Unusual response to the ajmaline test in a patient with Brugada syndrome

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We present a Brugada syndrome patient who suffered an aborted sudden death. The ajmaline test (1 mg/kg body weight) induced accentuated alternans ST-segment elevation in V1–V2 without ventricular arrhythmias. It could represent silent ischaemia not detected before, failure of myocardial regions to repolarize in alternate beats due to transmural dispersion of conduction and refractoriness in the right ventricular outflow tract or a rate dependent sodium channel block by ajmaline.

We need more studies to know whether this electrocardiographic sign is a risk factor for life-threatening ventricular arrhythmias in Brugada syndrome patients. (Europace 2003; 5: 371–373) © 2003 Published by Elsevier Ltd on behalf of The European Society of Cardiology.

Key Words: Brugada syndrome, ajmaline test, alternans ST-segment elevation.

Case report

Brugada syndrome (BS) is characterized by a right bundle branch block pattern with ST-segment elevation (STE) in V1–V3 leads and a propensity for episodes of sudden cardiac death or syncope caused by life-threatening cardiac arrhythmias in a structurally normal heart[1,2].

We present a patient who suffered an aborted sudden death by ventricular fibrillation (VF); electrocardiograms, effort and Holter tests, laboratory analysis, echocardiography study, coronary angiography and left ventriculography were all normal. The ajmaline test (1 mg/kg body weight) unmasked the electrocardiographic pattern, with marked alternans ST elevation in V1–V2 (Fig. 1), without ventricular arrhythmias. Programmed electrical stimulation (at three cycle lengths, 600, 500 and 400 ms, up to three extrastimuli from the right ventricular apex) was negative; HV was normal. The patient initially refused implantation of an automatic defibrillator, and therefore received amiodarone and propranolol for 4 years and 10 months, until implantation of a device 2 years ago. On follow-up, he is without drugs and recurrences.

Discussion

Although the electrocardiographic manifestations of the syndrome can transiently disappear, intravenous administration of ajmaline, procainamide and flecainide can reveal the electrocardiographic pattern[3,4]. There have been reports of accentuated ST elevation in right precordial leads and T wave alternans after intravenous administration of procainamide and pilocarpine in patients with BS, and also concomitant with vasospastic angina[5,6].

Alternans ST elevation is known to be a predictor of life-threatening ventricular arrhythmias[7,8]. Mechanisms of this electrocardiographic sign are not totally known; the relationships between it and myocardial ischaemia have been shown[9–11], and has explained the possible mechanism. This is failure of myocardial regions to repolarize in alternate beats due to variation in conduction and refractoriness between ischaemic and non-ischaemic myocardial zones[11]. Calcium transient alternans currents
are an important cause of electrical alternans during ischaemia, due to properties of intracellular calcium to regulate transmembrane currents and a variation in the duration of action potential from beat to beat [12,13]. Tachibana et al. [14] demonstrated that flecainide (sodium channel blocker) induced alternans ST elevation greater in epicardial than endocardial sites, and triggered VF in the intact canine heart. They found that verapamil did not suppress alternans ST elevation in their studies, but 4-aminopyridine did. This drug blocks $I_{to}$ (potassium current outward) therefore they concluded that potassium was most important for the alternans ST elevation in their cases. Others [15] had demonstrated before that 4-aminopyridine had an opposite effect to flecainide in the action potential mainly in epicardial cells, and this, therefore, supports the results of Tachibana et al.

Antzelevitch and others [16–19] demonstrated ionic mechanisms for the electrocardiographic pattern and actions of class I agents in the BS. The loss of the action potential dome in right ventricular epicardium but not endocardium underlies the ST elevation; and is dependent on the balance of currents active during phase 1 of action potential (principally $I_{to}$, $I_{Na}$, and $I_{Ca}$). Any agent capable of causing an outward shift in the current active at the end of phase 1 of right ventricular epicardium, increasing $I_{K}$ and/or decreasing $I_{Na}$ and $I_{Ca}$, can contribute to loss of the action potential dome and cause an accentuated dispersion of repolarization. Loss of the action potential dome in the right ventricular epicardium is thought to accentuate further the transmural voltage gradient and thus to create the arrhythmogenic substrate.

All of these conditions, effects of sodium channel blockers and potassium channel openers in the right ventricular epicardium and not in the endocardium provoking variation of conduction and refactoriness in the right ventricular outflow tract, can be seen in BS patients.

In the opinion of Antzelevitch (personal communication), ajmaline, because it dissociates from the sodium channel relatively slowly, produces a profound use-dependent block of the sodium channel that is rate dependent. The level of sodium channel block for a given beat is determined by the preceding diastolic interval. At specific rates, block leading to loss of the action potential dome in right ventricular epicardium can lead to a prolongation of the diastolic interval sufficient to reduce the sodium channel block for the next beat in

Figure 1 Twelve surface ECG leads during basal condition (left) and after administration of 70 mg of intravenous ajmaline (right). Note presence of accentuated alternans ST segment elevation in leads V1–V2.
some right ventricular epicardial sites. Less prominent STE would be expected. The shorter diastolic interval at these sites would now generate a more potent sodium channel block, facilitating loss of the action potential dome and more prominent STE. Alternans of the ST segment could thus be established.

In our patient, the ajmaline test unmasked the electrocardiographic pattern. We do not know exactly why STE displayed alternans. It could represent silent ischaemia not detected before, failure of myocardial regions to repolarize in alternate beats due to transmural dispersion of conduction and refractoriness in the right ventricular outflow tract or rate dependent sodium channel block by ajmaline.

We need more studies to know if alternans ST elevation is a risk factor for life-threatening ventricular arrhythmias in BS patients.

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References


