood' patients. We suggest a step-by-step approach that can help us to make as first a correct diagnosis and then to examine properly the arrhythmic risk. In our case, an ICD implantation was recommended for secondary prevention after VF, but, for primary prevention, we still do not have any guidelines. So, it is advisable to take advantage of multimodality techniques and identify the phenotypic risk features in order to avoid a malignant cardiac event with early ICD implantation. Our case contributes to adding to the literature regarding the clinical and instrumental characteristics of patients with mitral valve prolapse and SCD.

Executive summary

- There is a defined association between mitral valve prolapse and sudden cardiac death.
- Mitral anulus disjunction (MAD) is often associated with Barlow's disease and is considered a phenotypic risk feature.
- Mitral valve prolapse with MAD and systolic curling lead to a progressive fibrotic substitution of myocardial wall, increasing the probability of malignant arrhythmias.
- Cardiac magnetic resonance is a promising diagnostic tool for arrhythmic risk stratification.
- The presence of late gadolinium enhancement lead us to consider mitral valve prolapse and MAD as a novel form of 'scar-related' cardiomyopathy.
- Risk stratification is still challenging, red flags such as a clinical history of syncope, ventricular arrhythmias at Holter monitoring and late gadolinium enhancement finding, require more attention.

Author contributions

Writing original draft: AG Robles, L Piscitelli and R Costantino; Conceptualization: AG Robles and DRR Chieppa; Imaging curation: DRR Chieppa, V Forte and AI Guaricci; Critical review: S Romano and L Sciarra; Supervision: F Bartolomucci, M Zingaro and I Rosa.

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Informed consent disclosure

The patient gave informed consent to the anonymous use of their clinical data for scientific purposes.

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