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CASE REPORT
Electrophysiology

Unconventional diagnosis of bradyarrhythmic syncope in Brugada syndrome: a case report

Francesca Esposito *, Felice Nappi, Francesco Urraro, Paolo Vitillo, and Francesco Rotondi

Department of Cardiology, AORN 'San Giuseppe Moscati', Contrada Amoretta, Avellino 83100, Italy

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Background The Brugada syndrome (BrS) is an inherited disorder associated with the risk of ventricular fibrillation and sudden cardiac death (SCD). The current main therapy is an implantable cardioverter-defibrillator (ICD). However, the risk stratification and management of patients remain challenging. Here, we present a case of BrS representative of the pitfalls that clinicians may encounter in the management of Brugada patients in routine clinical practice.

Case summary A 39-year-old man with BrS and recurring syncope was implanted with a subcutaneous ICD (S-ICD) (EMBLEM MRI S-ICD, Boston Scientific). Syncope recurred some months later. Subcutaneous ICD interrogation showed no arrhythmic events, but SMART Pass (high-pass filter) deactivation was noted. A query was sent to Boston Scientific clinical service, unveiling an extremely long asystolic pause as syncope determinant. Subcutaneous ICD was explanted and replaced by conventional single chamber ICD in the pre-pectoral region.

Discussion Brugada syndrome patients with high-risk features are candidates for ICD implantation to prevent SCD. Recent evidence highlighted that symptomatic patients carry a substantially higher risk compared with asymptomatic ones. Syncope may represent a pivotal symptom in BrS patients, but young patients with Type 1 Brugada pattern may experience syncope other than from tachyarrhythmias. Subcutaneous ICD is an advisable option in young ICD recipients to avoid lifetime complication related to standard transvenous systems. However, S-ICD lacks pacing capabilities and, therefore, is not indicated when an anti-bradycardia system is needed. The diagnostic workup of syncope in Brugada patients may be ineffective in elucidating the underlying aetiology whose understanding is essential to offer a personalized therapeutic approach.

Keywords Brugada syndrome • Syncope • Subcutaneous implantable cardioverter-defibrillator • Asystole • Case report

ESC curriculum 5.2 Transient loss of consciousness • 5.7 Bradycardia • 5.8 Cardiac ion channel dysfunction • 5.10 Implantable cardioverter-defibrillators

Learning points

- Understanding the aetiology of syncope in patients with Brugada syndrome may be challenging, and common diagnostic tests may be misleading or not exhaustive.
- Subcutaneous implantable cardioverter-defibrillator is a valuable option in young implantable cardioverter-defibrillator recipients to avoid lifetime complication related to standard transvenous systems. However, this device is not equipped for bradyarrhythmias' detection and treatment; thus, the need for pacing must be carefully ruled out in Brugada patients before its implant.

* Corresponding author. Tel: +39 0825203100, Email: francescaesposito84@yahoo.it
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Introduction

Brugada syndrome (BrS) is associated to an increased lifetime risk of malignant arrhythmias and sudden cardiac death (SCD).[1] Identification and timely treatment of patients at risk may be challenging. Arrhythmic syncope is a high-risk feature and establishing the aetiology of syncope plays a pivotal role in both risk stratification and treatment. Here, we report the case of a young BrS patient with recurrent syncope and undiagnosed major bradycardia unconventionally detected by a subcutaneous implantable cardioverter-defibrillator (S-ICD).

Summary figure

Date	Event
Past	• History of recurrent syncope with prodromes diagnosed as neuromediated (cardioinhibitory) at head-up tilt test.
Time 0	• Access to the emergency room for traumatic syncope. • Blood samples and physical exam: unremarkable. • Spontaneous Type 1 Brugada pattern at electrocardiogram (ECG). • Echocardiography: normal. • Hospitalization for further investigations.
Week 1	• Electrophysiological (EP) study with up to two extra stimuli: normal baseline intervals but easy inducibility of ventricular fibrillation (VF). • Coronary angiography: normal. • Blood sampling for genetic testing. • S-ICD implant.
Week 5	• Recurrence of syncope. • Outpatient S-ICD interrogation: no major arrhythmias, evidence of SMART Pass deactivation. • Query to Boston Scientific clinical service to check the reason for SMART Pass deactivation: report showing an asystolic pause of about 29 s.
Week 8	• Hospital readmission for S-ICD explant and implant of conventional transvenous ICD.
Week 10	• Family screening (genetic testing + 12-lead ECG with standard and high parasternal leads): normal.
Three-year follow-up	• The patient has experienced neither syncope nor ventricular arrhythmias (semi-annually outpatient visits).

Case summary

A 39-year-old Caucasian man was admitted to our hospital for traumatic syncope with jaw fracture. Syncope occurred while performing as an actor in the theatre. He experienced very brief prodromes but did not immediately assume a supine position due to being engaged in the performance activity. Bystanders did not report any shaking during the syncopal episode and he did not experience incontinence. He had a history of recurring syncope with short prodromes (mainly dizziness and blurred vision) since adolescence. Family history and physical exam were unremarkable. He did not take any medications. Twelve-lead ECG was consistent with spontaneous Type 1 Brugada pattern in both standard and high precordial leads. Electrocardiogram showed Type 1 coved-type ST elevation of 2 mm in V1, a PQ interval of 180 ms and a QRS duration of 90 ms (*Figure 1*). Neither QRS fragmentation nor early repolarization was present. Echocardiographic examination showed normal function and dimensions of the heart chambers and excluded valvular heart disease. A head-up tilt test performed several years earlier was positive for cardioinhibitory syncope with short prodromes. Therefore, syncopal episodes had been referred to as neuromediated. Genetic testing for SCN5A was pursued and showed a variant of uncertain significance (NM_001160161.2 c.1398G>T p.Leu466Phe Eterozigote DN).[2] A Shanghai score of 4.5 was calculated. In light of the uncertain aetiology of syncopal episodes, the patient was referred for an EP study with up to two extra stimuli. Invasive testing showed normal baseline intervals [Atrial-His Bundle (AH) interval 120 ms and His Bundle-Ventricular (HV) interval 46 ms] but resulted positive for easy inducibility of VF (see Supplementary material online, *Figure S1*). Carotid sinus massage was not performed due to the young age of the patient and lack of clinical features suggestive of carotid sinus syndromes.[3] Coronary artery disease was ruled out by coronary angiography. A cardiac magnetic resonance was attempted, but the patient was not able to undergo the exam due to claustrophobia. According to the European Society of Cardiology (ESC) guidelines, an implantable cardiac defibrillator (ICD) was indicated (Class IIa, level of evidence C).[4] Considering the patient's age and preference (actor rejecting the hypothesis of a frontal chest scar), a three-lead surface ECG screening followed by a S-ICD system implantation (EMBLEM MRI S-ICD, Boston Scientific) was performed. Post-procedural defibrillation test demonstrated inducible VF that was interrupted with a 65-J DC shock. One month later, the patient experienced a new syncope while driving. Subcutaneous ICD interrogation was negative for major arrhythmias, but the SMART Pass (high-pass filter) had turned off (*Figure 2*). The SMART Pass is a 9 Hz high-pass filter developed to reduce inappropriate shocks due to T-wave over-sensing. It works by reducing T wave amplitude without affecting the sensing of the QRS complexes, thus improving the QRS-to-T wave ratio. In an effort to avoid under-sensing of low-amplitude ventricular arrhythmias, SMART Pass is specifically designed to auto-deactivate in the presence of low-amplitude signals (0.25 mV).[5] We asked Boston Scientific clinical service to check the reason why and the company sent us a report showing an asystolic pause of about 29 s, compatible with an extended sinus pause (*Figure 3*). After a detailed informed interview with the patient and psychological counselling, we decided for S-ICD explant and implantation of a conventional single chamber ICD in the pre-pectoral region. To date, he has experienced neither syncope nor ventricular arrhythmias. The proband's parents and siblings were referred for genetic screening and underwent a 12-lead ECG with standard and high parasternal leads, along with clinical history review. All relatives were gene negative and had normal phenotypes, with no Brugada pattern identified on ECG.

Discussion

Brugada syndrome patients carry a higher risk of life-threatening arrhythmias compared with general population.[1] Apart from very high-risk patients (aborted SCD/documented ventricular fibrillation or tachycardia) in whom ICD implantation is mandatory, lifetime risk is consistently higher in patients symptomatic for syncope compared with asymptomatic ones.[6] Latest ESC guidelines recommend ICD implantation in BrS patients with arrhythmic syncope (Class IIa),[4] but the

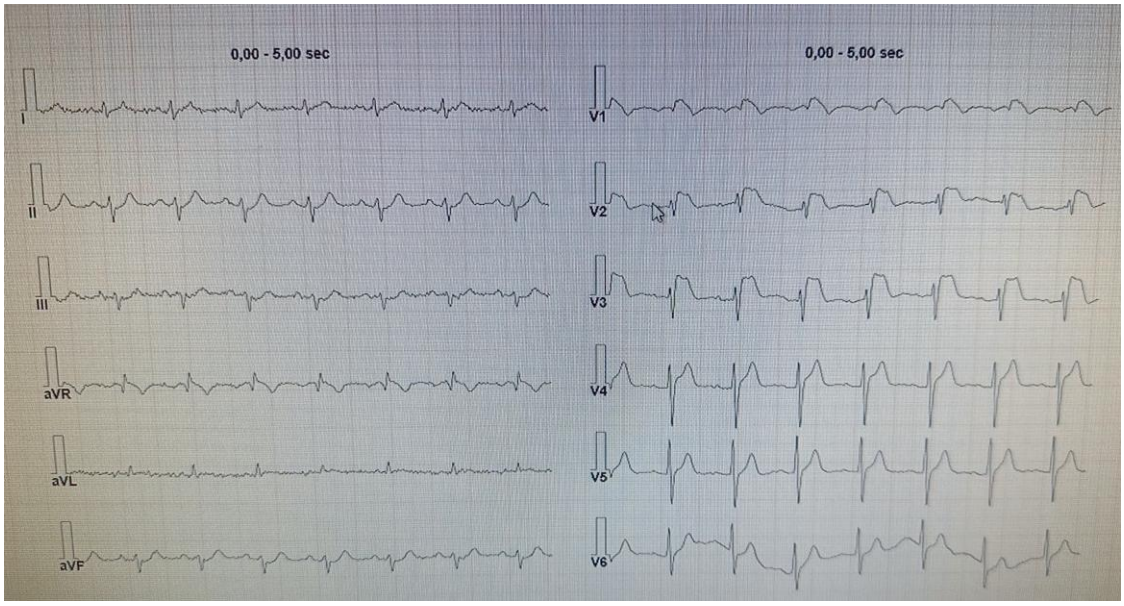

Figure 1 Standard 12-lead electrocardiogram of the patient showing Type 1 Brugada pattern with coved-type 2 mm ST-elevation in V1.

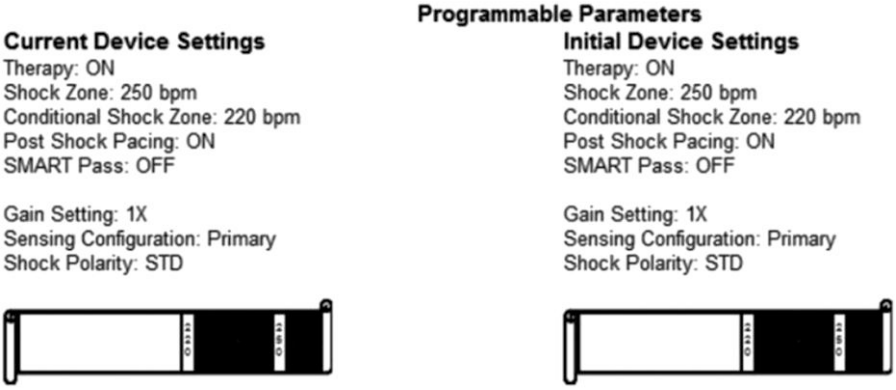

Figure 2 Subcutaneous implantable cardioverter-defibrillator interrogation showing SMART Pass deactivation at follow-up.

nature of syncopal episodes may be difficult to ascertain in some cases. Certain patients with unexplained syncope may present high risk features (high-risk Shanghai score and red flags for arrhythmic aetiology) and the implantation of a loop recorder[3] may appear an unsatisfiable solution, especially in case of traumatic presentation. Electrophysiological study is not an adequate risk predictor. However, induction of ventricular arrhythmias at EP study with programmed electrical stimulation with double extra stimuli has been associated to a worse prognosis in BrS patients with Type 1 ECG.[7] Therefore, it may prompt towards ICD implantation, especially in the presence of syncope of unclear significance with high-risk features. Subcutaneous ICD is effective in delivering lifesaving shocks in Brugada patients at risk of SCD, avoiding the need for intracardiac leads and related complications. However, this device lacks pacing capabilities when an anti-bradycardia system is advisable. SMART Pass proved effective in preventing T wave over-sensing-induced inappropriate shocks in S-ICD recipients with BrS.[5,8] In the present case, SMART Pass deactivation, due to an extremely long asystolic pause, unveiled an unexpected cause of syncope and highlighted patient's need for pacing. It is noteworthy that sinus node disease (SND) has been reported in 1.1–8.8% of patients with clinically diagnosed BrS,[9] while first-degree atrioventricular block is the most represented conduction disturbance in BrS patients and is independently linked to outcome.[10] The simultaneous presence of these manifestations finds its bases in ionic channel dysfunction that may underlie complex phenotypes in the context of overlap syndromes. For example, phenotypic overlap of Type 3 long QT syndrome, BrS, cardiac conduction disease, and SND is observed with SCN5A mutations.[11] Therefore, S-ICD is a valuable option in young patients with Brugada syndrome, but major bradycardia should be carefully ruled out before implantation to sort out patients who could benefit most from conventional transvenous systems. The choice of a single chamber ICD may be a reasonable option in young patients needing backup pacing during episodic asystole, to minimize long-term risks linked to permanent transvenous leads.

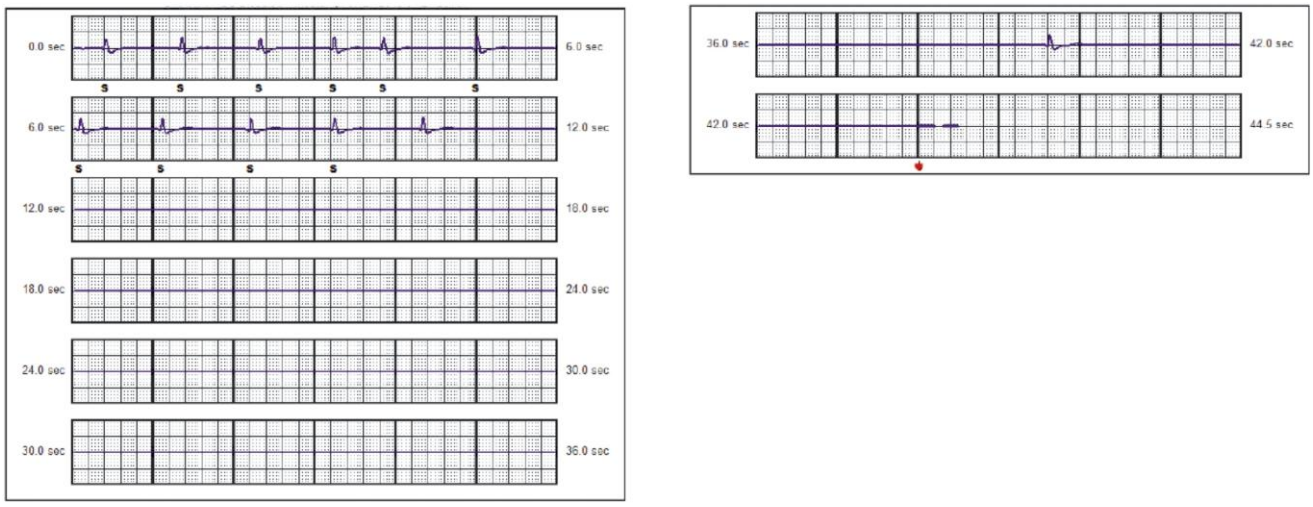

Figure 3 Extremely long (about 29 s) asystolic pause revealed by Boston Scientific clinical service after the query relative to SMART Pass deactivation. The tracing shows sinus bradycardia and slight heart rate deceleration just preceding the asystole, compatible with an extended sinus pause.

Patient's perspective

Implantable cardioverter-defibrillator implantation was not easily accepted by the patient mainly due to scar-related issues. Despite the S-ICD generator is bigger, at first instance, the patient preferred this device to a transvenous system due to its posterolateral location, less evident in frontal shots during his job as an actor. Anyway, once the need for pacing had emerged, he strongly wanted to prevent further traumatic syncope. Psychological counselling and detailed informed interview with the referring physician, joint with attention to the aesthetical aspects of the procedure (intradermal linear suture), helped him to accept the conventional transvenous system.

Conclusion

The diagnostic workup of syncope in BrS may be complex. Further studies are needed to fully elucidate the role of diagnostic tools in Brugada patients to provide a therapeutic approach tailored on individual risk profile.

Lead author biography

Francesca Esposito is an electrophysiologist at the "Moscati" hospital in Avellino, Italy. She graduated at the "Federico II" University of Naples in Italy, where she also graduated as a PhD in Clinical and Experimental medicine. She was a fellow at the IRCCS "Maugeri" were she studied the molecular mechanisms and clinical and genetic diagnosis of channelopathies under the mentorship of Professor Silvia Priori.

Supplementary material

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

Consent: The authors confirm that written consent for submission and publication of this case report including images and associated text has been received from the patient in line with COPE guidance.

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Data availability

The data underlying this article are available in the article itself.

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