Journal of Rare Cardiovascular Diseases 2017; 3 (3): 92–97
www.jrcd.eu

CASE REPORT
Rare arrhythmias

Exercise ECG unmasked Brugada sign: manifestation of the risk of sports-associated sudden cardiac arrest (RCD code: V-1A.1)

Paweł Tomasz Matusik[1,2]*, Monika Komar[3], Jakub Podolec[4], Grzegorz Karkowski[1], Jacek Lelakowski[5], Piotr Podolec[3]

[1] Department of Electrocardiology, The John Paul II Hospital, Kraków, Poland; [2] Jagiellonian University Medical College, Kraków, Poland; [3] Department of Cardiac and Vascular Diseases, Institute of Cardiology, Jagiellonian University Medical College and the John Paul II Hospital, Kraków, Poland; [4] Department of Interventional Cardiology, Institute of Cardiology, Jagiellonian University Medical College and the John Paul II Hospital, Kraków, Poland; [5] Department of Electrocardiology, Institute of Cardiology, Jagiellonian University Medical College and the John Paul II Hospital, Kraków, Poland

Abstract

Sports-associated sudden cardiac arrest (SCA) constitutes an important problem. Causes of SCA during sport activities include Brugada syndrome (BrS) among others. We describe a 29-year-old male, without a history of cardiovascular disease, who suffered from SCA during football training and despite intensive treatment, after almost 4 weeks of hospitalization, unfortunately died. Detailed medical documentation review showed grade I atrioventricular block, intraventricular conduction abnormalities and BrS type 2 morphology of ST-segment elevation on resting 12-lead electrocardiogram (ECG). The patient had a history of syncope during physical activity. Further echocardiographic study did not reveal significant structural heart disease. Submaximal exercise testing was performed and showed ventricular extrasystoles during physical activity and type 1 BrS morphology of ST-segment elevation during recovery phase. We compared observed ECG changes to those present in a healthy football player and described noticeable similarities. Exercise ECG testing, especially in patients after syncope of probable arrhythmic etiology, may unmask BrS ECG pattern and lead to BrS diagnosis. JRCD 2017; 3 (3): 92–97

Key words: Brugada syndrome, exercise ECG, electrocardiogram, rare disease

Background

Sports-associated sudden cardiac arrest (SCA) constitutes an important clinical problem. Among middle age population, about 5% of SCA occur during sports activities [1]. The causes of SCA during exercise include Brugada syndrome (BrS), which belongs to class V of classification of rare cardiovascular diseases [2,3]. Current European Society of Cardiology (ESC) guidelines recommend diagnosis of BrS in the setting of ST-segment elevation ≥2 mm with type 1 BrS morphology in at least one lead (V1 and/or V2) placed in the second, third or fourth intercostal space [4]. According to guidelines typical electrocardiographic (ECG) BrS pattern, with coved type ST-T configuration [5], may occur spontaneously or after intravenous administration of sodium channel blockers [4]. Several reports indicate, that BrS ECG pattern may be also revealed during physical exercise testing (ExT) [6,7].

Case presentation

We describe a 29-year-old male patient, competitive football player, without previously diagnosed cardiovascular disease, who suffered from SCA during football training, spontaneously, without chest injury. Basic life support was performed initially by bystanders and then cardiopulmonary resuscitation (CPR) was provided by medical personnel including a team of air ambulance services using Lund Hospital Cardiac Arrest System (LUCAS). During CPR, 8 defibrillations were delivered (in the course of CPR polymorphic ventricular tachycardia was observed), and finally return of spontaneous circulation (ROSC) was achieved, and the patient was stabilized. He was transferred to the hospital, where neuroprotection was introduced – sedation, mild hyperventilation, hypothermia, and the treatment with diuretics (furosemide, potassium canrenoate and mannitol were used during

Conflict of interest: none declared. Submitted: February 4, 2017. Accepted: May 9, 2017.

* Corresponding author: Department of Electrocardiology, The John Paul II Hospital, 80 Prądnicka St., 31-202 Kraków, Poland; tel.: +48 12 614 2381, +48 12 614 2006, +48 12 633 2399; fax: +48 12 614 2226; e-mail: pawel.matusik@wp.eu

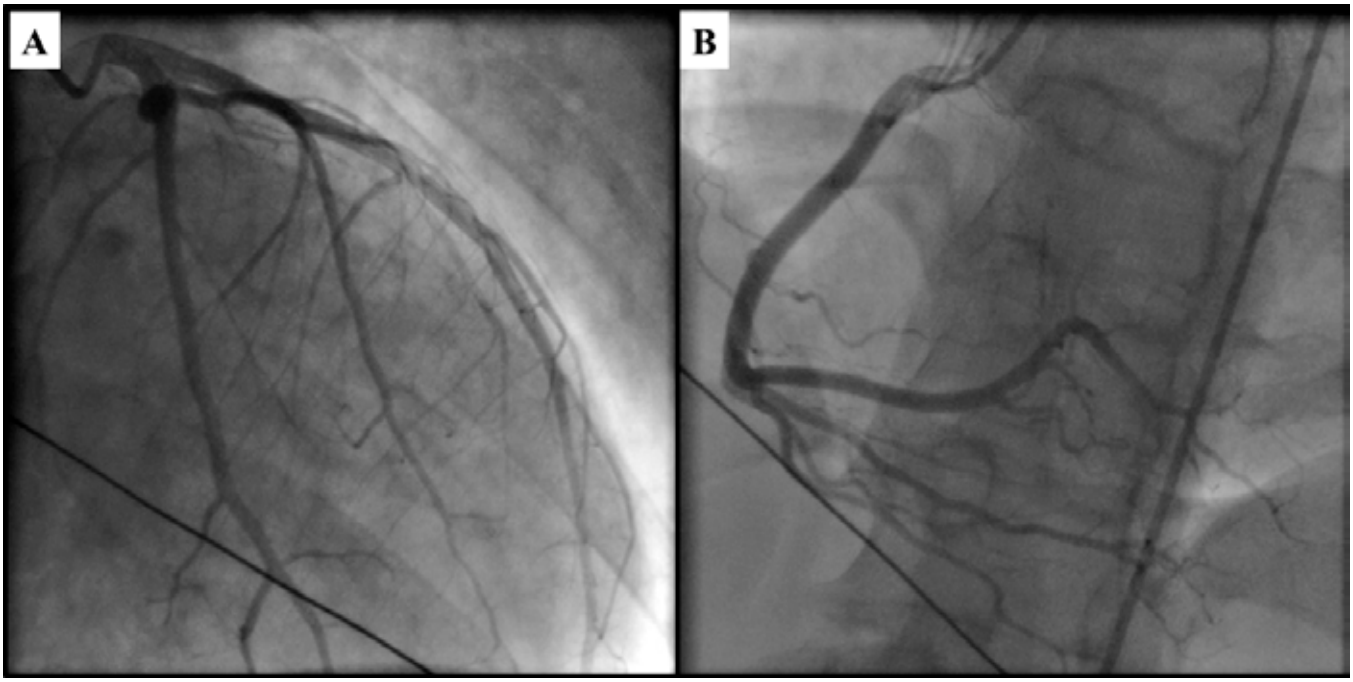

Figure 1. Coronary angiography of both left (Panel A) and right (Panel B) coronary arteries showing normal coronary circulation and no coronary artery disease

the hospital stay). Laboratory studies obtained after admission to hospital, about 80 minutes after SCA, revealed increased white blood cell count of 28.29 × 1000/μl (normal range, 3.8–10.0 × 1000/μl), neutrophils of 18.5 × 1000/μl (normal range, 2.0–7.8 × 1000/μl), lymphocytes of 7.7 × 1000/μl (normal range, 0.6–4.1 × 1000/μl), monocytes of 1.66 × 1000/μl (normal range, 0.2–1.0 × 1000/μl), while normal red blood cell count of 5.43x1000 000/μl (normal range, 4.2–6.0 × 1 000 000/μl), hemoglobin of 15.9 g/dl (normal range, 14.0–18.0 g/dl), hematocrit of 47.9% (normal range, 40.0–54.0%) and platelets count of 262 × 1000/μl (normal range, 140–440 × 1000/μl) were observed. Moreover, increased creatinine kinase-MB fraction (CK-MB) of 164 U/L (normal range, 0–24 U/l) was observed during blood sample hemolysis, increased high-sensitivity troponin T levels of 0.464 ng/ml, 4.320 ng/ml and 5.180 ng/ml (normal range, <0.014 ng/ml) and low potassium level of 3.0 mmol/l (normal range, 3.5–5.1 mmol/l). Echocardiography revealed decreased left ventricular ejection fraction (LVEF) of 40%, no pericardial fluid, no significant valvular pathologies or systolic anterior motion of the mitral valve. Coronary angiography revealed normal coronary arteries without atherosclerotic lesions (Figure 1). In computed tomography (CT), without contrast agent, there was no intracranial bleeding or acute stroke. A 24-hour ECG Holter monitoring demonstrated sinus rhythm, episodes of junctional beats and mean heart rate of 83 (54-116) beats per minute (bpm). Moreover 1587 ventricular extrasystolic beats and 2540 supraventricular extrasystolies were found. Subsequent CT angiography did not show vascular malformations in the intracerebral arteries. In the course of further hospitalization the patient did not recover consciousness and gradual brain edema with features of intussusception were observed in the subsequent CT scans of the head. After neurosurgical consultation patient was disqualified from neurosurgical intervention. Due to suspicion of brain death an electroencephalogram was performed and revealed non-reactive comma with the dominant activity of slow waves with a frequency of 2–4 Hz in all leads. In cerebral angiography no flow in intracerebral arteries was found. Furthermore, brain scintigraphy (SPECT) was performed and did not show accumulation of radioactive marker in the brain structures also indicating no blood flow in the brain circulation. Therefore, based on overall clinical picture and the results of above mentioned tests, repeated examinations by the commission according to brain death evaluation protocol were performed. Despite intensive treatment, after almost 4 weeks of hospitalization death of the brain was diagnosed.

The history revealed alcohol consumption the day before SCA and positive history of sudden deaths in his family (about 40 and about 25 years of age). Detailed previous medical documentation review had shown a resting, supine 12-lead ECG, performed over 3 years before SCA, with normal sinus rhythm, about 60 bpm, right axis deviation, PQ=240 ms (the widest P wave in lead II), QRS=130 ms (in lead I), QTc=381 ms (in lead V4), first degree atrioventricular block (AVB), right bundle branch block (RBBB), left posterior fascicular block (LPFB) and BrS type 2 morphology of ST-segment elevation (Figure 2). 24-hour blood pressure (BP) monitoring had revealed slightly elevated blood pressure during whole day (137.3/66.3 mmHg), normal BP and heart rate circardian rhythm, with average, whole day heart rate of 55.4 bpm (Figure 3).

The patient, about 9 months before SCA, had a history of syncope during physical activity. Afterwards studied in the setting of emergency department potassium level was 3.87 mmol/l (normal range, for different laboratory, 3.5–5.5 mmol/l), therefore electrolytes had been supplemented and the patient had been referred to further cardiological consultation with recommendation of physical exercise limitation.

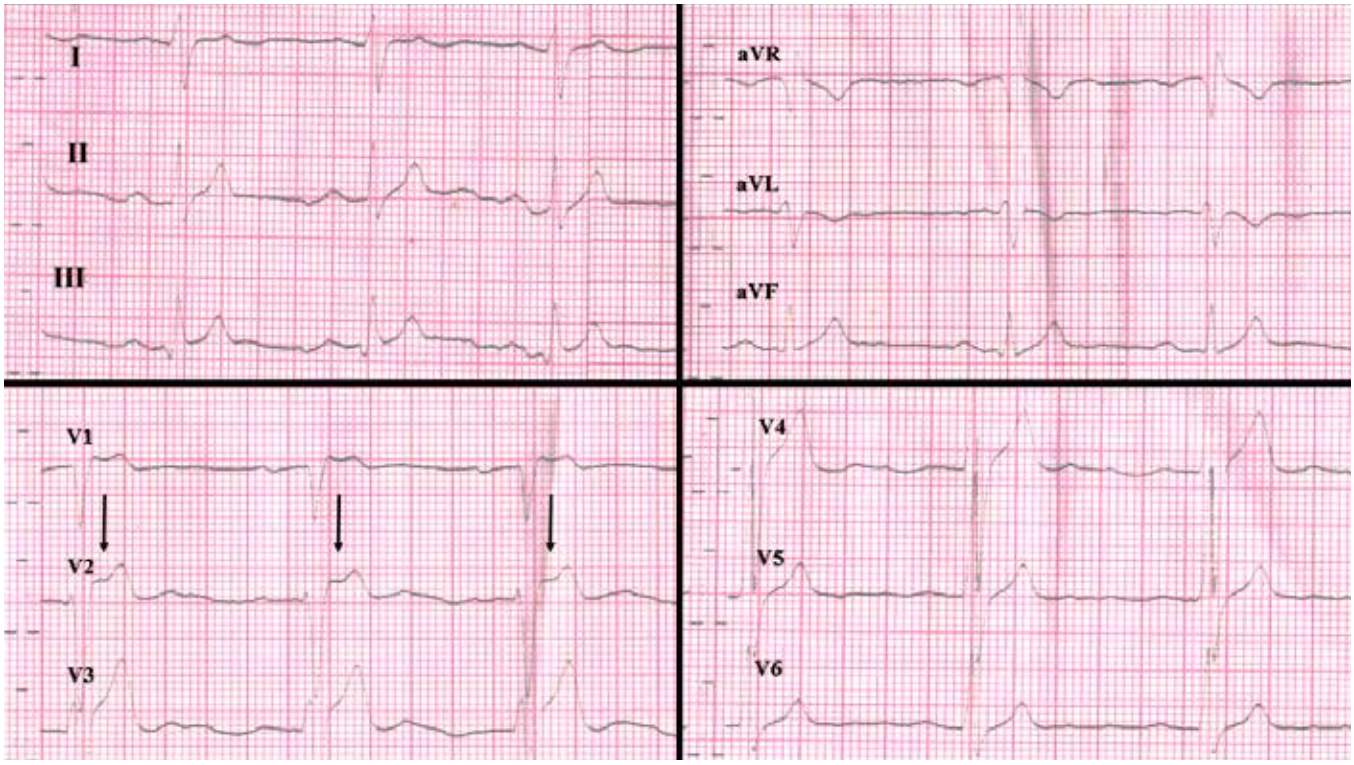

Figure 2. Supine, resting 12-lead electrocardiogram revealing Brugada syndrome type 2 ST-segment elevation (arrows). Detailed description in the main text

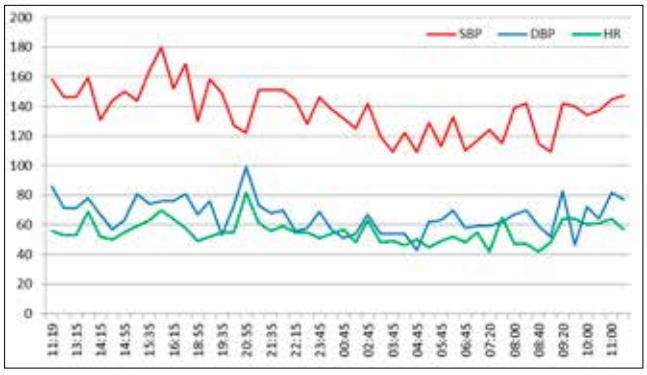

Figure 3. 24-hour blood pressure monitoring result including heart rate measurements. SBP – systolic blood pressure, DBP – diastolic blood pressure, HR – heart rate

Echocardiographic study had revealed normal cardiac chambers size, left ventricular ejection fraction of 70%, interventricular septum and inferolateral wall thickness of 11 mm, normal mitral inflow, preserved global and segmental contractility, small prolapse of anterior leaflet of mitral valve, mild mitral and tricuspid regurgitation and thin interatrial septum.

During further clinical examination the patient had undergone submaximal ExT. Before the ExT the resting heart rate was 66 bpm, while resting blood pressure was 160/85 mm Hg. During 13 minutes and 19 seconds of exercise the patient had achieved peak heart rate of 166 bpm (86% of age-predicted maximum), his peak blood pressure had been 200/70 mm Hg and he had achieved an exercise workload of 17.2 metabolic equivalents (METS). Importantly, ventricular extrasystoles had been noticed during ExT (Figure 4). After ExT the resting heart rate had been 75 bpm, while blood pressure – 150/85 mm Hg. Moreover detailed assessment of ECG obtained during ExT had revealed type 2 BrS ECG pattern during rest and typical for BrS type 1 morphology of ST-segment elevation during recovery phase in V1 and V2 (Figure 4, Panel A and C).

Discussion

Syncope and cardiac arrest may be associated with several cardiovascular diseases including BrS, takotsubo cardiomyopathy and severe aortic stenosis [8–11]. The differential diagnosis, beside BrS, should include other causes of sudden cardiac death (SCD) in young athletes, which may be divided into electrical cardiac abnormalities (other cardiac channelopathies, congenital long QT syndrome and catecholaminergic polymorphic ventricular tachycardia and Wolff-Parkinson-White syndrome), structural cardiac abnormalities (hypertrophic cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy, congenital coronary artery anomalies, Marfan syndrome, mitral valve prolapse/aortic stenosis) and acquired cardiac abnormalities (including myocarditis, commotio cordis, drugs, hypothermia and hyperthermia) [12].

As syncope or SCA may be the first manifestation of BrS [13], it is crucial to look for signs of BrS during detailed ECG assessment in patients with history of syncope and/or SCA. Changes in the 12-lead ECG observed in described case could at least in part correspond to that observed in patients who actively participate in

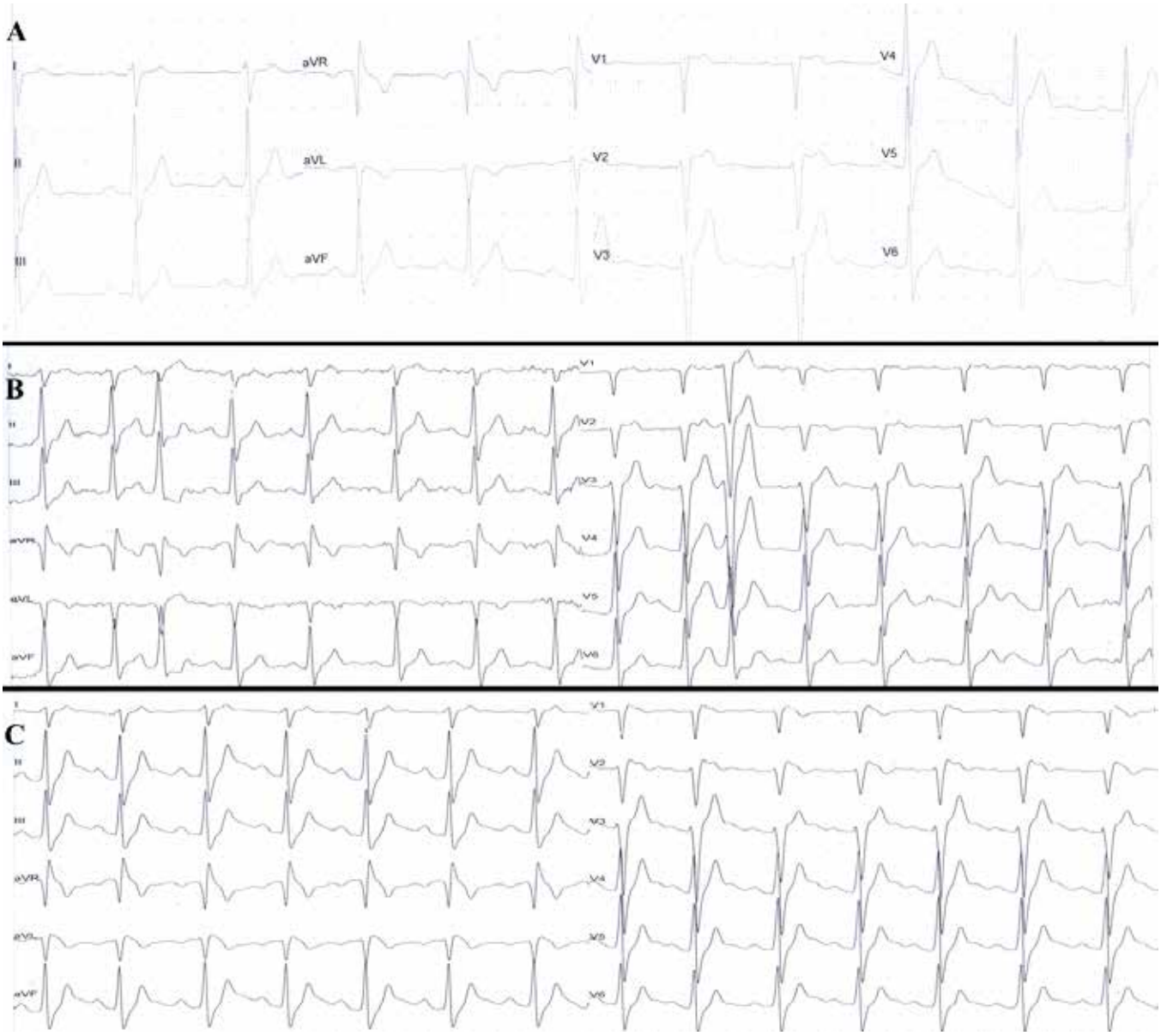

Figure 4. Electrocardiograms during exercise testing. Panel A: Rest. Panel B: Physical exercise. Panel C: Recovery phase (second minute of the recovery phase). Detailed description in the main text

exercise. Minimum of 4 hours a week of regular and long-term intensive physical activity corresponds to unique ECG characteristics which reflect increased vagal activity and cardiac chamber enlargement [14]. Those changes, among others, include first-degree AV block, incomplete RBBB and early repolarization (J-point elevation, J waves, concave ST-segment elevation or terminal QRS slurring) and are considered normal in athletes [14]. Moreover, in black/African athletes convex ('domed') ST-segment elevation with inverted T waves in V1-4 may be observed [14]. These ECG characteristics in athletes, especially rSr' QRS complexes, may be misleading in BrS diagnostic process [15]. Introduced specific criteria for evaluation of rSr' QRS morphology in leads V1-V2 may facilitate patient management [16]. Importantly, asymptomatic athletes with RBBB or left bundle branch block who do not develop type II second-degree AVB or complete AVB, with no heart disease that precludes participation, can participate in competitive athletics [17].

Unveiling of BrS ECG pattern during physical exercise or during recovery phase had been described previously [6, 7]. One of the previously described patients had, similarly to our case, type 2 BrS ECG pattern with 'saddleback' ST-elevation in resting supine ECG [18].

In a study done by Makimoto et al. it was demonstrated that ST-segment elevation augmentation during ExT at early recovery phase, especially in patients after syncope, was associated with poor prognosis in BrS [19]. On the other hand, it is not unusual in sportsmen during ExT who achieve high exercise capacity to develop ST-segment deviations that are hard to assess. Figure 5 (Panel A-C) shows an example of ECG recording during ExT performed by a control, healthy 30-year-old sportsman (football player). The control athlete before ExT had the resting heart rate of 69 bpm, while resting blood pressure was 130/80 mm Hg. During 15 minutes and 56 seconds of exercise the control athlete achieved peak heart rate

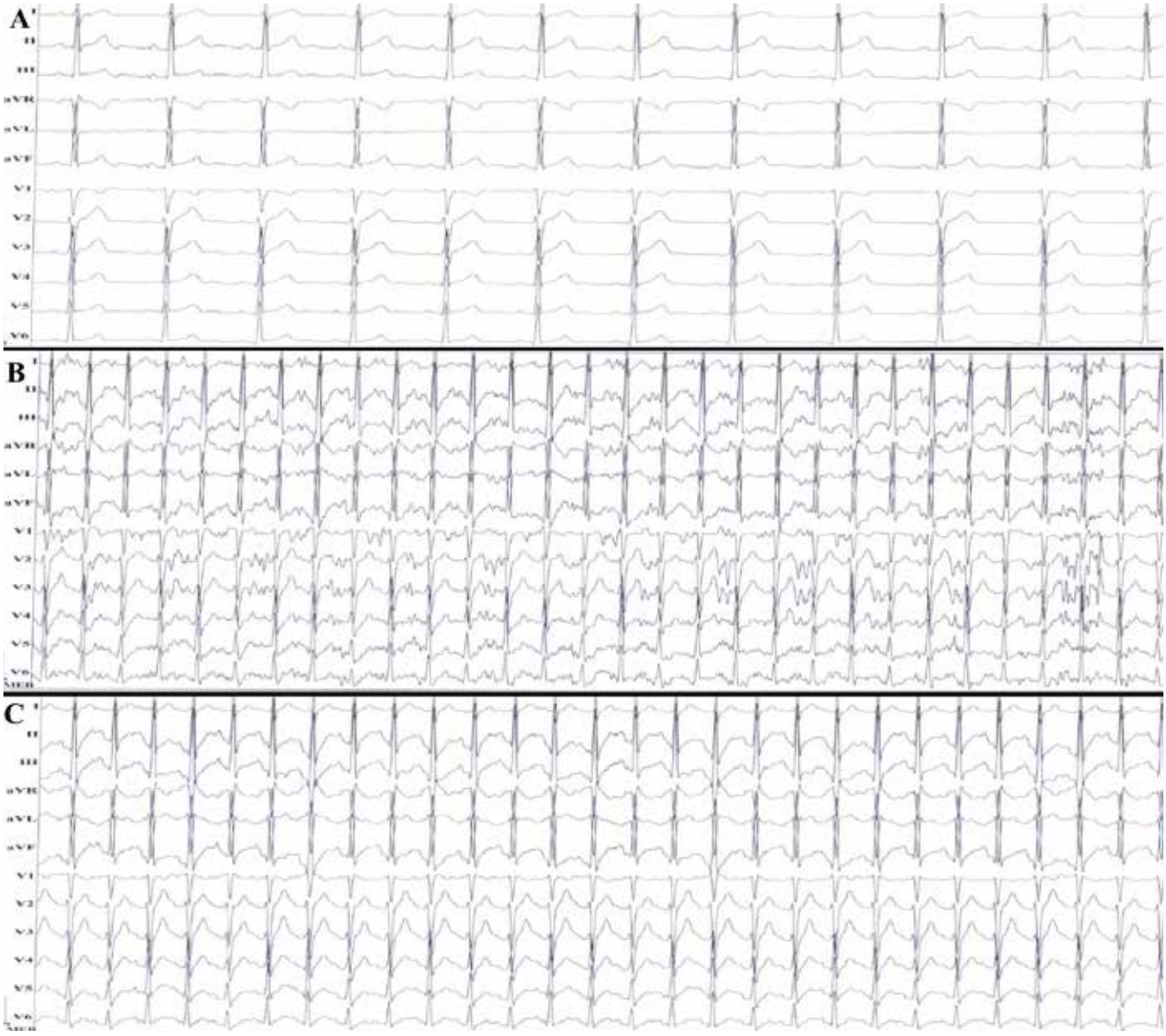

Figure 5. Electrocardiograms during exercise testing in a control, healthy sportsman. Panel A: Rest. Panel B: Physical exercise. Panel C: Recovery phase. Detailed description in the main text

of 176 bpm (93% of age-predicted maximum), while peak blood pressure was 185/65 mm Hg. The control sportsman achieved an exercise workload of 17.0 METS. After the ExT the resting heart rate was 109 bpm, while blood pressure was 150/80 mm Hg. The ECG obtained during ExT shows visible ST-segment elevations in precordial leads during rest and periods with ST morphology resembling type 1 BrS ECG pattern in V1 during early recovery phase (Brugada-like pattern) [5].

BrS ECG pattern may be observed in other clinical scenarios. For example, abnormal ECG filter setting (e.g. 1.5 Hz instead of 0.05 Hz) may simulate ECG BrS pattern (example of Brugada phenocopy) [20–22]. BrS ECG pattern may be observed during Taxus poisoning or intracoronary acetylocholine injection [23, 24]. Interestingly, pharmacological unmasking of Brugada sign was associated with repolarization abnormalities indicating ischemic myocardial region in the course of acute myocardial infarction of uncertain anatomical location [25].

Malignant ventricular arrhythmias in BrS typically occur at rest, after increased vagal activity and/or cancelation of sympathetic activity [26]. SCA in BrS is not typically associated with exercise [12]. In reported patient both syncope and SCA occurred during physical activity (football trainings). It is very probable that in the case of our patient SCA resulted from a 'perfect storm', which was triggered by transient factors (possible interaction between previous alcohol consumption, strenuous physical exercise [which may be associated with profound bradycardia and exercise-induced hyperthermia [12]], electrolyte imbalance [which could be exaggerated by sweat electrolyte loss during physical activity [27]]) and vulnerable substrate (genetic predisposition of myocardium to ventricular arrhythmias).

According to ESC recommendations for competitive sports participation in athletes with cardiovascular disease (published in 2005) patients with BrS should be restricted from competitive sports, while in healthy genetic BrS carriers without phenotypic expression this recommendation is uncertain [28]. 2015 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of SCD do not directly address aspect of BrS patients participation in competitive sports [4]. On the other hand, recent scientific statement from American Heart Association and American College of Cardiology states, that even in previously symptomatic BrS patients (in patients asymptomatic on treatment for at least 3 months) competitive sports participation may be considered assuming precautionary measures and specific treatments are introduced [29]. Patients with BrS after implantable cardioverter defibrillator (ICD) implantation should be advised about limitations in exercise participation associated with the presence of the device [30].

It is very important for patients with BrS to avoid large meals, electrolyte disturbances, excessive alcohol intake, drugs that may induce BrS ECG morphology and hyperthermia (including prompt use of antipyretic drugs in the case of fever) [4,30]. Especially in BrS patients after cardiac arrest and/or with sure sustained spontaneous ventricular tachycardia ICD implantation is recommended [4]. Moreover, in the case of BrS diagnosis, family members screening for BrS, plays significant role in comprehensive clinical care.

Conclusions

Exercise ECG testing, especially in patients after syncope of probable arrhythmic etiology, may unmask BrS ECG pattern and lead to BrS diagnosis. Therefore, special attention should be paid to the assessment of typical for BrS ST-segment elevation during exercise ECG testing.

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