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CASE REPORT
Arrhythmias/Electrophysiology

Brugada syndrome in a young patient with type 1 myotonic dystrophy requiring an implantable cardioverter defibrillator for primary prevention: a case report

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Background Cardiac electrical disturbances represent the most frequent cardiac manifestations of myotonic dystrophy Type 1 (MD1). Limited data suggest that the prevalence of Brugada syndrome in MD1 may be increased compared to the general population.

Case summary We report a case of a 22-year-old asymptomatic man with repolarization abnormalities in leads V1–V3 suggestive of Type III Brugada pattern. The patient had a family history of MD and incidents of sudden death in relatives. Drug-induced Brugada Type 1 syndrome was revealed after procainamide challenge. A ventricular stimulation study was positive since a polymorphic ventricular tachycardia was induced after two extrastimuli. The patient underwent implantation of a single chamber cardiac defibrillator (ICD). Eight months after the procedure he suffered an appropriate ICD shock due to rapid polymorphic ventricular tachycardia.

Discussion Brugada syndrome is linked with MD1. Potential life-threatening arrhythmias may develop in the adult life of MD1 patients. Electrocardiographic surveillance and tailored invasive treatment with ICDs can prevent sudden cardiac death in this setting.

Keywords Brugada syndrome • Myotonic dystrophy • Implantable cardioverter defibrillator • Ventricular stimulation study • Case report

Learning points

- Conduction disturbances, atrial fibrillation, and tachyarrhythmias may develop in the adult life of myotonic dystrophy 1 patients.
- The prevalence of Brugada syndrome in myotonic dystrophy 1 may be increased compared to the general population.
- Implantable cardioverter defibrillator therapy guided by electrophysiologic evaluation can prevent sudden cardiac death in this setting.

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Introduction

Brugada syndrome (BS) is a primary arrhythmic disorder associated with an increased risk for ventricular fibrillation and sudden cardiac death (SCD).[1] The only treatment that has a proven efficacy in reducing the risk of SCD in BS is the implantable cardioverter defibrillator (ICD).[1] Considerable controversy still exists about the prognostic value of electrophysiological study (EPS) as a tool for SCD risk stratification in BS.[2,3]

Muscular dystrophies are a group of inherited diseases affecting skeletal and cardiac muscle. Cardiac involvement occurs as a degenerative process and the most frequent manifestations are dilated cardiomyopathy and arrhythmias.[4] The myotonic dystrophies (Type 1 and 2, MD) represent a subset of inherited muscular dystrophies. Cardiac electrical disturbances such as atrioventricular conduction blocks, sinus node dysfunction, atrial fibrillation, and ventricular tachyarrhythmias represent the most frequent cardiac manifestations of MD1 and seem to have significant impact on clinical outcomes given that up to one in three of patients die suddenly.[4]

Timeline

Day	Events
1	The patient referred for evaluation from the Department of Neurology. His electrocardiogram (ECG) showing repolarization abnormalities with mild ST elevation in V1–V3 leads suggestive of Type 3 Brugada pattern
2	An echocardiographic examination was significant only for a mild prolapse of the anterior mitral valve leaflet without any significant regurgitation
3	A procainamide provocation test for Brugada syndrome was performed and at the end of the test the ECG changed towards a typical Type 1 Brugada pattern
7	The ventricular stimulation study was performed and polymorphic ventricular tachycardia/ventricular fibrillation was induced with two extrastimuli in the right ventricular apex
20	A single chamber implantable cardioverter defibrillator (ICD) was implanted to the patient for primary prevention of sudden cardiac death
20 + 8 months	The patient suffered an appropriate ICD shock due to rapid polymorphic ventricular tachycardia

Case presentation

A 22-year-old man was referred from the neurology department due to transient sinus bradycardia during his admission for fever and transient loss of orientation in time and place. The patient was suspected to suffer from a central nervous system infection but this was not actually proven from the subsequent investigation in the neurology department. The patient's personal medical history was unremarkable of any known condition although it was evident that he had some kind of mild mental retardation. No history of syncope or presyncope was evident. He had a known family history of MD (mother and grandfather), while three incidents of sudden death at young ages (23-, 40-, and 42-year-old subjects) in mother's relatives were also reported (they had no established diagnosis of a specific disease). Physical examination did not reveal any abnormal finding while the patient was afebrile. Systemic arterial blood pressure was 105/68 mmHg, heart rate at rest 62 b.p.m., and arterial oxygen saturation 98%. On heart auscultation normal rhythmic heart sounds without any heart murmurs were evident and no increased central venous pressure was found. Lung auscultation revealed no abnormal sounds while no peripheral oedema was present. Neurological and opthalmological examination was reported to be normal at that moment. Surface electrocardiogram (ECG) (*Figure 1A*), while the patient was afebrile, showed normal sinus rhythm without any conduction abnormalities while repolarization abnormalities with mild ST elevation in V1–V2 leads suggestive of Type 3 Brugada ECG pattern were present (*Figure 1A*). An echocardiographic examination showed normal dimensions and contractility of both ventricles without signs of hypertrophy. No signs of diastolic dysfunction were evident. A mild prolapse of the anterior mitral valve leaflet was noted without any significant regurgitation.

A procainamide provocation test for BS was performed (10 mg/kg i.v. infusion of procainamide over 10 min) and at the end of the test the ECG changed towards a typical Type 1 Brugada pattern (*Figure 1B*). After a thorough discussion with the patient and his family an EPS was suggested for further arrhythmic risk stratification mainly due to his family history of sudden death incidents. The ventricular stimulation study was performed and polymorphic ventricular tachycardia/ventricular fibrillation was induced at a drive train cycle length of 400 ms and two extrastimuli (S1–S2: 240 ms, S2–S3: 260 ms) in the right ventricular apex (*Figure 2*). All other measurements of the electrophysiologic study were within normal limits. The patient was screened for MD and following an extensive clinical and laboratory investigation including electromyography he was finally diagnosed with MD1, while a genetic testing for MD confirmed the diagnosis. Subsequently, a single chamber ICD was implanted to the patient for primary prevention of SCD. Subcutaneous ICD was excluded based on the high incidence of conduction disorders in the life of MD patients. No antiarrhythmic medication was started throughout the course of the diagnostic evaluation of the patients or the follow-up period. Family screening for MD and BS was also performed and revealed that his brother is suffering from MD without evidence of Brugada pattern on ECG. Of note, 8 months after the procedure the patient suffered an appropriate ICD shock due to rapid polymorphic ventricular tachycardia (*Figure 3*). A pedigree chart is depicted in *Figure 4*.

Discussion

Patients with MD1 have a high prevalence of both electrical and structural abnormalities with infra-Hisian block being the main contributor to SCD. Asymptomatic patients with MD1 may have cardiac involvement that may be masked by their muscular disability and

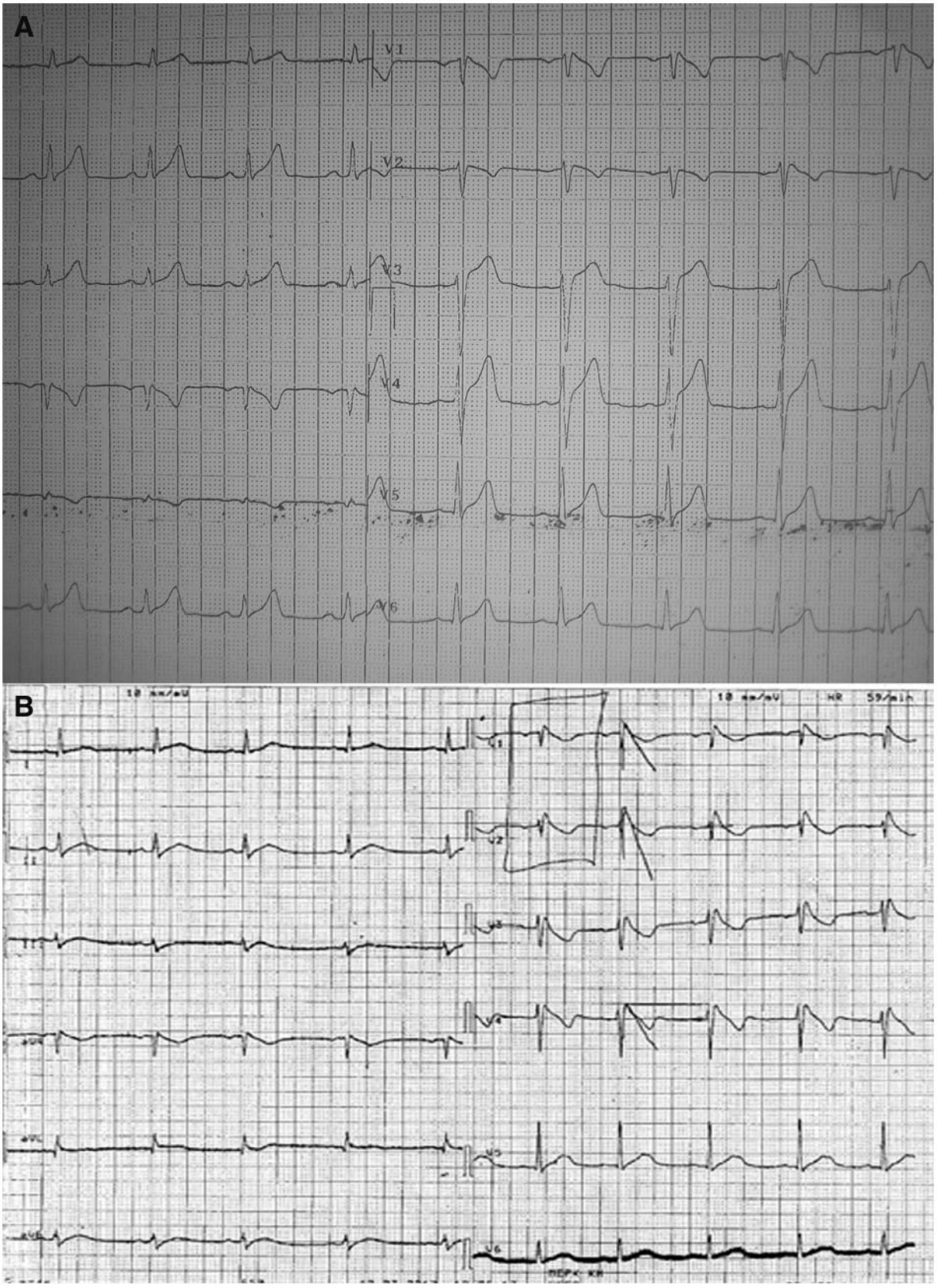

Figure 1 Electrocardiogram of the patient (*A*) at baseline showing concave ST elevations <2 mm and negative T waves in leads V1–V2 and (*B*) at the end of procainamide infusion showing Brugada Type 1 pattern in right high precordial leads.

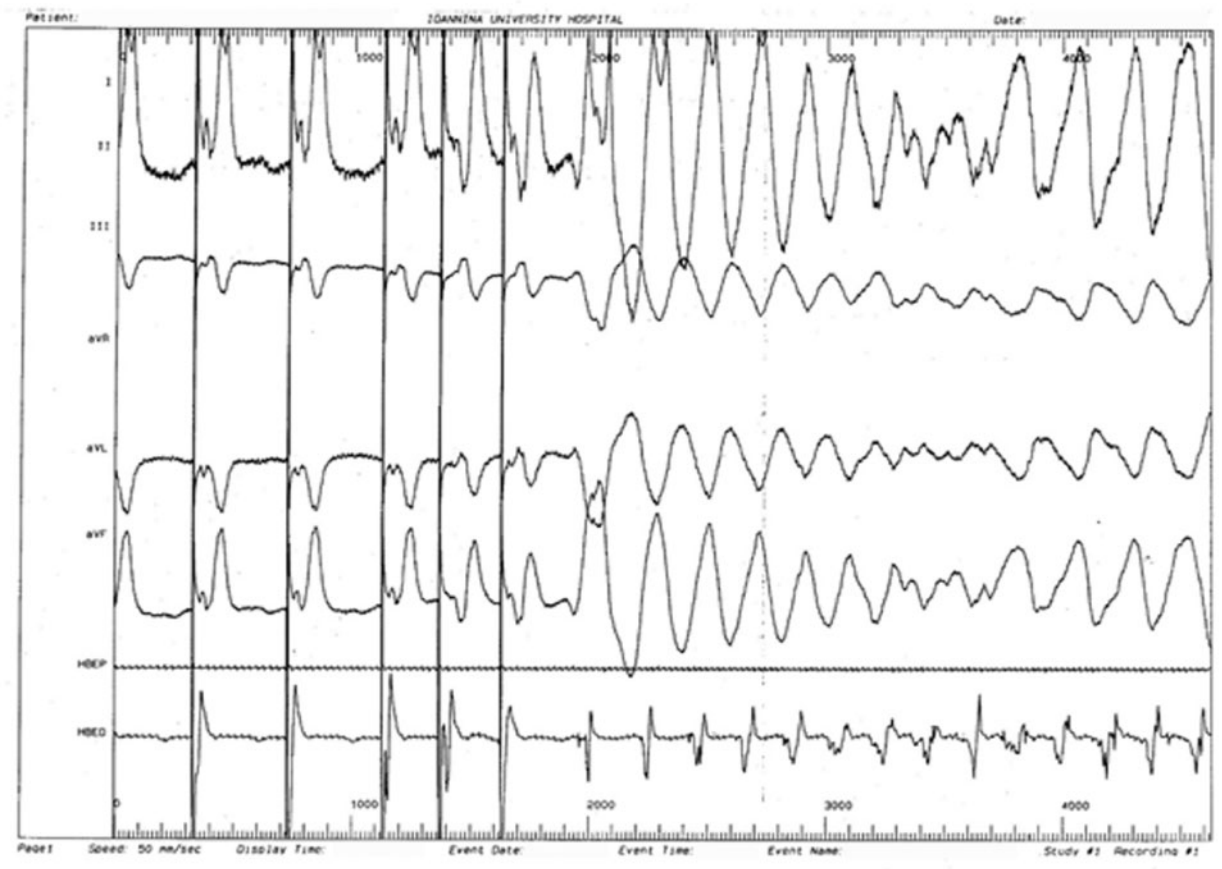

Figure 2 Ventricular stimulation study showing provocation of polymorphic ventricular tachycardia after application of two extrastimuli.

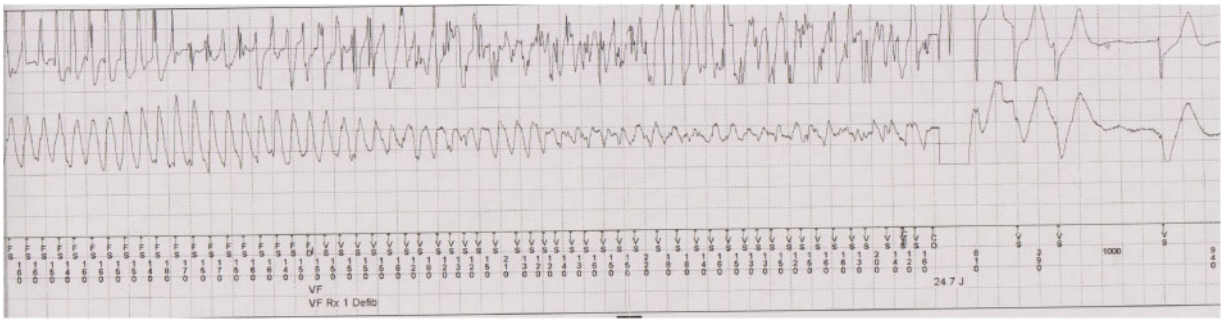

Figure 3 Device interrogation showing the episode of polymorphic ventricular tachycardia (VT)/ventricular fibrillation (VF) and the appropriate shock.

reduced exercise capacity. Conduction disturbances affect roughly 30–75% of MD1 patients and are a result of fibrosis, focal fatty infiltration, and also lymphocytic infiltration.[4] Prolongation of the PR interval occurs in 20–40% of patients and QRS widening in 5–25% of patients. These conduction abnormalities frequently progress to symptomatic AV block and necessitate pacemaker implantation. Electrocardiographic and electrophysiological criteria that identify patients needing device implantation have been proposed. Specifically, those with a PR interval >240 ms, a QRS wider than 120 and/or HV ≥70 ms are at higher risk of SCD.[4] Despite pacing therapies, patients with MD continue to die suddenly probably due to the occurrence of ventricular tachyarrhythmias.[4] Based on these

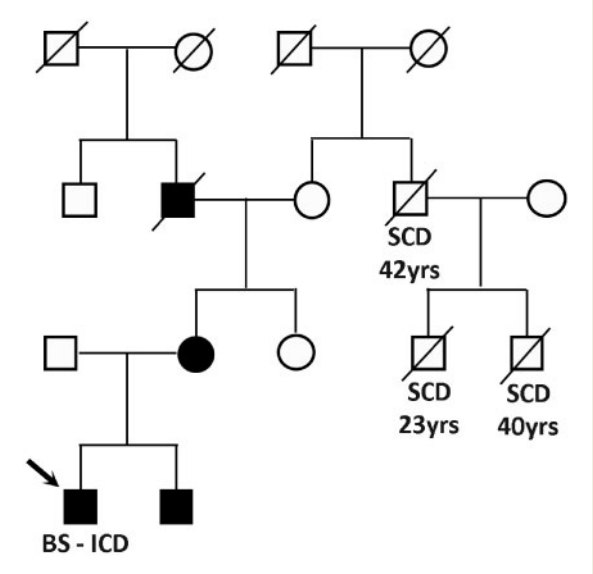

Figure 4 The pedigree chart of the patient's family. Bold black indicates the diagnosis of myotonic dystrophy. The patient with Brugada syndrome who implanted a defibrillator is indicated by the arrow.

assumptions, whenever an indication for a permanent pacemaker has been established in MD1 patients the need for an ICD may be further considered (Class IIb, level of evidence B indication according to ESC Practice Guidelines).[5] Arrhythmias often develop later in the course of disease in the adult life. However, since early treatment can be effective in preventing the occurrence of SCD, surveillance for arrhythmias should start earlier in patient's life.[4]

It has been previously reported that the prevalence of spontaneous Type 1 Brugada ECG pattern in MD1 patients was 7.7/1000 which is much higher than the 0.2–0.5/1000 prevalence observed in apparently healthy populations.[1] Furthermore, ~20% of MD1 patients may exhibit Brugada ECG Type 1 pattern after drug challenge (ajmaline or flecainide) even those with minor right precordial lead abnormalities at baseline.[6,7] There are only few data regarding the prognostic importance of a Brugada pattern in MD1 patients while the management of these patients should be individualized. Evidence that alterations in the properties of the sodium current (similar to those observed in BS) contribute to the increased risk for ventricular arrhythmias in MD1 patients has emerged from animal models but also from observations in humans.[8,9] MD1 patients diagnosed with BS after a drug challenge were tested for a genetic mutation in SCN5A and none of these patients showed such a mutation. SCN5A is a gene encoding a subunit of a membrane myocardial sodium channel, whose mutations are related to BS and other arrhythmic syndromes such as long QT 3 syndrome.[1] These findings support the notion that loss of function of sodium channel due to missplicing of SCN5A may be involved.[10]

In general, ventricular stimulation studies are not currently recommended by the guidelines in patients with drug-induced BS. However, Pedro Brugada's group have studied a large cohort of BS patients and advocate electrophysiologic testing which seems to have good predictive value especially when less aggressive protocols (up to two extrastimuli) are used.[3,11] In our patient who was not having spontaneous Type 1 BS this strategy and the subsequent ICD implantation proved to be life-saving.

Conclusion

Patients with MD1 have increased incidence of BS. Of note, potentially life-threatening arrhythmias may develop in the adult life of MD1 patients. Electrocardiographic surveillance and tailored invasive treatment with ICDs can prevent SCD in this setting.

Lead author biography

Panagiotis Korantzopoulos is Associate Professor in the First Department of Cardiology of Ioannina Medical School, Greece. He is an arrhythmia and electrophysiological device specialist. He has been awarded the EHRA accreditation in Cardiac Pacing and Implantable Cardiac Defibrillators and he is also Fellow of the EHRA. Research interests: arrhythmias, atrial fibrillation, Brugada syndrome, pacemakers, ICDs, electrocardiology, repolarization indexes, meta-analyses. He is reviewer in 48 international biomedical journals. Publications in journals indexed in Pubmed: 216; Total citations: 3148; H-index: 29 (May 2019).

Supplementary material

Supplementary material is available at *European Heart Journal - Case Reports* online.

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

Consent: The author/s confirm that written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: none declared.

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