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BRUGADA SYNDROME

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In 1992, Brugada syndrom was introduced as a new clinical entity linking typical but variable ST segment changes in the right precordial leads to an increased vulnerability for lethal ventricular arrhythmias. The diagnosis of Brugada syndrome is based on clinical and electrocardiographic features. Recent studies illustrate the dynamic character of these ECG patterns. Whenever a large number of baseline ECGs was available during a follow-up, the diagnostic pattern could be documented only in approximately 25% of the tracings. Because the presence of the spontaneous coved type I ECG pattern is thought to be a useful predictor of future arrhythmic events in asymptomatic patients, these findings are of great clinical importance. ICD implantation is an option for the patients with Brugada syndrome and ventricular tachycardia or fibrillation. Extensive research is ongoing to find alternative pharmacological options for these patients, especially for patients in whom ICD implantation is contraindicated for various reasons. *Acta Medica Medianae 2015;54(2):37-40*

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Introduction

In 1992, Brugada syndrome was introduced as a new clinical entity linking typical but variable ST segment changes in the right precordial leads to an increased vulnerability for lethal ventricular arrhythmias. In the affected patients, no structural heart disease could be identified despite thorough invasive and noninvasive investigation. Brugada syndrome is genetically transmissible disease manifesting as an autosomal dominant and age-dependent trait. Up to now, more than 80 causative gene mutations have been identified, mostly located on the SCN5A gene, encoding the pore-forming subunit of the cardiac sodium channel. The tremendous phenotypic variations within families and the overlap with other channelopathies illustrate the complex genetic heterogenity underlying this syndrome (1).

The diagnosis of Brugada syndrome is based on clinical and electrocardiographic features. Patients present with syncope or (aborted) sudden cardiac death due to malignant ventricular arrhy-thmias. No apparent structural heart disease can be found. Three different ECG patterns all featuring ST segment elevations in the right pre-cordial leads have been recognized:

Type I is the only pattern that is diagnostic of Brugada syndrome. It consists of a coved type ST segment elevation greater than 2mm, followed by a descending negative T wave in at least one right precordial lead V1-V3.

Types II and III are saddleback-shaped patterns, with a high initial augmentation followed by an ST elevation greater than 2mm for type II and less than 2mm for type III. Both patterns are suggestive of but not diagnostic of Brugada syndrome (2).

Multiple case reports of ECG patterns that mimic those of Brugada syndrome have been published. Possible causes of ST segment elevation in the right precordial leads are: drugs (class Ic and Ia, verapamil, Ca channel blockers), acute ischemia in RVOT, hyperthermia and hypothermia, elevated insulin level, etc.

Recent studies illustrate the dynamic character of these ECG patterns. Whenever a large number of baseline ECGs was available during the

follow-up, the diagnostic pattern could be documented in approximately 25% of the tracings. Because the presence of the spontaneous coved type I ECG pattern is thought to be a useful predictor of future arrhythmic events in asymptomatic patients, these findings are of great clinical importance (3). The class IC antiarrhythmic drug test provided a tool to unmask these concealed forms. Intravenous administration of ajmaline, flecainide or procainamide was able to elicit the diagnostic coved-type Brugada syndrome ECG pattern (4). On the basis of the results of comparative studies and clinical experience, ajmaline, in a dose of 1mg/kg, is considered to be the preferred drug. Recently, the full stomach drug test was proposed as an alternative tool in diagnosing Brugada syndrome. The episodes of syncope and sudden death are caused by fast polymorphic ventricular tachycardia or ventricular fibrillation. These arrhythmias appear with no warning. The first patient with Brugada syndrome was seen in 1986. Indigenous populations of Asia knew about the problem for many decades. In the Philippines the problem was known as "bangungut", in Japan as "pokuri" (unexpected sudden death during sleep). Currently, more than 70 SCN5A mutations have been linked to Brugada syndrome, all creating an impaired sodium influx. The loss of function SCN5A mutations also have been described as being responsible for Lev-Lenegre disease, or progressive conduction defect. This phenotypic overlap is illustrated by the frequent occurrence of conduction abnormalities in patients with Brugada syndrome. In addition, SCN5A was previously shown to be the cause of LQT3 syndrome, a form of Romano-Ward long QT syndrome. The differences in the clinical findings between LQT3 and Brugada are due to the different biophysical features dictated by the position of the mutations within the gene (5).

Case report

Patient D.A. was admitted to the Clinic of Cardiovascular Diseases because of a sudden onset of weakness. Patient was sent from private clinic where an ECG was performed which showed changes in the form of a right bundle brunch block (Figure 1). Patient did not previously suffer from any disease nor had surgery. His father died from myocardial infarction at the age of 47; his mother and sister did not report any significant illness. He was immediately admitted to coronary care unit and was monitored. Complete laboratory analyses were performed which showed no deviation from normal values. New ECG was recorded and it showed right bundle branch block with ST-segment elevation of 2mm in leads V1-V3 (Figure 1). D-dimer and troponin were within normal ranges. Echocardiography was performed one day after admission and it showed a normal structure of the atria and ventricles, with preserved global and regional wall motion of the left ventricle and normal valvular apparatus and ejection fraction of 65%. The patient was monitored for 48h after which it was decided that 24-hours Holter monitoring should be repeated. The obtained tracings showed that the average heart rate was 48/min, the minimal heart rate was 39/min and maximal was 90/minutes. During monitoring, the patient was in sinus rhythm. It was decided that a two-chamber frequency adaptive cardioverter defibrillator DDDR pace-maker should be implanted. On the next day, in a local anesthesia after a preparation of cephalic vein, one electrode was placed at the top of the right ventricle, and through the same vein the second electrode was placed in the right atrial appendage (Figure 2). The patient received antibiotics for another 4 days and he was discharged in good general health. After 2 weeks, stitches were removed and the patient was advised to undergo genetic mapping for SCN5A gene. After one month, at the second clinical control, the patient showed results of genetic mapping for SCN5A gene which was positive.

Asymptomatic patients may be diagnosed when the atypical ECG pattern is detected during routine examination. This ECG pattern cannot be distinguished from that in symptomatic patients. In others, the characteristic ECG pattern is recorded during screening after the sudden death of a family member with this syndrome. On the other hand, another group of symptomatic patients have been diagnosed after suffering syncope and ventricular fibrillation. Subsequently, some of these patients are correctly diagnosed at

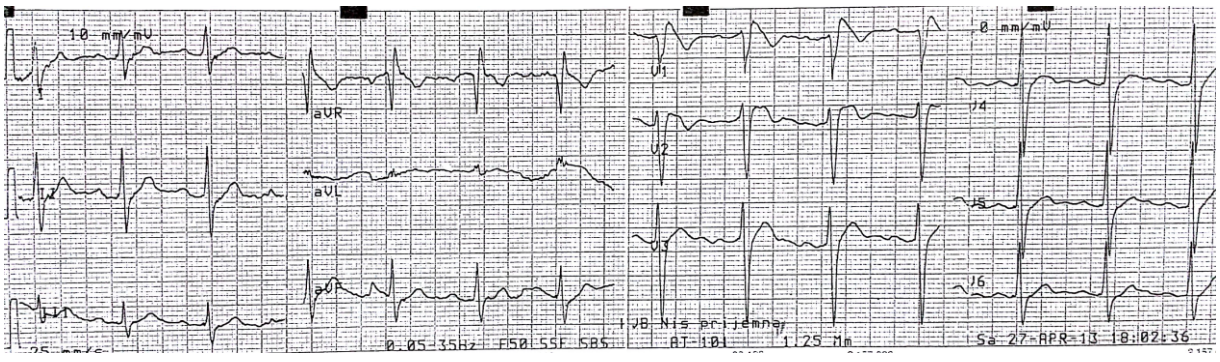

Figure 1. ECG with signs of Brugada syndrome type I

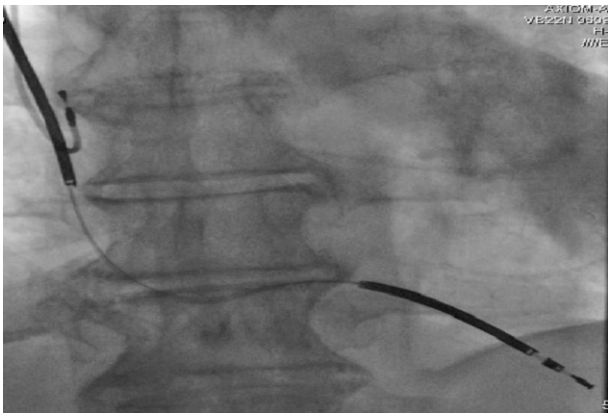

Figure 2. Two-chamber ICD

follow-up when ECG pattern changes spontaneously from normal to the typical pattern for the syndrome. This is also the case for those persons in whom the disease is unmasked by the administration of an antiarrhythmic drug given for other arrhythmias, e.g. atrial fibrillation (6).

Quinidine and dimethyl lithospermate B (Danshen extract) have been suggested as drugs that reduce the tendency for ventricular arrhythmias. Larger patient groups and longer follow-up periods are necessary to evaluate these products (6-8).

Conclusion

ICD implantation is an option for the patients with Brugada syndrome and ventricular tachycardia or fibrillation. Extensive research is ongoing to find alternative pharmacological options for these patients, especially for patients in whom ICD implantation is contraindicated for various reasons.

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BRUGADA SINDROM

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Brugada sindrom je 1992. godine uveden kao novi klinički entitet, sa tipičnim promenama na ST segmentu u desnim prekordijalnim odvodima koji povećavaju vulnerabilnost za letalne ventrikularne aritmije. Dijagnoza Brugada sindroma je bazirana na tipičnim EKG promenama. Nekoliko studija je pokazalo dinamičnost EKG promena, ali je dijagnoza na osnovu karakterističnih EKG promena postavljena u 25% slučajeva. Prezentacija EKG promena tipa I Brugada sindroma je značajni prediktor asimptomatskih bolesnika i od velikog kliničkog značaja. Implantacija ICD je terapijska opcija za bolesnike sa Brugada sindromom i VT ili VF. Dalja istraživanja su neophodna radi alternativne medikamentne terapije, naročito onih bolesnika kod kojih je ICD implantacija kontra-indikovana iz različitih razloga. *Acta Medica Medianae 2015;54(2):37-40.*

Ključne reči: *Brugada sindrom, ICD implantacija*