An autopsic examination case of diagnosed Brugada syndrome

Satoshi Furukawa¹, ⁴, Satomu Morita¹, Hayato Okunaga¹, Lisa Wingenfeld¹, Akari Takaya¹, Tokiko Nakagawa¹, Ikuo Sakaguchi¹, Yoshio Yamamoto², Takasi Ashihara³, Minoru Horie³, Katsuji Nishi³, Masahito Hitosugi¹

¹Department of Legal Medicine, Shiga University of Medical Science, Shiga, Japan
²Iga Research Institute of Mie University, Mie, Japan
³Department of Cardiovascular and Respiratory Medicine, Shiga University of Medical Science, Shiga, Japan
⁴Department of Legal Medicine, Shiga University of Medical Science, Setatsukinowa, Otsu City, Shiga 520-2192, Japan

Email address:
31041220@belle.shiga-med.ac.jp (S. Furukawa)

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Abstract: Brugada syndrome is a cardiac disorder characterized by typical ECG alterations, and it is associated with a high risk for sudden cardiac death, affecting young subjects with structurally normal hearts. The prevalence of this disorder is still uncertain, presenting marked geographical differences. The syndrome has a genetic basis, and several mutations have been identified in genes encoding subunits of cardiac sodium, potassium, and calcium channels, as well as in genes involved in the trafficking or regulation of these channels. We experienced an autopsy case of the sudden death by diagnosed Brugada syndrome. We present the case report and autopsic findings.

Keywords: Brugada Syndrome, Sudden Death, Coved and Saddleback Type ST Elevation, Autopsy, Histological Findings

1. Introduction

Brugada syndrome (BS) has originally been described as an autosomal-dominant inherited arrhythmic disorder characterized by ST elevation with successive negative T wave in the right precordial leads without structural cardiac abnormalities [1,2]. Patients are at risk for sudden cardiac death (SCD) due to ventricular fibrillation (VF). Since 1953, the ECG pattern similar to coved-type ST-segment elevation was reported as a normal variant in the healthy population or related to VF with structural abnormality [3-5]. BS is a genetically determined disease, characterized by typical electrocardiographic signs, and it predisposes to sudden cardiac death (SCD) secondary to polymorphic ventricular tachycardia (PVT)/ventricular fibrillation (VF) in the absence of structural heart disease. It was first described in 1992 by Pedro and Josep Brugada [1]. Brugada and Brugada linked an abnormal ECG with right bundle branch block pattern and coved-type ST elevation over the right precordial leads to primary ventricular fibrillation (VF) and sudden cardiac death (SCD) in patients with structurally normal hearts [1]. It instantly became known as Brugada syndrome (BS) and has drawn the worldwide attention of cardiologists, electrophysiologists and molecular biologists/geneticists. We present an autopsy case of diagnosed BS.

2. Case Report

A 33-year-old man was found lying on the floor in his house. He had pointed the electrocardiogram (ECG) abnormality five years before in the medical examination. The ECG showed the coved and saddleback type ST elevation in leads V1 through V3. (Figure 1) His mother was dead of unknown origin in her thirties. The ECG classified the Brugada pattern and he diagnosed Brugada syndrome.

The autopsy was performed on the day following death. The body was 162 cm in height and 63.8 kg in weight. Postmortem lividity was large in his back. A large number of
petechia in the conjunctiva was also recognized. (Figure 2)
The heart weighed 297.7g.

Autopsy findings revealed that the intervals of cardiac cells were wide to each other, and there were inflammation, small hemorrhage and fibrosis in the right ventricle especially. (Figure. 3-6)

3. Discussion

The clinical spectrum of the BS patient ranges from asymptomatic to SCD [6].

Patients may have a late onset of VF, despite having had an abnormal ECG pattern for decades [6,7]. Syncope or seizures because of self-terminating VF episodes are also common, as are agonal respiration and difficulty in arousal at night, again caused by self-terminating VF episodes [6,7]. The majority of BS patients are relatively young, between 20 and 40 years of age, but the youngest patient diagnosed with the syndrome was 2 days old and the oldest 84 years [6,8]. Despite an autosomal dominant inheritance pattern, BS prevalence is up to 10-fold higher in males and with greater severity [7,9]. Worldwide, the syndrome is probably responsible for 4-12% of all sudden deaths and at least 20% of sudden deaths in patients with structurally normal hearts [2,6]. There is also a difference between the incidence of the Brugada type 1 ECG pattern and the syndrome itself, as defined by the 2005 Consensus criteria. Miyasaka et al observed a type 1 Brugada ECG pattern in 12 per 10,000 inhabitants; type 2 and 3 ECGs were more prevalent, appearing in 58 per 10,000 inhabitants [10]. The prevalence of a Brugada ECG is higher in Asia (0.36%) and Europe (0.25%) than in the USA (0.03%) [11]. However, the true prevalence of BS is unknown because the ECG pattern can be wax and wane, making it very likely that the true incidence is underestimated.
Proven to be good risk factors, except for a history of VT/biphasic T-wave. This ST-T segment morphology is phase 0 of the action potential (AP), causing slow protein, sarcolemma, because of decreased expression of the sodium channel.

J-point elevation without ST elevation ≥1 mm. ST elevation ≥2 mm without T-wave inversion. Type 3 pattern shows a J-point elevation without ST elevation ≥1 mm.

The diagnostic criteria of BS consist of 2 parts: (1) detection of the typical ECG abnormality and (2) clinical characteristics [6]. The 2 Brugada consensus reports classified the Brugada ECG pattern into 3 types (Table 1): (1) type 1 pattern has ST elevation ≥2 mm, giving rise to a coved-type ST-segment, in electrical continuity with a negative T-wave and without a separating isoelectric; (2) type 2 has a high take-off ST-segment elevation. In this variant, the J-point elevation (≥2 mm) gives rise to a gradually descending elevated ST-segment (remaining >1mm above the baseline) and a positive or biphasic T-wave. This ST-T segment morphology is referred to as the saddleback type; (3) type 3 is the coved-or saddleback-type with <1 mm ST-elevation ST-segment elevation [2,6]. In conjunction with the ECG abnormality, 1 of the following criteria is necessary: (1) a history of VT/VF, (2) a family history of SCD, (3) a family history of coved-type ECG, (4) agonal respiration during sleep, or (5) inducibility of VT/VF by programmed electrical stimulation (PES). In 1998, Chen et al reported the first case of diagnosed BS.

In recent years, it has become clear that the right ventricular outflow tract (RVOT) is the likely arrhythmogenic substrate site, and the RVOT is the only cardiac structure lying just beneath the second and third intercostal spaces. The consensus reports recommend the following clinical manifestations: (1) history of spontaneous VT/VF episode or aborted SCD; (2) family history of SCD or coved-type ECG; (3) agonal respiration during sleep; or (4) inducibility of VT/VF by programmed electrical stimulation (PES). In 1998, Chen et al reported the first mutation, linked to BS, in the SCN5A gene, which encodes for the α-subunit of the sodium channel [12]. Since then, there have been an increasing number of gene mutations identified [6,11,13].

Functional studies demonstrate that SCN5A mutations in BS patients cause loss of function of the sodium channel because of decreased expression of the sodium channel protein, sarcolemma, expression of non-functional channels or altered gating properties (delayed activation, earlier inactivation, faster inactivation, enhanced slow inactivation and delayed recovery from inactivation) [14-20]. The loss of function of the sodium channel results in a decrease in the sodium current, which in turn impairs the fast upstroke of phase 0 of the action potential (AP), causing slow conduction in the heart.

Even though SCN5A mutations are the most common type found in 11–28% of BS probands, the genetics of BS have become heterogeneous. In addition to the SCN5A mutations, more mutations are found in the gene encoding the proteins of the potassium and calcium channels. SCN5A mutations may cause not only BS but other diseases as well. Indeed, SCN5A mutations have also been associated with long QT syndrome, cardiac conduction disease, sick sinus syndrome, atrial fibrillation (AF), and dilated cardiomyopathy with overlap syndromes identified in specific families [16, 21-25]. We reported the autopsy case of diagnosed BS.

Table 1. Three types of Brugada ECG patterns.

| Type 1 | Brugada Pattern |
| Type 2 | Brugada Pattern |
| Type 3 | Brugada Pattern |

Type 1 is a coved-type pattern and type 2 is a saddleback-type, which has ST elevation ≥2 mm without T-wave inversion. Type 3 pattern shows a J-point elevation without ST elevation ≥1 mm.

References


