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Treatment of the Patient with Brugada Syndrome – a Case Report

Liječenje bolesnika s Brugadinim sindromom – prikaz slučaja

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Abstract. ***Aim*:** Brugada syndrome is a rare genetic disorder that can be recognized by characteristic changes in ECG records. The syndrome is more common in Southeast Asian countries than in the rest of the world. Considering the increasing presence of foreign workers from Southeast Asia in Europe, this work aims to draw attention of healthcare professionals and educate them on early recognition and prompt stratification of patients at risk. ***Case report*:** This paper presents the case of a patient hospitalized due to out-of-hospital cardiac arrest. After hemodynamic stabilization at the emergency department, ECG showed changes indicative of Brugada pattern type 1. Cardiac arrest soon occurred again due to polymorphic ventricular tachycardia. This time, despite numerous defibrillations and therapy, the return of spontaneous circulation was not achieved initially. The electrical storm was finally terminated by the administration of isoproterenol, a β-adrenoreceptor agonist recommended by the Guidelines of the European Society of Cardiology. In the further course, the hospital stay, development of complications, their treatment, and the implantation of a cardioverter defibrillator in secondary prevention are described. ***Conclusion*:** The specificity of this syndrome is the increased risk of sudden cardiac death in healthy and young individuals, mostly men. The Guidelines give clear recommendations on the management of symptomatic patients, as well as those with Brugada pattern type 1. No clear guidelines are given for pattern types 2 and 3. Therefore, the consensus of experts expressed in the Shanghai scoring system can be used for risk stratification and further treatment. It is of great importance to recognize ECG records with the Brugada pattern and to promptly refer the patient for further evaluation with the aim of primary prevention of sudden cardiac death.

Keywords: Brugada syndrome; Isoproterenol; Sudden Cardiac Death; Ventricular Tachycardia

Sažetak. ***Cilj*:** Brugadin sindrom predstavlja rijedak genetski poremećaj koji se može prepoznati po karakterističnim promjenama EKG zapisa. Sindrom je češći u zemljama jugoistočne Azije u odnosu na ostatak svijeta. S obzirom na sve veću prisutnost stranih radnika iz područja jugoistočne Azije u Europi, cilj je ovoga rada skrenuti pozornost zdravstvenih djelatnika na sindrom i educirati ih radi ranog prepoznavanja i pravovremene stratifikacije rizičnih bolesnika. ***Prikaz slučaja*:** Ovim radom prikazuje se slučaj bolesnika hospitaliziranog zbog izvanbolničkog srčanog zastoja. Nakon hemodinamske stabilizacije na hitnom prijamu učinjen je EKG kojim su uočene promjene indikativne za Brugadin obrazac tipa 1. Tijekom obrade ubrzo je ponovno došlo do srčanog aresta uslijed polimorfne ventrikularne tahikardije. Ovoga puta, usprkos brojnim defibrilacijama i terapiji, inicijalno nije postignut povratak spontane cirkulacije. Električna oluja okončana je tek primjenom izoproterenola, agonista β-adrenoreceptora preporučenog smjernicama Europskog kardiološkog društva u slučaju električne oluje u bolesnika s Brugadinim sindromom. U daljnjem tijeku prikaza opisuje se boravak u bolnici i liječenje bolesnika, razvoj komplikacija, njihovo zbrinjavanje i implantacija kardioverter-defibrilatora u sekundarnoj prevenciji. ***Zaključak*:** Specifičnost ovog sindroma je povećan rizik iznenadne srčane smrti u zdravih i relativno mladih ljudi, većinom muškaraca. Smjernice daju jasne preporuke o zbrinjavanju simptomatskih bolesnika, kao i onih s Brugadinim obrascem tipa 1. Za obrasce tipa 2 i 3 nisu dane jasne smjernice, stoga za stratifikaciju rizika i daljnje postupanje može poslužiti

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konsenzus eksperata izražen u Šangajskom bodovnom sustavu. Od velike je važnosti prepoznati EKG zapise s Brugadinim obrascem te pravovremeno uputiti bolesnika na daljnju obradu u cilju primarne prevencije iznenadne srčane smrti.

Ključne riječi: Brugadin sindrom; iznenadna srčana smrt; izoproterenol; ventrikularna tahikardija

Brugada syndrome is a rare disorder characterized by changes in the ECG due to a mutation in the cardiac sodium channel gene. It often manifests itself as sudden cardiac death in young, previously healthy men. The syndrome is more common in Southeast Asian countries.

INTRODUCTION

Brugada syndrome (BrS) was first described a little more than 30 years ago and continues to attract the attention of many doctors, especially cardiologists – arrhythmologists due to the increased risk of sudden cardiac death (SCD) in previously healthy individuals[1]. It is a rare hereditary disease associated with the mutation of certain genes, and its prevalence ranges from 1 to 5 per 10,000 inhabitants in Europe and up to 12 per 10,000 in Southeast Asia[2]. Almost four-fifths of patients are men, and the average age of symptoms onset is around 40 years. In some regions, BrS has specific names, so in the Philippines it is also called *Bangungut*, which represents a male person who dies of an unclear cause in his sleep with agonal breathing during a nightmare[3]. In Japan, the term *Pokkuri* prevails, which means a sudden and good death, without a long illness[4]. Other names such as *Sleeping sickness* in Hawaii or *Lai Tai syndrome* in Thailand have also been recorded.

CASE REPORT

A 36-year-old patient was hospitalized at the Clinic for Cardiovascular Diseases of the Rijeka Clinical Hospital Centre (KBC Rijeka) after an out-of-hospital cardiac arrest. According to the available documentation, the patient was a foreign worker of South Asian origin on temporary work in Croatia without any medical history. The emergency medicine doctor stated that the call for intervention was made by the patient, who complained of difficult breathing and palpitations. When the emergency staff arrived, vital parameters were normal, but during transport to the hospital, cardiac arrest in ventricular fibrillation (VF) soon occurred. Cardiopulmonary resuscitation (CPR) measures were taken and defibrillation of VF was performed twice with the return of spontaneous circulation (ROSC). On arrival at the Integrated Emergency Hospital Admission (IEHP) of KBC Rijeka, the patient was in a disturbed state of consciousness, GCS 3, and was breathing spontaneously through an I-gel mask. The pupils were narrow and light-reactive. Soon, he was intubated and connected to mechanical lung ventilation. An ECG was performed and a domed ST elevation was observed in the V1 and V2 leads (Figure 1). A few minutes later bigeminy of ventricular extrasystoles (VES) was monitored. VES bigeminy soon turned into repetitive polymorphic ventricular tachycardia – *VT storm* refractory to repeated defibrillations and administered therapy (amiodarone 300 mg i.v., metoprolol 5 mg i.v., magnesium 2 g i.v. and potassium chloride).

Considering the ECG findings indicative of Brugada syndrome with refractory VT, immediate administration of isoproterenol was indicated. 1 microgram per minute of isoproterenol was administered i.v. (0.2 mg of isoproterenol in 50 mL of 0.9% NaCl intravenously via perfusor at a flow rate of 15 mL/h), which achieved rapid and complete rhythmic stabilization of the patient.

Laboratory findings revealed slightly elevated leukocytes (13.1 x 10^9), troponin T (37 ng/L), and significantly decreased potassium (2.4 mmol/L). Immediately after receiving the findings, parenteral potassium replacement with potassium chloride was started. Before admission, a CT pulmonary angiogram (CTPA) and a CT scan of the brain were performed. CT scan of the brain showed proper differentiation of grey and white matter of the cerebrum and cerebellum, without recent lesions. The consumption of narcotics was ruled out by the toxicological analysis of urine. Ultrasound of the heart in IEHP ruled out significant structural abnormalities of the heart as a

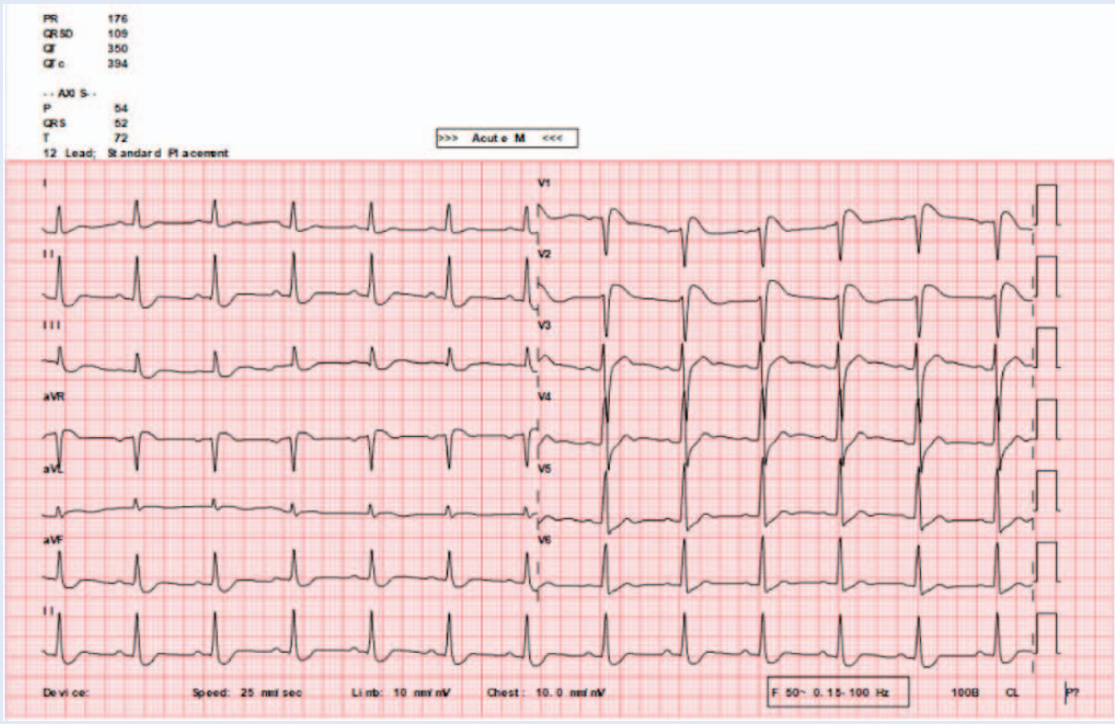

Figure 1. Patient's ECG at the arrival to IEHP

possible cause of cardiac arrest. A review of the patient's past medical history through electronic health records showed that he was examined twice by a general physician under the International Classification of Diseases (ICD-10) diagnosis R55 Syncope and collapse. The further stay at the Intensive Cardiac Care Department was complicated by an increase in inflammatory parameters (CRP 222 mg/L), but the microbiological isolates (blood cultures, urine culture, tracheal aspirate) that arrived later were sterile. On the second day of treatment, despite the prescribed antipyretics, the patient became highly febrile, and as a result, repeated polymorphic VT occurred again. This time it was successfully interrupted by two defibrillations and repeated intravenous administration of isoproterenol. In the further course, hemodynamic and rhythmic parameters were stable and a good response to empiric therapy was observed, which ultimately resulted in separation from mechanical breathing support on the sixth day of treatment. During the stay, an ultrasound of the heart was performed. It showed the proper size and left ventricular ejection fraction, without signs of hypocontractility. Considering the regular findings of the ultrasound, the absence of an increase in troponin or ischemic ECG changes, the previously performed CTPA, which did not describe any signs of coronary arteries pathology, and the absence of risk factors, we considered that it was not necessary to perform a coronary angiography to rule out ischemic heart disease as the cause of the arrhythmia. A few days after, the patient was transferred to the Arrhythmias Department, and with the help of a translator, the nature of the disease was explained to him. For secondary prevention of SCD, on the 13th day of treatment, a VVIR cardioverter defibrillator was implanted, which was connected to a ventricular DF4 defibrillation single coil electrode positioned in the apex of the right ventricle via the left cephalic vein. Control testing of the device was in order. Before discharge, the patient was given clear instructions about the importance of preventing risk factors, such as control of elevated body temperature, adequate nutrition while avoiding large meals, prohibition of alcohol consumption and avoidance of drugs contraindicated in patients with BrS. One month after initial admission the pa-

tient underwent a control examination. In the meantime, he felt well, and the tested parameters of the device were normal, with the ST changes of the V1 and V2 leads still present.

DISCUSSION

As mentioned in the introductory part of the paper, in 1992 the Brugada brothers published an article in which they studied the SCD of eight patients. Right bundle branch block and ST elevation of precordial leads V1 and V2 were common in the mentioned patients, and in some patients also in V3. The mentioned changes could not be explained by electrolyte disturbances, myocardial ischemia or structural heart disease[1]. Seven years later, the Brugada brothers published a new article in which they defined the disease as genetically determined with an autosomal dominant pattern of inheritance[5]. In the paper, they describe three different mutations that affect the function and structure of sodium channels through the SCN5A gene, and they assume that BrS is the cause of up to 50% of SCD in patients with a structurally normal heart. In the conclusion of the paper, the brothers state that amiodarone and beta blockers do not prevent SCD, and the only effective therapy is an implantable cardioverter defibrillator (ICD), with the hope that gene therapy will offer the cure of the future. In papers written a few years later, the above ECG pattern was called the Brugada type 1 pattern[6]. Along with type 1, two other forms are described. Type 2 also has an elevated J point of ≥ 2 mm with a saddle-shaped ST segment that is elevated ≥1 mm and a positive or biphasic T wave. On the other hand, type 3 compared to type 2 has a positive T wave and the ST segment is elevated by less than 1 mm (Figure 2). In the meantime, numerous papers have been written on the topic of Brugada syndrome, and in 2022 new Guidelines from the European Society of Cardiology (ESC) dealing with ventricular arrhythmias and prevention of SCD were published[7]. They summarize the most important knowledge about Brugada syndrome and give certain recommendations on how to treat patients. In the Guidelines, the Type 1 ECG pattern is described somewhat differently compared to the patient's ECG from the first work of the Brugada brothers. J point elevation of more than 2 mV with concave ST elevation and T wave inversion in V1 or V2 lead are listed as criteria. It is important to note that the above pattern can be constantly present or can be induced by fever or sodium channel blockers used in diagnostic tests. Unfortunately, there has been no progress in genetic diagnostics, and SCN5A is still the only gene that can be reliably associated with BrS in approximately 20% of patients[8].

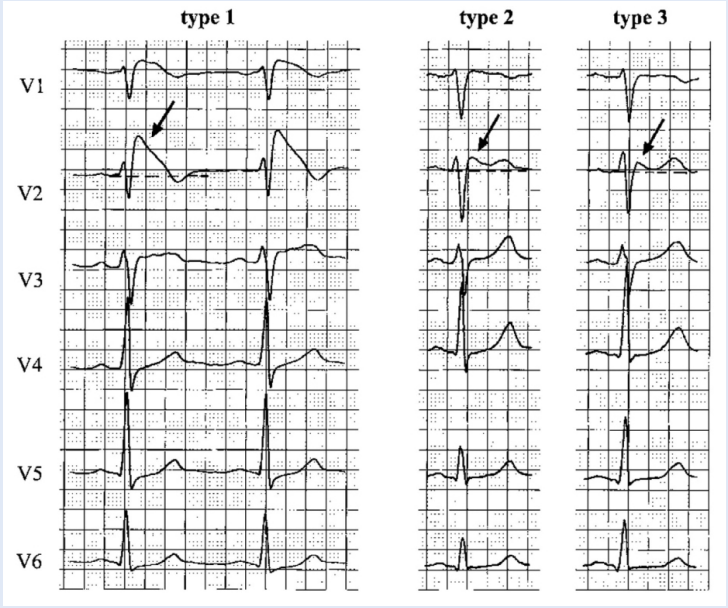

Figure 2. Brugada patterns

Almost a third of patients with BrS present with syncope, which means that most are asymptomatic[9]. Given the relatively rare incidence of the disease, it is understandable that it is not possible to conduct research on a larger number of people, therefore the level of all recommendations, except for one, is classified as level C – expert consensus, data from smaller or retrospective studies and registries. The patient presented in this work falls under the symptomatic category and, according to ESC recommendations, meets both criteria for recommended ICD implantation, namely cardiac arrest and documented sustained VT as part of BrS. It is important to emphasize that only one of the above two conditions is sufficient for the implantation of an ICD. Likewise, according to the Guidelines in case of VT storm, treatment with isoproterenol infusion, which was also used in the presented case

Table 1. Proposed Shanghai score system for the diagnosis of BrS

	Points
I. ECG*	
A. Spontaneous type 1 Brugada ECG pattern at nominal or high leads	3.5
B. Fever-induced type 1 Brugada ECG pattern at nominal or high leads	3
C. Type 2 or 3 Brugada ECG pattern that converts with provocative drug challenge	2
II. Clinical history**	
A. Unexplained cardiac arrest or documented VF/polymorphic VT	3
B. Nocturnal agonal respirations	2
C. Suspected arrhythmic syncope	2
D. Syncope of unclear mechanism/unclear etiology	1
E. Atrial flutter/fibrillation in patients <30 years without alternative etiology	0.5
III. Family history	
A. First or second degree relative with definite BrS	2
B. Suspicious SCD (fever, nocturnal, Brugada aggravating drugs) in a first or second degree relative	1
C. Unexplained SCD <45 years in first or second degree relative with negative autopsy	0.5
IV. Genetic test result	
A. Probable pathogenic mutation in BrS susceptibility gene	0.5

* One item must be present. ** If there are several items, only one with highest score can be counted.
Score: ≥3.5 points: probable/definite BrS; 2-3 points: possible BrS; <2 points: non-diagnostic

and successfully terminated VT, should be considered. From all of the above, it can be concluded that the treatment of symptomatic patients diagnosed with BrS is recommended. If by any chance the aforementioned patient was referred earlier by the family doctor for syncope, according to the Guidelines, the implantation of a "loop recorder" should be considered, and the implantation of an ICD comes into consideration only if the arrhythmogenic cause of the syncope is confirmed. Electrophysiological testing and induction of VT can also be considered. It is interesting that the Guidelines decidedly do not mention the Brugada pattern type 2 or 3, but state that BrS should be considered in patients with an induced pattern type 1 and at least one of the listed criteria: arrhythmogenic syncope or agonal breathing at night, positive family history of BrS or sudden death (under the age of 45). Therefore, only the Brugada type 1 pattern has a diagnostic value, while type 2 can raise the suspicion of BrS, but the diagnosis can only be established after the induction of the type 1 pattern[10]. Given the vagueness of clinical Guidelines regarding Brugada patterns types 2 and 3, a group of leading experts from several societies including representatives of the Heart Rhythm Society (HRS), the European Heart Rhythm Association (EHRA) and the Asian-Pacific Heart Rhythm Society (APHRS) met in Shanghai in 2015[11]. As a result of the joint meeting, a consensus emerged, part of which is the proposed Shanghai scoring system which aims to more adequately stratify patients (Table 1). The goal of the system is to diagnose Brugada syndrome based on ECG, personal and family history, and genetic testing. If the Score is higher than 3.5, BrS is probable and/or definite. With 2 to 3 points BrS is possible, and with less than 2 points it is nondiagnostic.

As a consensus of HRS, EHRA and APHRS, the Shanghai scoring system emerged. It aims to replace the shortcomings of the current Guidelines regarding pattern types 2 and 3, based on ECG, personal and family history, and genetic testing.

CONCLUSION

Although BrS is not common in European countries, it is necessary to educate the medical staff who come across ECG records to recognize the

Brugada pattern and promptly refer the patient for adequate further diagnosis and treatment. One should certainly consider the significant influx of young male labor force from the countries of South and Southeast Asia, where the prevalence of BrS is twice as high. Given that the treatment of BrS has not changed significantly in the last 25 years, work needs to be done to establish the most adequate screening of patients and primary prevention of SCD. There remains hope for the fulfilment of the assumption made by the Brugada brothers in 1999 about the progress of genetic therapy. Until then, the recommendations of the recently published ESC Guidelines on the treatment of ventricular arrhythmias and the prevention of SCD should be followed, along with consideration of the consensus of experts manifested by the Shanghai scoring system.

Conflicts of Interest: Authors declare no conflicts of interest.

REFERENCES

1. Brugada P, Brugada J. Right bundle branch block, persistent ST segment elevation and sudden cardiac death: a distinct clinical and electrocardiographic syndrome. A multicenter report. J Am Coll Cardiol 1992;20:1391–6.
2. Brugada J. Management of patients with a Brugada ECG pattern. E-journal Cardiol Practice [Internet]. 2009;7. [cited 2024 Jan 12]. Available from: https://www.escardio.org/Journals/E-Journal-of-Cardiology-Practice/Volume-7/Management-of-patients-with-a-Brugada-ECG-pattern.
3. Gaw AC, Lee B, Gervacio-Domingo G, Antzelevitch C, Divinagracia R, Jocano F Jr. Unraveling the Enigma of Bangungut: Is Sudden Unexplained Nocturnal Death Syndrome (SUNDS) in the Philippines a Disease Allelic to the Brugada Syndrome? Philipp J Intern Med 2011;49: 165-176.
4. Nakajima K, Takeichi S, Nakajima Y, Fujita MQ. Pokkuri Death Syndrome; sudden cardiac death cases without coronary atherosclerosis in South Asian young males. Forensic Sci Int 2011;207:6-13.
5. Brugada J, Brugada P, Brugada R. The syndrome of right bundle branch block ST segment elevation in V1 to V3 and sudden death--the Brugada syndrome. Europace 1999;1:156-66.
6. Wilde AA, Antzelevitch C, Borggrefe M, Brugada J, Brugada R, Brugada P et al. Proposed diagnostic criteria for the Brugada syndrome: consensus report. Circulation 2002;106:2514-9.
7. Zeppenfeld K, Tfelt-Hansen J, de Riva M, Winkel BG, Behr ER, Bloom NA et al. 2022 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: Developed by the task force for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death of the European Society of Cardiology (ESC) Endorsed by the Association for European Paediatric and Congenital Cardiology (AEPC). Eur Heart J 2022;43:3997–4126.
8. Hosseini SM, Kim R, Udupa S, Costain G, Jobling R, Liston E et al. Reappraisal of Reported Genes for Sudden Arrhythmic Death: Evidence-Based Evaluation of Gene Validity for Brugada Syndrome. Circulation 2018;138:1195-1205.
9. Mascia G, Della Bona R, Ameri P, Canepa M, Porto I, Brignole M. Brugada syndrome and syncope: A systematic review. J Cardiovasc Electrophysiol 2020;31:3334-3338.
10. Sieira J, Brugada P. The definition of the Brugada syndrome. Eur Heart J 2017;38:3029-3034.
11. Antzelevitch C, Yan GX, Ackerman MJ, Borggrefe M, Corrado D, Guo J et al. J-Wave syndromes expert consensus conference report: Emerging concepts and gaps in knowledge. Europace 2017;19:665-694.