Infant Case with a Malignant Form of Brugada Syndrome

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Infant with Brugada Syndrome. We report a 6-month-old Japanese infant with a malignant form of Brugada syndrome, who had frequent episodes of ventricular fibrillation (VF) and nonsustained polymorphic ventricular tachycardia (VT). To the best of our knowledge, this infant is the youngest patient reported to have Brugada syndrome. Continuous infusion of a β-adrenergic agonist and intravenous injection of a parasympathetic antagonist suppressed the electrical storm of polymorphic VT and VF. Combined oral administration of a β1-adrenergic agonist, a parasympathetic antagonist, and quinidine has successfully suppressed recurrences of VT or VF for 6 months, and the combination may have the potential to decrease the incidence of VT or VF as an adjunctive therapy with prophylactic placement of an implantable cardioverter defibrillator. (J Cardiovusc Electrophysiol, Vol. 11, pp. 1277-1280, November 2000)

Introduction

In 1992, Brugada and Brugada1 described eight patients, including three children, who had a history of aborted sudden cardiac death due to ventricular fibrillation (VF), right bundle branch block, and specific ST segment elevation in the right precordial leads (V1 to V3) in the absence of any structural heart disease. Brugada syndrome is observed more often in male adults from Asian countries, including Thailand and Japan, than in the United States or European countries.2-14 At present, there is no specific pharmacologic treatment to prevent sudden death in patients with the Brugada syndrome.4 In this report, we describe a 6-month-old Japanese infant with a malignant form of Brugada syndrome, who had frequent episodes of VF and nonsustained polymorphic ventricular tachycardia (VT). The electrical storms of VF and polymorphic VT were treated successfully with intravenous administration of a β-adrenergic agonist (isoproterenol) and a parasympathetic antagonist (atropine).

Case Report

A 6-month-old male Japanese infant, one of a pair of dizygotic twins, was admitted to our hospital because of recurrent episodes of cyanosis after crying. The other twin died unexpectedly during sleep at the age of 4 months. The ECG findings appeared normal in all family members in whom standard 12-lead ECG could be performed. The patient was 61 cm tall (−2.1 SD) and weighed 6.3 kg (−1.4 SD). Results of physical examination were normal. Electrolyte levels were as follows: sodium 145 mEq/L, potassium 4.6 mEq/L, chloride 113 mEq/L, and calcium 4.1 mg/dL. He had normal chest X-ray films and echocardiograms. Magnetic resonance image revealed no abnormal findings in the right and left ventricles. Twelve-lead ECG at admission showed coved-type ST segment elevation in leads V1 and V2, prominent J wave in leads V1 to V6, and normal corrected QT intervals (387 msec17) (Fig. 1). Nonsustained polymorphic VT was recorded 734 times a day by Holter monitoring and were recorded more frequently during sleep than while awake (Fig. 2). DC cardioversion was needed to terminate polymorphic VT or VF that did not terminate spontaneously. Recurrent VF, family history of sudden death, ST segment elevation in leads V1 and V6, and absence of organic heart disease established a diagnosis of Brugada syndrome. Intravenous administration of propranolol 1.3 mg/kg per day increased the amplitude of ST segment elevation in leads V1 and V2 (Fig. 3A), as well as the incidence of polymorphic VT (1,144 times a day). Immediately after continuous infusion of MgSO4 (0.3 mg/kg per min), polymorphic VT developed with syncope. Intravenous injection of a Class IB antiarrhythmic drug (mexitelaine) did not change the amplitude of ST segment elevation or J wave, and resulted in only a slight decrease in the incidence of polymorphic VT and VF (343 times a day). In contrast, continuous infusion of a β-adrenergic agonist (isoproterenol), as well as intravenous injection of a parasympathetic antagonist (atropine), dramatically decreased the amplitude of ST segment elevation and J wave, and totally suppressed polymorphic VT and VF. Therefore, we started oral administration of a β1-adrenergic agonist, denopamine (0.44 mg/kg per day), atropine (0.05 mg/kg per day), and quinidine (6.2 mg/kg per day). The amplitude of ST segment elevation in leads V1 and V2, and J wave in leads V5 to V6 was decreased prominently compared with that of the baseline ECG (Fig. 3B). Prophylactic placement of an implantable cardioverter defibrillator was performed in this

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Manuscript received 17 March 2000; Accepted for publication 30 June 2000.
Figure 1. Twelve-lead ECG recorded at admission in the absence of treatment. Coved-type ST segment elevation in leads V1 and V2 and prominent J wave in leads V4 to V6 are seen.

Discussion

Brugada syndrome, which originally was reported by Brugada and Brugada\(^1\) in 1992, is considered to be a subgroup of idiopathic VF. A considerable number of patients with Brugada syndrome have been reported, mainly from Asian countries, and >80\% of those were adult males (44 ± 22 years).\(^2-14\) Likewise, a familial occurrence has long been recognized. Mutations in the cardiac ion channel gene were identified in patients with Brugada syndrome.\(^15\) Thus, Brugada syndrome is one of the highlighted forms of inherited arrhythmias that may cause sudden cardiac death in the adult population. However, the incidence of Brugada syndrome in children is very rare despite the findings that 3 of 8 patients in the report by Brugada and Brugada were children. Two of the children were siblings who each had the first episode of aborted sudden death at the age of 2 years. The other child was an 8-year-old girl. To the best of our knowledge, the youngest reported patient with Brugada syndrome was a 14-month-old girl.\(^16\) Thus, this case reports the youngest patient documented to have Brugada syndrome. Moreover, the other twin died suddenly during sleep at the age of 4 months, which suggests that Brugada syndrome should be recognized as being related to sudden cardiac death and syncope, even in infants and children.

Recent experimental studies by Yan and Antzelevitch\(^17,18\) suggested that an increase in an \(I_{Ca}\)-mediated phase 1 notch and a subsequent loss of the action potential (AP) dome in the right ventricular epicardium, but not the endocardium, produce a transmural voltage gradient, resulting in ST segment and J point elevation in the right precordial leads. Moreover, heterogeneous loss of the AP dome in the epicardium predisposes the right ventricle to development of phase 2 reentry, giving rise to premature beats that initiate VF. Because maintenance of the AP dome is determined by the balance of currents active at the end of phase 1 of the AP (principally \(I_{Na}\), \(I_{K}^{\alpha}\), and \(I_{Na}\)), any agents that cause an outward shift in current active at the end of phase 1 (e.g., augmenting \(I_{Na}\) and suppressing \(I_{Ca}\) and \(I_{Na}\)) can increase the magnitude of the AP notch and lose the AP dome in the epicardium, resulting in ST segment and J point elevation.\(^3,7\) In our patient, both \(\beta\)-adrenergic agonists (isoproterenol and denopamine) and a parasympathetic antagonist (atropine) decreased the amplitude of the ST segment and J wave, as well as suppressed VT and VF. These findings are consistent with the clinical observation that ST segment elevation in patients with Brugada syndrome is reduced or totally normalized after administration of \(\beta\)-adrenergic agonists.\(^19\) Quinidine was effective in decreasing ST segment elevation and suppressing VF, which was similar to the success of Belhassen et al.\(^19\) However, a \(\beta\)-adrenergic antagonist (propranolol) and MgSO\(_4\) aggravated ST segment elevation and the incidence of VT and VF. These findings are consistent with the clinical study that beta blockers are ineffective for Brugada syndrome.\(^20\) \(\beta\)-Adrenergic agonists and parasympathetic antagonists augment \(I_{Ca}\), quinidine blocks...
I\textsubscript{Ca} and \(\beta\)-adrenergic antagonists and MgSO\textsubscript{4} suppress I\textsubscript{Ca}. Thus, our data parallel the results of the experimental studies by Yan and Antzelevitch.\textsuperscript{17,18} Our case shows that intravenous administration of isoproterenol and/or atropine may be the therapy of choice to suppress the electrical storm of VT or VF in patients with Brugada syndrome. Our data also indicate that oral therapy with denopamine, atropine, and quinidine may have the potential to decrease the incidence of VT or VF as an adjunctive therapy with prophylactic placement of an implantable cardioverter defibrillator.

Acknowledgments: We are grateful to Dr. Wataru Shimizu of the National Cardiovascular Center for his important suggestions regarding the management of our patient and his scientific contributions to this case report. We extend many thanks to Professor Makoto Uchiyama and Dr. Seiichi Sato for their constant support.

References


