Flecainide Suppresses Bidirectional Ventricular Tachycardia and Reverses Tachycardia-Induced Cardiomyopathy in Andersen-Tawil Syndrome

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BVT and Andersen-Tawil Syndrome. Bidirectional ventricular tachycardia (BVT), although a rare arrhythmia in the general population, is frequently observed in patients with Andersen-Tawil syndrome and long QT interval. However, the pharmacologic treatment of this arrhythmia remains unknown. In the present study, we documented the favorable antiarrhythmic action of flecainide in a young woman with sustained BVT and Andersen-Tawil syndrome. She presented with incessant BVT that could only be terminated with flecainide. During sinus rhythm, a prolonged QT interval was observed. Genetic studies revealed a mutation in the K+ channel gene KCNJ2. Over a 4-year follow-up period, recurrence of her arrhythmia occurred twice. The first episode was due to noncompliance and resolved with resumption of flecainide therapy. The second recurrence was associated with a tachycardia-induced cardiomyopathy and resolved when the dose of flecainide was increased from 200 to 300 mg daily. This report suggests that flecainide can be effective in controlling BVT associated with Andersen-Tawil syndrome and indicates that the left ventricular dysfunction is secondary to the arrhythmia and not due to an associated phenotypic manifestation of the disorder. (J Cardiovasc Electrophysiol, Vol. 19, pp. 95-97, January 2008.)

Case Report

A 16-year-old female was referred for evaluation of sustained bidirectional ventricular tachycardia (BVT) associated with dizziness. The patient had no known heart disease, was on no medications, and had no family history of heart disease or sudden death. Physical examination was normal except for mild symmetric lower extremity weakness. Serum laboratory assessments, chest x-ray, echocardiography, and cardiac magnetic resonance imaging were all normal. On admission, an electrocardiogram showed BVT with alternating QRS complexes (Fig. 1). Atrial and ventricular transesophageal stimulation failed to terminate the arrhythmia. Multiple drugs given intravenously were also unsuccessful, including lidocaine, propranolol, diltiazem, potassium chloride, and magnesium sulfate. Administration of oral flecainide 100 mg twice a day suppressed the arrhythmia and allowed resumption of sinus rhythm with a distinct long QT interval and biphasic T waves (Fig. 2). Genetic analysis demonstrated an R67W mutation in the K+ channel gene KCNJ2. The patient refused ICD implantation and was discharged on oral flecainide 100 mg twice a day suppressing the arrhythmia. Multiple drugs given intravenously were also unsuccessful, including lidocaine, propranolol, diltiazem, potassium chloride, and magnesium sulfate. Administration of oral flecainide 100 mg twice a day suppressed the arrhythmia and allowed resumption of sinus rhythm with a distinct long QT interval and biphasic T waves (Fig. 2). Genetic analysis demonstrated an R67W mutation in the K+ channel gene KCNJ2. The patient refused ICD implantation and was discharged on oral flecainide 100 mg twice a day suppressing the arrhythmia.

During a 4-year follow-up period, the patient had two recurrences of BVT. The first episode was due to noncompliance and the arrhythmia disappeared when the patient resumed flecainide treatment. The second episode occurred 3 years later while on flecainide and was associated with congestive heart failure and globally depressed left ventricular function (ejection fraction 25%). The arrhythmia was controlled when the daily dose of flecainide was increased to 300 mg. A repeat echocardiogram obtained 3 months later showed a normal left ventricular function (ejection fraction 55%), consistent with a tachycardia-induced cardiomyopathy.

Discussion

Bidirectional ventricular tachycardia (BVT) is a rare arrhythmia, characterized by QRS complexes with alternating morphologies.1-3 The more common type of BVT is a pattern of right bundle branch block with alternating left anterior and left posterior hemiblock.2 Bidirectional VT can occur during digitalis toxicity,1,2 but in some patients no obvious abnormalities are found.3

Recently, this arrhythmia has been reported in patients carrying a mutation of the KCNJ2 gene located in the chromosome 17q23, causing variable phenotypic abnormalities known as Andersen-Tawil syndrome.4,5 This gene encodes for the α subunit of the potassium channel Kir2.1, resulting in a prolonged QT interval, BVT, torsades de pointes, and periodic paralysis.6 Andersen-Tawil syndrome can present as an autosomal dominant or sporadic disorder.7,8 Ventricular arrhythmias associated with the Andersen-Tawil syndrome are characteristically aggravated during hypokalemia, and some patients can develop ventricular fibrillation.9 Although

This study was supported by an MDA grant.

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Manuscript received 16 April 2007; Revised manuscript received 25 May 2007; Accepted for publication 29 May 2007.

doi: 10.1111/j.1540-8167.2007.00910.x
flecainide has been recently reported to be effective in treating polymorphic ventricular tachycardia in the Andersen-Tawil syndrome, however, effective pharmacologic treatment has not been reported. In the present case, flecainide suppressed BVT acutely and over a 4-year period, although it required close monitoring to reduce recurrences. The mechanism by which flecainide suppressed BVT in our patient is not fully understood. However, calcium overload and sodium currents elicited by the sodium/calcium exchanger may explain the antiarrhythmic action of flecainide in our patient. In patients with Andersen-Tawil syndrome and BVT, the markedly prolonged QT interval is the result of a depressed I_{K1} current, leading to calcium overload and oscillations during the terminal phase of the action potential. These “late” oscillations distinguish Andersen-Tawil syndrome from other forms of long QT in which the oscillations occur during phase 2 or early phase 3 of the action potential. Therefore, intracellular calcium overload and triggered activity appear as the likely mechanisms for the arrhythmias associated with the Andersen-Tawil syndrome. In this regard, the sodium-calcium exchanger-dependent “late” oscillatory potentials (delayed after depolarizations) resemble those observed during digitalis toxicity under experimental conditions. In fact, tetrodotoxin (a specific and potent sodium channel blocker) reduces calcium overload and arrhythmias associated with digitalis intoxication. Therefore, a common mechanism, i.e., calcium overload and enhanced sodium-calcium exchange, may explain the presence of BVT during both digitalis toxicity, as well as in patients with Andersen-Tawil syndrome. Under these conditions, the sodium/calcium exchanger may not be able to effectively exchange sodium for calcium, leading to calcium overload and oscillations during the terminal phase of the action potential.
conditions, a potent sodium channel blocker like flecainide can reduce the oscillatory potentials that initiate BVT. In support of this hypothesis, in rabbit myocardium, inhibition of sodium channels by flecainide and other class I antiarrhythmic drugs alter the sodium-calcium exchange, resulting in a decrease in calcium through the exchanger and the calcium content in the sarcoplasmic reticulum.

The present case also demonstrates that flecainide can not only eliminate sustained BVT in the Andersen-Tawil syndrome, but also can normalize the depressed left ventricular function, suggesting that these patients can develop a tachycardia-induced cardiomyopathy. This observation suggests that the left ventricular dysfunction is not necessarily another phenotypic manifestation of this entity, but rather the result of an incessant ventricular arrhythmia.

References

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