Vagal Stimulation Induces Brugada Syndrome-like J-ST Segment Elevation in Electrocardiography

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Abstract

Brugada syndrome is a sudden cardiac death syndrome due to ventricular fibrillation (Vf). Vagal activity increase has been clinically described as contributing to the occurrence of Vf in this syndrome. However, significance of vagal stimulation remains unclear. We experienced a case with Brugada syndrome-like electrocardiographic (ECG) morphology which might have been induced by vagal stimulation increase. Therefore, we attempted to experimentally confirm it in canine model.

The patient was a 53-year-old male. Pilsicainide (1 mg/kg) was intravenously administrated to make the diagnosis that the origin of his Vf was included to Brugada syndrome. Though the ECG remained unchanged following the administration of pilsicainide, typical Brugada syndrome-like ECG, with the coved type ST segment elevation was induced and was accompanied by nausea and vomiting. In one out of 3 canines enrolled, typical Brugada syndrome-like ECG morphology was induced when vagal nerve was stimulated. The degree of elevation of the J point (terminal of QRS and ST segment) and ST segment was varied according to the strength of vagal stimulation. We learned that the typical Brugada syndrome-like ECG morphology was inducible with vagal stimulation in a part.

Key words

Brugada syndrome, vagal stimulation, electrocardiography, sudden cardiac death

INTRODUCTION

Brugada syndrome ¹) is a sudden cardiac death syndrome due to ventricular fibrillation (Vf), which occurs in middle aged men without any evidence of obvious heart disease. The mechanism of this syndrome is believed to be due to heterogeneity of the action potential which is observed between the right ventricular myocytes located on the epicardial side and those located on the endocardial side, and is based on Na channel gene, SCN5A, mutation. On the other hand, vagal activity increase has been clini-
cally described as contributing to the occurrence of Vf in this syndrome 2–5. However, significance of vagal stimulation remains unclear. We experienced a case with Brugada syndrome-like electrocardiographic (ECG) morphology which might have been induced by vagal stimulation increase. Therefore, we attempted to experimentally confirm whether or not vagal stimulation induces the Brugada syndrome-like ECG morphology.

**CASE REPORT**

The patient was a 53-year-old male who had experienced repeated episodes of syncope over 6 months. He was then admitted to examine the cardiogenic origin of his symptoms. A neurological origin had already been ruled out by Tilt-up test, cranial MRI, and electroencephalography. Although the Holter monitoring and echocardiogram exhibited normal findings, a treadmill test and coronary angiogram revealed ischemic heart disease (with a 75% stenosis of the right coronary artery) without symptoms. But the left and right ventriculography showed that there was normal cardiac function. Percutaneous transluminal coronary angioplasty (PTCA) to the right coronary artery stenosis was successful. An electrophysiological study (EPS) was performed one week after the PTCA. Ventricular fibrillation (Vf) was repeatedly induced by ventricular extra-stimulus method (2 paired extra-stimuli).

Pilsicainide (1 mg/kg) was intravenously administrated to make the diagnosis that the origin of his Vf was included to Brugada syndrome. Though the ECG remained unchanged following the administration of pilsicainide (Fig. 1), typical Brugada syndrome-like ECG, with the coved type ST segment elevation in the right precordial leads was induced and was accompanied by nausea and vomiting (Fig. 2). One week later, pilsicainide administration was attempted again. Neither vomiting nor significant ST segment elevation was exhibited. He was diagnosed with Brugada syndrome, and an implanted cardioverter defibrillator (ICD) was implanted.

**EXPERIMENT**

Because Brugada syndrome-like ECG morphology was induced when he was nauseous and vomited, we believed that the induction of that ECG morphology might have been related to autonomic stimulation. Therefore, we experimentally confirmed in the canine model that the Brugada syndrome-like ECG morphology was induced by vagal stimulation. A standard 12 lead ECG was recorded in an anesthetized canine (pentobarbital 30 mg/kg iv), and positive pressure respiration was applied. The ECG was recorded in the supine position, using EPLab (Quinton Electrophysiology Co., Canada). After opening the cervical wall, an electrical stimulation system was attached to the right vagal nerve with specially designed needle electrodes. The various strengths of

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**Fig. 1** Electrocardiography (right precordial leads) before and 5 minutes after administration of pilsicainide (1 mg/kg).

**Fig. 2** Development of the typical Brugada syndrome-like electrocardiographic morphology (lead V2) when nausea and vomiting occurred: Artifact due to postural change.
the stimulation used were 3.3 Hz – 5 V, 5 Hz – 5 V, and 10 Hz – 5 V for a 20 second interval. Each application was for an interval of greater than one minute. A BC-03 Cardiac Stimulator (FUKUDA DENSHI CO LTD, Tokyo Japan) was used for the stimulation.

In one out of 3 canines enrolled, typical Brugada syndrome-like ECG morphology was induced when the vagal nerve was stimulated. The degree of elevation of the J point (terminal of QRS and ST segment) and ST segment was varied according to the strength of vagal stimulation (Fig. 3).

From this experiment, we learned that the ECG morphology, which was altered by the vagal stimulation, was likely due to Brugada syndrome in a part of canines.

**DISCUSSION**

Vagal stimulation induces the sinus bradycardia and the atrio-ventricular block. Direct effect of vagal stimulation on the ventricles was demonstrated by Litovsky et al. However, it is not known whether or not vagal stimulation has an affect on the morphology of QRS complex and ST-T wave on the body surface ECG. From the clinical evidences of patients with Brugada syndrome, the increase in the vagal nerve activity has been shown to contribute to the ST segment elevation and the occurrence of Vf. The ST segment elevation in this syndrome is explained by a genetic Na channel disturbance in the myocardium. Namely, between the myocytes of the epicardium and those of the endocardium, in which there is a distinction of transient outward current (Ito) density which forms the early phase of the action potential (phase 1), thus causing an inactivation of the Ca current activity, resulting in shortening of the action potential of the epicardial sided myocyte. This distinction of phase 2 and 3 causes the Brugada syndrome-like ST segment elevation on the ECG. An increase in the vagal nerve activity possibly causes the decrease in the Ca current, therefore it may contribute to the ST segment elevation. In the present case, pilsicainide, pure Na channel blocker, did not unmask the ST segment elevation, but did induce nausea and vomiting. Furthermore, in our canine model the Brugada syndrome-like ST segment was revealed by vagal stimulation. In the genetic studies of Brugada syndrome, a gene mutation related to Ito current and Ca current has not been confirmed. It should be noted that Brugada syndrome-like ECG morphology is inducible only by vagal stimulation.

**CONCLUSION**

We experienced a case with repeated episodes of syncope that was caused by Brugada syndrome which was possibly unmasked by vagal stimulation. We then experimentally confirmed the influence of vagal stimulation on the ECG morphology using the canine model. We learned that the typical Brugada syndrome-like ECG morphology was inducible with vagal stimulation in a part.

**References**


抄 録

迷走神経刺激による Brugada 症候群様心電図波形の誘発

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Brugada 症候群は心臓性突然死と関連する症候群である。臨床的に迷走神経緊張促進因子であることが考えられているが、その神経刺激の意義は明確ではない。Brugada 症候群様心電図波形の発現に迷走神経刺激が関与したと考えられた例を経験したので、犬を用いて実験的に確認した。

症例は 53 歳の男性で、Brugada 症候群の診断のためにビルジカイニド (1 mg/kg) が投与された。心電図は変化しなかったが、悪心と嘔吐があった。それに伴い、典型的な Brugada 症候群様波形が見られた。

犬の実験では、3 頭中 1 頭で、電気的迷走神経刺激による Brugada 症候群様波形の誘発が見られた。J 点（QRS–ST 部分移行部）と ST 部分の上昇の程度は迷走神経刺激強度依存した。典型的な Brugada 症候群様波形が迷走神経刺激により誘発される例があることがわかった。

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