"Torsade de pointes" in a patient with variant angina

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Key words:
Angina;
Arrhythmias, ventricular;
Coronary spasm;
Torsade de pointes.

Ventricular tachyarrhythmias have been well documented in patients with variant angina. Episodes of torsade de pointes have been described infrequently.

We report a case of a 60-year-old male with a previous history of one vessel artery disease and a successful coronary angioplasty with stenting of the left anterior descending artery, who experienced an episode of angina at rest and electrocardiographic evidence of self-terminating torsade de pointes. After a negative coronary angiography and a positive hyperventilation test, the diagnosis of variant angina was considered and beta-blockers discontinued and calcium channel antagonists prescribed. No other episodes of angina were documented during the following 6 months of follow-up.

(Ital Heart J 2004; 5 (7): 554-558)

Received January 29, 2004; accepted February 25, 2004.

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Introduction

Variant angina may be associated with serious complications such as myocardial infarction, ventricular tachyarrhythmias, and sudden cardiac death.

Although episodes of polymorphic ventricular tachycardia (VT) have been well documented, episodes of torsade de pointes have rarely been described. Despite the typical ECG pattern, the etiology has to be carefully investigated for an appropriate management. Indeed, short- and long-term measures are available for torsades de pointes associated with long QT syndromes (LQTS), including the removal of torsadogenic agents, the suppression of early afterdepolarization with magnesium, the acceleration of the basic heart rate with isoproterenol or cardiac pacing and beta-blocker administration[1]. Differently, in patients with a normal QT, it is recommended to consider and treat torsades de pointes as a common polymorphic VT (polymorphic VT showing a pattern of torsade de pointes)[2]. Particularly, in patients with variant angina, beta-blockade may prolong or precipitate coronary spasm and, consequently, ischemia-induced arrhythmias. Calcium channel antagonists and nitrates are very effective in preventing coronary spasm and the related arrhythmias, including torsade de pointes.

Case report

A 60-year-old male with a recent history of two episodes of angina at rest was admitted for cardiological evaluation. The patient's cardiac risk factors included a family history of coronary artery disease and dyslipidemia. Moreover, the patient had a previous history of one vessel artery disease and a successful coronary angioplasty with stenting of the left anterior descending artery. His routine medications included aspirin, atenolol and atorvastatin.

At the time of admission, the patient's blood pressure was 120/80 mmHg and the heart rate 53 b/min; ECG showed sinus rhythm with normal PR and QT intervals and negative T waves in the anterior leads. Chest X-ray and blood chemical analysis were normal. Transthoracic echocardiography showed a normal cardiac structure and left ventricular contraction without abnormalities of the regional wall kinetics.

The day after, he complained of central chest tightness, associated with ECG documentation of nonsustained polymorphic VT and a short run of self-terminating torsade de pointes (Fig. 1). Cardiac catheterization performed the same day revealed irregularities of the left descending coronary artery without significant stenosis. The diagnosis of variant angina was considered, but pharmacological tests to demonstrate coronary spasm were not performed in view of the recent life-threatening ventricular arrhythmia.

Two days later, a hyperventilation test performed in the morning was positive (Fig. 2), with ECG evidence of ST-segment elevation (> 0.2 mV) in the anterior leads

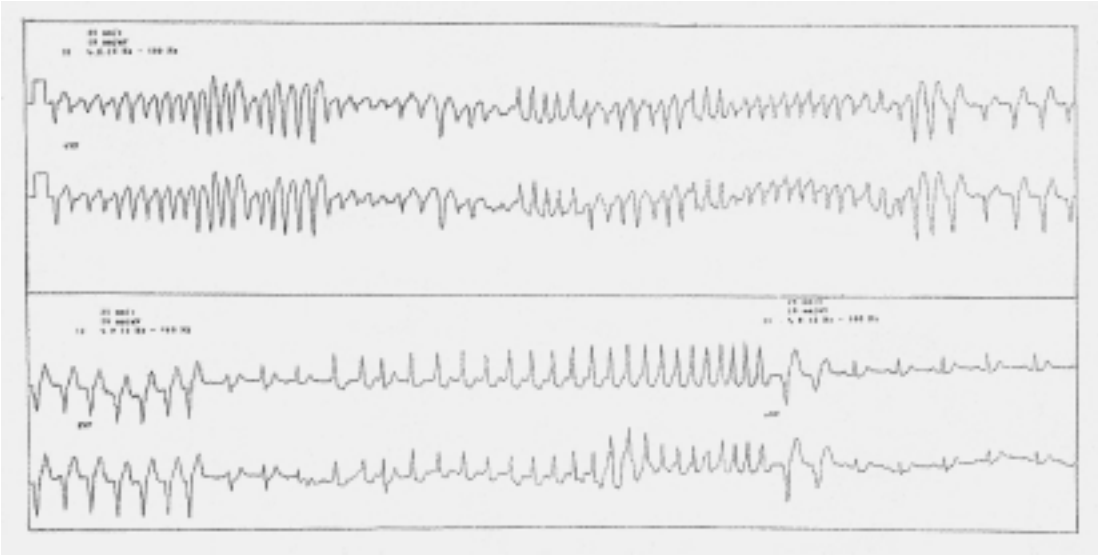

Figure 1. *ECG recorded during an episode of chest pain, showing a self-terminating torsade de pointes (polymorphic ventricular tachycardia with a pattern of torsade de pointes).*

and short runs of VT associated with chest pain, efficaciously treated with intravenous nitroglycerin. Beta-blockers were replaced with isosorbide mononitrate 80 mg and verapamil 240 mg daily. A control hyperventilation pre-discharge test was negative. During a follow-up period of 6 months the patient was free of symptoms and no other episodes of ventricular arrhythmias were documented.

Discussion

Torsade de pointes, first characterized in 1966 by Dessertenne, is a polymorphic VT showing a peculiar ECG pattern characterized by QRS complexes that appear to "twist" around the isoelectric line. The most typical form is associated with syndromes characterized by an evident delay in myocardial repolarization (LQTS), an abnormality caused by mutations in genes encoding specific ion channels (congenital LQTS), by metabolic abnormalities or by drugs (acquired LQTS) and the resulting heterogeneity in repolarization allows the onset of a reentrant arrhythmia (torsade de pointes). It is usually preceded by pauses (due to sinus arrhythmia, sinus arrest or, more commonly, to "post-extrasystolic" pauses) and in a typical sequence, longer post-extrasystolic pauses are followed by longer and faster runs of torsade de pointes ("pause-dependent" torsade de pointes). Torsade de pointes is a life-threatening arrhythmia because, even though it is often nonsustained and is self-terminating, it may degenerate to ventricular fibrillation and require DC shock[1].

Infrequently, this arrhythmia has been reported in patients with a normal QT interval and vasospastic angina. Previous reports showed that coronary spasm may induce life-threatening arrhythmias, and that it was associated with sudden death in patients with variant angina. Ventricular arrhythmias precipitated by coronary spasm tend to be rapid and polymorphic, are usually not inducible during programmed stimulation, but may be induced by the hyperventilation test or by ergonovine infusion[3-5]. The precise mechanisms are still unclear, but in animal models the production of an injury current and the reexcitation of cells close to the ischemic border, or reentrant mechanism, have been associated with their initiation. Thus, it is possible that ischemia or reperfusion following a coronary spasm may induce or aggravate an abnormality of ventricular repolarization, providing the basis for the development of polymorphic VT[3,6]. Dispersion of ventricular repolarization is an important electrophysiological feature that is considered fundamental for the initiation of VT and fibrillation. This is particularly true in the setting of myocardial ischemia. An inhomogeneity of ventricular repolarization has been documented in patients with vasospastic angina using electrophysiological studies[7] and noninvasive methods. Particularly, in an attempt to quantify the dispersion of repolarization noninvasively in the clinical setting, the method of assessment of QT dispersion (QTd), defined as the difference between the maximum and minimum QT intervals on an ECG, has been proposed[8]. In spite of the various problems inherent to the technology currently used to determine QTd from the surface ECG, over the last 10 years numerous studies have used this noninvasive methodology to quantify the inhomogeneity of ventricular repolarization in different subsets of patients with coronary artery disease[9]. With regard to variant angina, Suzuki et al.[10], determining the QTd before the induction of coronary spasm by the intracoronary injection of acetylcholine and 30 min after the administration of isosorbide dinitrate, showed that the baseline QTd was significantly

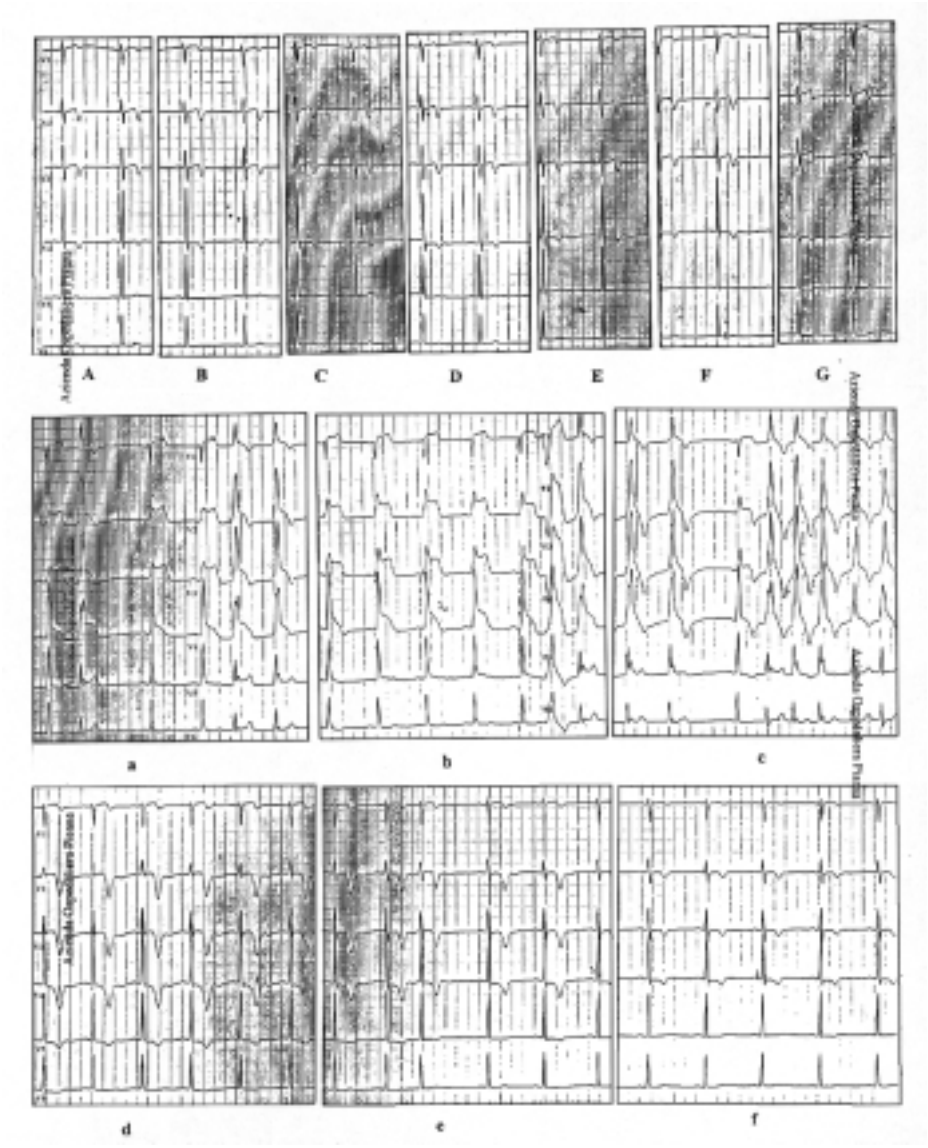

Figure 2. *Hyperventilation test. The patient was asked to hyperventilate vigorously for 6 min and a 12-lead ECG was recorded before* (A)*, and at 1, 2, 3, 4, 5, 6 min during (*B, C, D, E, F, G *respectively) and at 1, 2, 3, 4, 5, 6 min after the test (*a, b, c, d, e, f, g *respectively). After hyperventilation, the patient complained of severe chest pain and the ECG showed ST-segment elevation in the anterior leads, and ventricular premature contractions* (a, b) *and short runs of nonsustained ventricular tachycardia* (c)*. Intravenous nitroglycerin was immediately administered. The angina resolved immediately and the ECG showed evidence of deep negative T waves* (d, e, f).

greater than in patients with atypical chest pain (69 ± 24 vs 44 ± 19 ms, $p < 0.001$) and that only in the first group did the QTd decrease after administration of isosorbide dinitrate (to 48 ± 15 ms, $p < 0.001$). What is more, in the subgroup of patients with variant angina and ventricular arrhythmias, the QTd was significantly greater compared with the remaining patients. Similarly, Parchure et al.[11] provided evidence that QTd is increased in patients with variant angina complicated by cardiac arrest and syncope compared to patients without events, supporting the clinical notion of an increased risk for sudden arrhythmogenic death in these patients.

Thus, the data seem to indicate that patients with variant angina have a greater inhomogeneity of ventricular refractoriness, which may predispose them to life-threatening arrhythmias in the presence[12], and even in the absence, of signs of ischemia and that the noninvasive measurement of QTd may help identify patients at an increased risk of malignant arrhythmias. In our patient, the ECG variables were determined using previously described methods[10], at the time of admission (baseline), after the spontaneous episode of chest pain associated with polymorphic VT, during acute myocardial ischemia induced by the hyperventilation test and after the intravenous administration of nitroglycerin (Table I). Similarly to previous clinical studies[9], despite the normal ECG variables at baseline, QTd increased during acute myocardial ischemia and decreased after the administration of nitrates. This is in accordance with evidence that myocardial ischemia is associated with changes in the electrophysiological properties of

Table I. ECG variables in patients with variant angina.

	Spontaneous episode of polymorphic VT		Hyperventilation test	
	Baseline	After VT	During transmural acute ischemia	After ISDN
QTc max (ms)	419	447	447	413
QTc min (ms)	380	394	366	383
QTc mean (ms)	412.7 ± 14.9	421 ± 21.3	414.8 ± 33.6	406 ± 12.1
QT dispersion (ms)	40	50	80	30

ISDN = isosorbide dinitrate; QTc = rate-corrected QT interval; VT = ventricular tachycardia. Baseline, at admission; after ISDN, after the intravenous injection of nitrates (when chest pain and ischemic ST-segment changes were not observed); after VT, after the spontaneous episode of polymorphic VT.

the heart and, particularly, with an increased inhomogeneity of ventricular repolarization.

In the past, it has been discussed whether to consider torsade de pointes with a normal QT interval and myocardial ischemia as a separate entity or as a multiform VT (polymorphic VT showing a pattern of torsade de pointes)[13]. At present, it is recommended to consider this arrhythmia as a polymorphic VT[2], essentially for its therapeutic implications. Indeed, in contrast to the long-term management of torsades de pointes in patients with congenital LQTS, in which beta-blockers (at the maximum tolerated dose) remain the mainstay of therapy, in patients with variant angina beta-blockade may prolong or precipitate a coronary spasm and induce ventricular arrhythmias, an effect abolished by nitrates and calcium channel antagonists[14]. As coronary vasorelaxation is mediated by both beta1 and beta2 adrenoceptor stimulation, beta-blockers (almost the nonselective) may increase coronary vascular resistance in patients with variant angina, prolonging the duration of ischemic attacks[15,16].

Even though coronary angiography remains the gold standard for the diagnosis of spontaneous or pharmacologically induced spasm, it is not necessary to perform a provocation test with ergonovine or acetylcholine at cardiac catheterization in hyperventilation-positive patients, because the specificity of the test for coronary spasm is 100%[17]. What is more, it may be used to evaluate the long-term prognosis (patients with a positive hyperventilation test appeared to be at high risk for lethal arrhythmias and should be treated vigorously with calcium channel antagonists)[4,18]. Finally, in a previously positive hyperventilation test patient it may be useful for the evaluation and monitoring of the efficacy of drugs pre-discharge and during follow-up[17].

In conclusion, episodes of torsade de pointes in patients with a normal QT interval have to be considered and treated as a polymorphic VT; in particular, when they are due to coronary spasm (as in patients with variant angina), such episodes may improve following the discontinuation of beta-blockers and the administration of calcium channel antagonists.

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