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Ventricular fibrillation induction and diffuse abnormal ST-segment response to ajmaline in a patient with apparent pre-existing dynamic right bundle branch block

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Abstract. – OBJECTIVE: ST-segment elevation in the right precordial electrocardiography (ECG) leads in Brugada syndrome (BS) can be unmasked by class I anti-arrhythmic drugs (sodium channel blockers) administration. It is still debated whether this ECG pattern is better explained by abnormal repolarization or ventricular conduction and depolarization. Conduction diseases can conceal type 1 BS-like ECG in standard V1-V3 leads. ECG alterations were found also in alternative leads. The role of electrophysiology study (EPS) in sudden cardiac death risk stratification remains controversial, and could depend on the phenotypic expression of the cardiac sodium channels disease.

CASE REPORT: We describe unmasked diffuse J-point and ST-segment anomalies in peripheral and precordial ECG leads and ventricular fibrillation (VF) induction by EPS after ajmaline administration in a patient with pre-existing atypical right bundle branch block (RBBB) concealing subtle anomalies in standard V1-V3 leads. RBBB was influenced by the underlying BS-like ECG associating repolarization anomaly and pre-existing conduction disease. EPS induced VF when RBBB was associated with BS-like ECG, and failed to induce VF when RBBB was present alone.

CONCLUSIONS: BS phenotype heterogeneity requires further studies to improve the knowledge of its pathophysiological mechanisms associated with conduction diseases in order to better identify an individual therapy and prognostic stratification.

Key Words:
Brugada syndrome, Right bundle branch block, Electrophysiology study, Ajmaline, Ventricular fibrillation.

Introduction

Typical intermittent ST-segment elevation in the right precordial electrocardiography (ECG) leads in Brugada syndrome (BS) can be unmasked by class I anti-arrhythmic drugs administration. Whether this ECG pattern is better explained by abnormal repolarization or ventricular conduction/depolarization is still a matter of debate[1]. Conduction diseases can conceal/remind type 1 BS-like-ECG pattern in standard V1-V3 leads[1]. ECG alterations were found also in alternative leads[2]. The role of electrophysiology study (EPS) in sudden death risk stratification remains controversial, and could depend on the phenotypic expression of the channelopathy[3].

We describe for the first time a case of diffuse type 1 BS-like-ECG in the precordial and peripheral leads and ventricular fibrillation (VF) induction by EPS after ajmaline administration with pre-existing atypical right bundle branch block (RBBB).

Case Report

A 51-year-old man with an otherwise active life-style characterized by recreational sports, without structural heart disease, was referred because of repetitive sudden pre-syncope with trauma associated with abrupt onset of palpitations, more pronounced during warm baths or fever and never associated with physical exertion. Family history for sudden death was unclear.

Physical examination, laboratory and genetic testing were normal. Twelve-lead ECG showed sinus bradycardia with normal intervals, pre-existing atypical RBBB with QRS dynamic posi-

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tive terminal wave more evident during fever with beat-to-beat alternans, (Figure 1) subtle spontaneous intermittent J-point elevation and "coved-type" ST-segment elevation and negative T-wave in III, aVR, V1-V3, sometimes in V4. BS-like-ECG underlying the intraventricular conduction disease was suspected. Diagnostic drug-challenge performed by intravenous administration of ajmaline (1 mg/kg over 10 min) unmasked a diffuse abnormal response compatible with type 1 BS-like-ECG pattern superimposed to the pre-existing atypical RBBB during infusion and completely resolved after drug suspension: a greater "coved-type" down-sloping ST-segment elevation in aVR, III; 170% QRS duration increase (240 ms), increased J-wave duration with J-point elevation > 0.2 mV, convex ST-segment elevation and negative T-waves in V1-V4, aVR, III; deep and slurred S-waves in I, II, aVL, aVF, V6; QRS incisions in V1-V4; spontaneous frequent premature ventricular contractions (PVCs) in pairs and ventricular bigeminism originating from the left ventricle (LV) (Figure 2).

Following the definite evidence of spontaneous and drug-induced type 1 BS-like-ECG pattern in a symptomatic patient, ventricular arrhythmias risk stratification was performed by EPS showing basal sinus bradycardia, heart rate (HR) 48 bpm, intervals AH 117 ms, HV 50 ms, RBBB with QRS duration 144 ms, sinus node recovery time 937 ms (700 ms drive cycle), corrected sinus node recovery time 205 ms, atrioventricular node (AVN) Wenckebach 350 ms, AVN effective refractory period (ERP) 450-340 ms; programmed atrial stimulation did not induce arrhythmias, whereas programmed ventricular stimulation showed ventricular ERP 450-190 ms and easily induced VF (HR 290bpm) by double ventricular premature beats (S1:450 ms/S2:240 ms/S3:230 ms) not requiring direct current (DC)-shock (Figure 3, Panel A). As no signs of heart, pulmonary, neurological, or metabolic disease were detected, we confirmed the diagnosis of a BS phenotype variant characterized by the association of ECG abnormalities localized in multiple leads and RBBB. Implantation of a definite internal cardioverter defibrillator was indicated per international guidelines[4]. The patient was discharged in good conditions and was advised to follow BS recommendations.

After 3 years, the patient voluntarily repeated an EPS in another hospital to assess whether the arrhythmia risk was reduced or zeroed. No drug-challenge was performed. The new EPS did not induce ventricular arrhythmias. A baseline complete RBBB was present (Figure 3, Panel B).

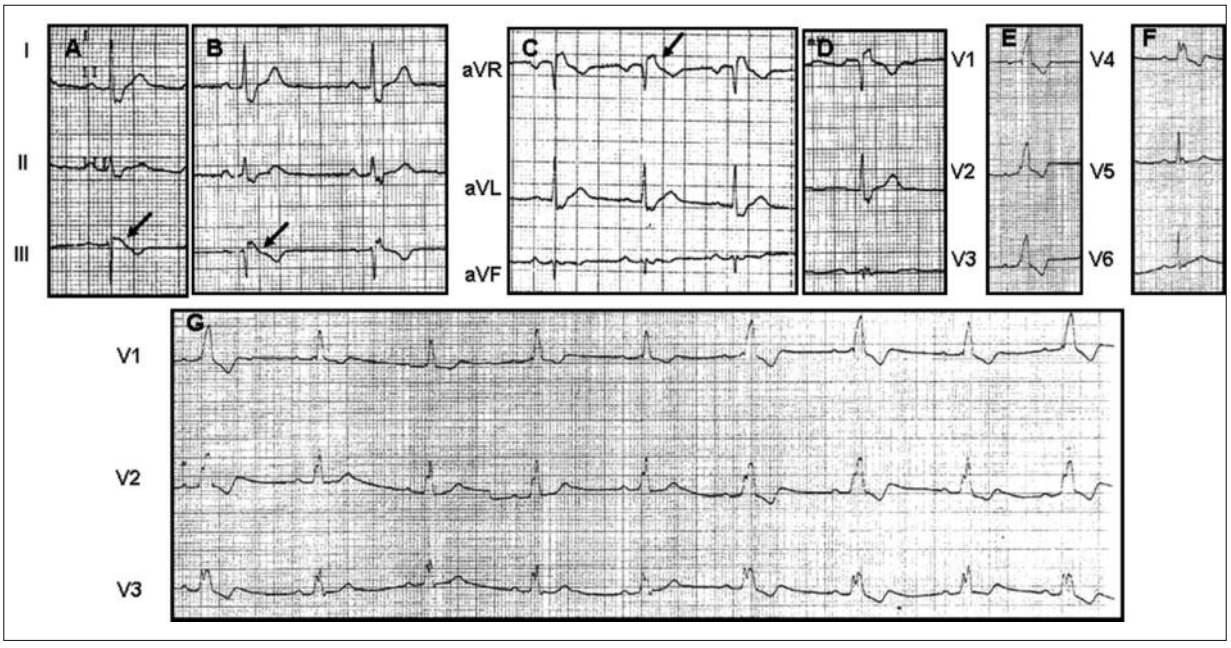

Figure 1. Baseline ECG with atypical RBBB with intermittent spontaneous subtle coved-type ST-segment in III (Panels ***A*** and ***B***, arrow), aVR (Panel ***C***, arrow) are shown. Panels ***E*** and ***F*** show the extension of RBBB in V1-V4. Panel ***G*** shows a dynamic RBBB in V1-V3.

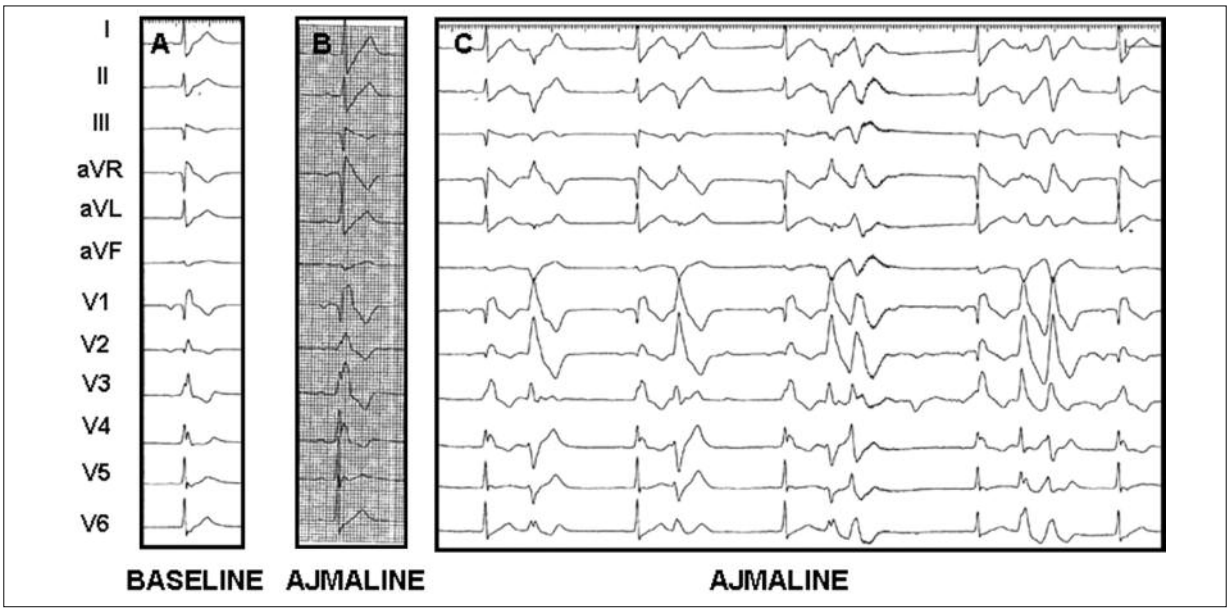

Figure 2. ECG before (Panel ***A***), and 10 min after administration of ajmaline showing accentuation of J-point and ST-segment elevation in V1-V4, aVR and III, where the typical BS abnormalities are masked by the pre-existing RBBB in V1-V3 (Panel ***B***). Panel C shows frequent spontaneous PVCs during ajmaline infusion from LV inferior lateral wall.

Discussion

This is the first description of easy VF induction at EPS and diffuse BS-like-ECG in peripheral and precordial leads unmasked by ajmaline administration in a patient with atypical pre-existing RBBB concealing sublte ST-segment alterations in standard leads.

Conduction diseases are frequently found in BS with/without conduction system structural le-

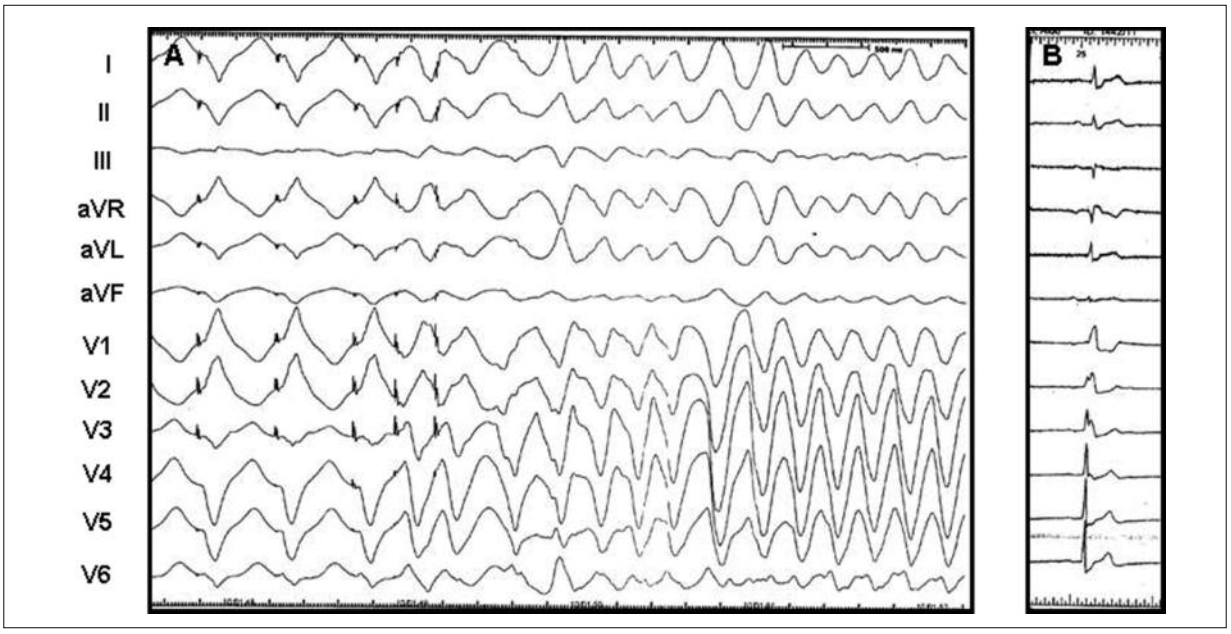

Figure 3. VF induction during programmed ventricular stimulation at EPS following ajmaline administration (Panel ***A***) when RBBB was associated with type 1 BS-like-ECG. The second EPS failed to induce VF when RBBB was present alone and with no drug-challenge (Panel ***B***).

sions[5]. The association and distinction between RBBB and BS-like-ECG remain unsolved. Transient RBBB normalization unmasks BS-like-ECG in V1-V3[6], but subtle ST-segment alterations can be missed or are hardly recognizable when RBBB normalization is unobtainable. In our case, BS-like-ECG in V1-V3 was masked by a fixed RBBB; therefore, the induction of diffuse anomalies in atypical ECG leads by ajmaline helped demonstrate the disease.

Atypical BS was observed in 10% of patients showing BS ECG phenotype in inferior or lateral peripheral leads, representing an independent predictor for malignant events[2]. A prominent R-wave and its morphology in aVR was also used as risk factor[7].

BS affects structurally normal hearts or with mild subclinical functional/morphological structural alterations of both ventricles with PVC morphologies originating from both ventricles, that might explain the localization of BS arrhythmogenic substrate in atypical sites[8]. In our case, diffuse ECG anomalies, and induced PVCs originating from the LV inferior lateral wall can result from a biventricular involvement.

Is it still debated whether the ECG pattern is better explained by an anomalous right ventricular (RV) repolarization or conduction/depolarization[1]. Typical BS-like-ECG has long been considered due to a repolarization defect of the right ventricular outflow tract (RVOT). Complete/incomplete RBBB results from an abnormal RBB central portion conduction, and delayed RV depolarization. When BS-like-ECG and RBBB are associated, the QRS in V1-V3 maintains a positive terminal end, and is the result of a more peripheral RVOT abnormal depolarization[1], or conduction delay[5]. Interestingly, a conduction delay with longer HV interval was associated with inducibility at EPS in BS supporting the conduction/depolarization anomaly hypothesis[3]. In our case, J-point and ST-segment were diverse and dynamic, suggesting that RBBB was influenced by the underlying BS-like-ECG with an association between repolarization anomaly and pre-existing conduction disease (and therefore altered depolarization)[1]. Such a highly heterogeneous substrate could be an adjunctive risk factor for ventricular arrhythmias.

The role of EPS in prognosis stratification is controversial and could depend on the dynamic genetic cardiac sodium channel disease phenotypic expression[3]. Sodium channel blockers confirm the diagnosis when BS-like-ECG is suspected, by maximizing the channelopathy and unmasking the ECG alterations, in particular when RBBB hides such pattern[6]. Negative EPS is worrying due to the dynamic nature of the ECG modifications and its unclear reproducibility, and when BS is suspected, drug challenge is mandatory. In our case, ajmaline maximized ECG anomalies when RBBB was present. Moreover, EPS induced VF when RBBB was associated with BS-like-ECG, and failed to induce VF when RBBB was present alone.

Conclusions

Our observation confirmed the possibility of BS phenotypic heterogeneity. Further studies on the complex pathophysiological mechanisms of diffuse BS alterations associated with conduction diseases are needed for individual therapy and prognostic stratification.

Conflict of Interest

The Authors declare that there are no conflicts of interest.

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