Who is the guilty among these two silent killers?

Bortolo Martini, MD,* Claudio Zolla, MD,* Francesco Guglielmi, MD,* Gian Luca Toffanin, MD,* Sergio Cannas, MD,* Nicolò Martini,† Rocco Arancio, MD*

*From the *Cardiac Unit, Santorso Hospital, Santorso, Italy, and †Ferrara Medical School, Ferrara, Italy.*

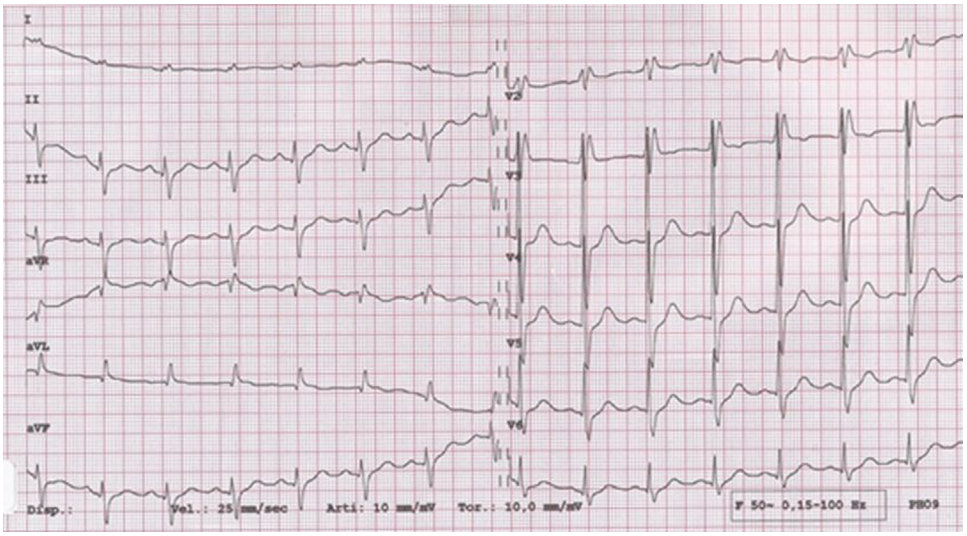

Figure 1 Electrocardiogram taken just after cardiac defibrillation. The traces show sinus rhythm and a resemblance to a type 1 pattern.

Introduction

Aborted sudden cardiac death (SCD) occurred in a previously asymptomatic 58-year-old woman with mitral valve prolapse. Electrocardiogram (ECG) soon after defibrillation and after flecainide challenge was consistent with type 1 Brugada pattern. Contrast magnetic resonance imaging (MRI) study of the left ventricle showed a delayed enhancement (suggesting fibrosis) of the inferior-basal left ventricular wall at the insertion of the posterior papillary muscle. Two lethal conditions, never reported before to occur together, affected this patient.

Case report

A 58-year-old woman suffered cardiac arrest while serving a client at her shop. Resuscitation maneuvers were performed by a friend and ventricular fibrillation was documented and promptly terminated by a DC shock delivered by a mobile emergency medical unit. After a brief period of atrial fibrillation, sinus rhythm spontaneously resumed and a 12-lead ECG showed a transient late coved wave in V_1-V_2 (Figure 1). The patient was treated with hypothermia (33°C) for 2 days and totally recovered. The ECG showed some minor late coved wave during cooling and returned to a persistent normal pattern after warming. A flecainide challenge test (2 mg/kg injected over 10 minutes) was performed 5 days after the aborted cardiac arrest and resulted in a Brugada type 1 ECG pattern with late QRS fragmentation in V_1 but no S wave in lead 1 (Figure 2). The patient's past history revealed a diagnosis of mitral valve prolapse (MVP) at 21 years of age with curling and moderate regurgitation, yearly normal ECGs, and the presence of late potentials during signal-averaged ECG. There was no history of syncope or significant ventricular arrhythmias on repeated Holter monitoring: only isolated ventricular premature contractions (VPCs), of both right bundle branch block and left bundle branch block morphology, could be determined. The patient's mother also suffered from MVP with significant mitral regurgitation, for which she underwent surgical repair at age 78. There was no family history of SCD or abnormal ECG patterns. Myocarditis and different channelopathies

KEYWORDS Ventricular fibrillation; Brugada syndrome; Mitral valve prolapse; Sudden cardiac death; Channelopathies; Arrhythmogenic right ventricular dysplasia/cardiomyopathy
(Heart Rhythm Case Reports 2017;3:33–35)

Address reprint requests and correspondence: Dr Bortolo Martini, Cardiac Unit, Santorso Hospital, Via Garziere 42, 36014 Santorso (Vicenza), Italy. E-mail address: bortolo.martini@gmail.com.

http://dx.doi.org/10.1016/j.hrcr.2016.08.013

KEY TEACHING POINTS

- Ventricular fibrillation can be due to Brugada syndrome and to mitral valve prolapse.
- An association of the 2 syndromes in the same patient is exceptional.
- Probably 1 of the conditions is an incidentaloma.

were excluded, as well as short-coupled torsades de pointes. The patient underwent comprehensive cardiac workup, as per our protocol in similar cases, which is devoted to investigating latent structural heart disease. At cardiac angiography no significant structural or wall motion abnormalities of either ventricle were detected, in particular arrhythmogenic cardiomyopathy. Only a slight derangement of the trabecular pattern was noted. The right ventricular outflow tract was normal. A patchy fibrosis of the inferobasal wall of the left ventricle, at the insertion of the papillary muscle, was ascertained by contrast-enhanced cardiac MRI (Figure 3). The patient was successfully implanted with a subcutaneous implantable cardioverter-defibrillator (ICD). Genetic studies are currently pending. Considering the absence of any familial history of ECG feature, we do not expect any new information from this study. No arrhythmias have recurred during a follow-up of 3 months after ICD implantation.

Discussion

This healthy and previously asymptomatic woman could have died because of Brugada syndrome (BrS)[1] or malignant MVP.[2] As MVP prevalence reaches 3% in the general population it is difficult to exclude a chance association, and recent data identify a subgroup of patients with ECG and fibrotic changes at high risk of SCD.[2] The estimated rate of SCD in MVP ranges from 0.2% to 0.4%/year.[2] Some controversy exists on the rate of SCD in BrS, as most of the patients have not a true syndrome but an asymptomatic ECG abnormality, either spontaneous or drug induced.[3] In this latter group, an annual rate of 0.5%, higher in those with a spontaneous type 1 ECG, was reported.[4] An organic cardiac structural heart disease is nowadays considered a substrate in both situations, although it was initially debated in BrS.[5,6] In malignant MVP localized fibrosis is present at the inferobasal portion of the left ventricular wall where early electrophysiological studies demonstrated the most common site of origin of ventricular premature beats.[7] In BrS a localized fibrosis of the right ventricular outflow tract, which induces conduction disturbances and possibly also some repolarization abnormalities, is assumed to be responsible for the lethal arrhythmias.[8] The origin of this common histologic abnormality could be the excessive traction on the papillary muscle by the MVP[2] and some acquired genetic or embryologic abnormality in BrS.[9] In our patient both electrical and structural abnormalities were present. There are several arguments suggesting MVP as the cause of the event: (1) female sex; (2) significant MVP with "curling" and fibrosis of the inferior left ventricle at MRI; (3) isolated VPCs mostly of right bundle branch block morphology; (4) family history of severe MVP. Against this hypothesis the patient's ECG did not show marked repolarization changes in the inferior leads. In contrast, several arguments support the diagnosis of BrS: (1) according to Sacher,[10] age and the absence of spontaneous ECG pattern; (2) similar ECG pattern soon after resuscitation, and type 1 after flecainide test, with a marked

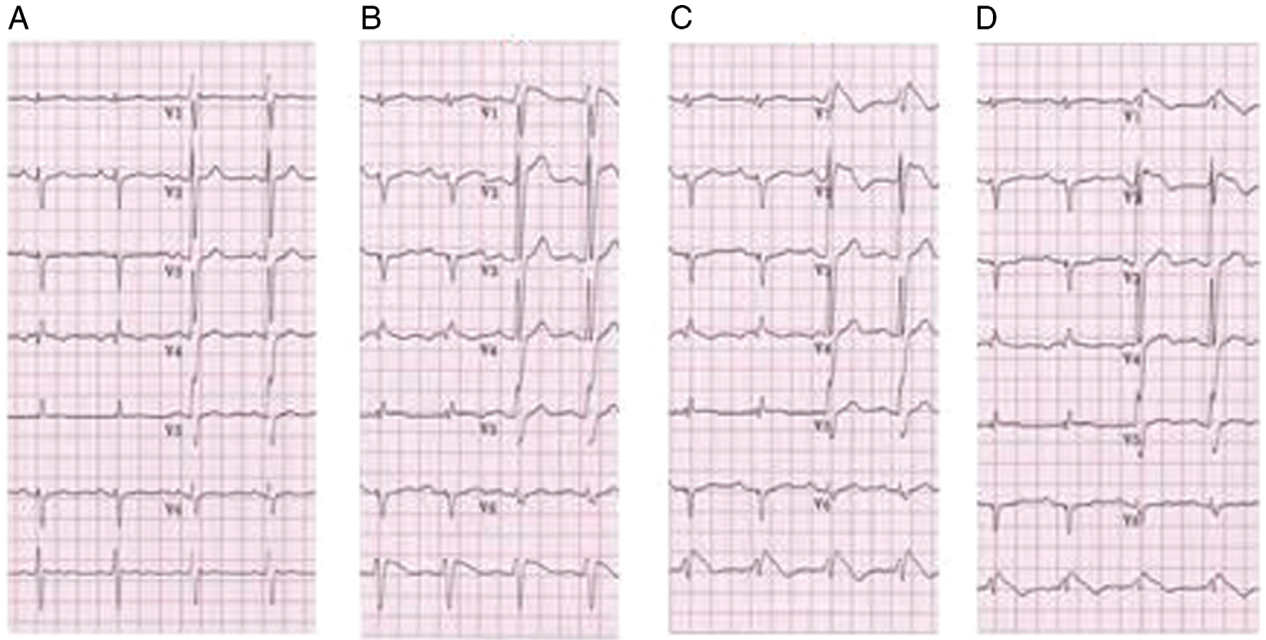

Figure 2 Flecainide challenge. **a:** At baseline electrocardiogram (ECG) with right precordial leads V_1-V_2 placed at the fourth intercostal space. Marked left axis deviation is present, but not type 1 ECG. **b:** After flecainide a type 1 ECG is present with some late QRS fragmentation. **c:** After flecainide with V_1-V_2 placed at the third intercostal space. **d:** After flecainide with V_1-V_2 placed at the second intercostal space.

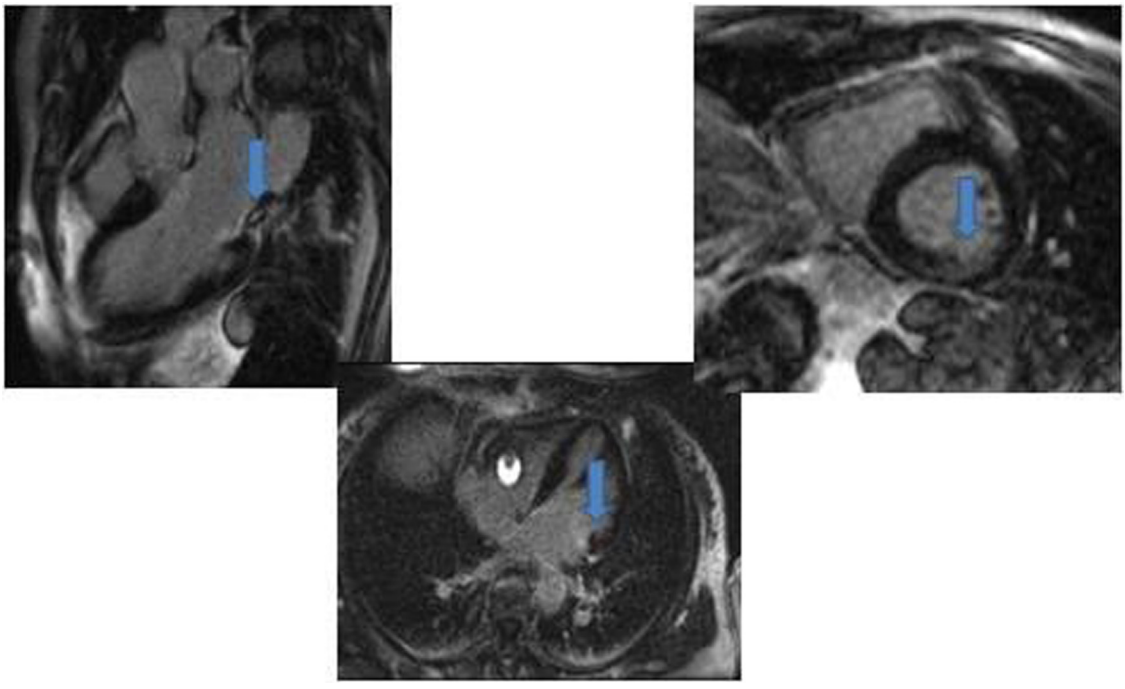

Figure 3 Contrast magnetic resonance imaging study of the left ventricle: delayed enhancement (suggesting fibrosis) of the inferior-basal left ventricular wall at the insertion of the posterior papillary muscle (*arrow*).

late coved wave in V_1; (3) positive late potentials; (4) some derangement of right ventricular trabecular pattern at angiography; (5) occurrence of ventricular fibrillation during normal activities; (6) isolated VPCs of left bundle branch block morphology at Holter monitoring.

In our opinion, it is actually impossible to establish what is the true cause of this aborted case of sudden death and what could be an alternative therapeutic approach.[11,12] In general most patients with an inducible Brugada pattern receive an ICD at that point, and do not have further investigations, which in our experience are still necessary to better understand these rare conditions.

Conclusion

SCD is always linked to a lethal electrical abnormality with both organic and functional components. When, unfortunately, not 1 but 2 rare and lethal situations coexist, it is difficult even for expert specialists to determine which is the killer and which is the silent bystander.

Acknowledgments

We thank Professor Bernard Belhassen from the Tel-Aviv Sourasky Medical Center for his helpful comments and critical reading of our manuscript.

Appendix

Supplementary data

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.hrcr.2016.08.013.

References

1. Havakuk O, Viskin S. A tale of two diseases. J Am Coll Cardiol 2016;67:100–108.
2. Basso C, Perazzolo Marra M, Rizzo S, et al. Arrhythmic mitral valve prolapse and sudden cardiac death. Circulation 2015;132:556–566.
3. Martini B. Brugada syndrome is not an ECG. Heart Rhythm 2016 Sep;13(9):e292.
4. Sieira J, Ciconte G, Conte G, et al. Asymptomatic Brugada syndrome: clinical characterization and long term prognosis. Circ Arrhythm Electrophysiol 2015;8:1144–1150.
5. Martini B, Nava A, Thiene G, Canciani B, Scognamiglio R, Daliento L, Dalla Volta S. Ventricular fibrillation without apparent heart disease: description of six cases. Am Heart J 1989;118:1203–1209.
6. Brugada P, Brugada J. Right bundle branch block, persistent ST segment elevation and sudden cardiac death: a distinct clinical and electrocardiographic syndrome. J Am Coll Cardiol 1992;20:1391–1396.
7. Lichstein E. Site of origin of ventricular premature beats in patients with mitral valve prolapse. Am Heart J 1980;100:450–457.
8. Ten Sande JN, Coronel R, Conrath CE, Driessen AH, De Groot JR, Tan HL, Nademanee K, Wilde AA, de Bakker JM, van Dessel PF. ST-segment elevation and fractionated electrograms in Brugada syndrome patients arise from the same structurally abnormal subepicardial RVOT area but have a different mechanism. Circ Arrhythm Electrophysiol 2015;8:1382–1392.
9. Brugada P. Brugada syndrome: more than 20 years of scientific excitement. J Cardiol 2016;67:215–220.
10. Sacher F, Meregalli P, Veltmann C, et al. Are women with severely symptomatic Brugada syndrome different from men? J Cardiovasc Electrophysiol 2008;19:1181–1185.
11. Brugada J, Pappone C, Berruezo A, Vicedomini G, Manguso F, Ciconte G, Giannelli L, Santinelli V. Brugada syndrome phenotype elimination by epicardial substrate ablation. Circ Arrhythm Electrophysiol 2015;8:1373–1381.
12. Syed FF, Ackerman MJ, McLeod CJ, Kapa S, Mulpuru SK, Sriram CS, Cannon BC, Asirvatham SJ, Noseworthy PA. Sites of successful ventricular fibrillation ablation in bileaflet mitral valve prolapse syndrome. Circ Arrhythm Electrophysiol 2016;9:e00400510, http://dx.doi.org/10.1161/CIRCEP.116.004005.