CASE REPORT

Long QT Syndrome. Electrocardiogram of Dangerous Drug Interactions

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ABSTRACT

Ventricular repolarization is not always evaluated properly at the moment of adopting certain medical management and its consequences might be fatal. Electrolyte disturbances and class III antiarrhythmic drug therapies are frequent associations in daily clinical practice and constitute two factors that have great repercussions as they may modify ventricular repolarization and generate malignant ventricular arrhythmias.
This case report deals with drug interactions, electrocardiographic changes and proarrhythmic effects.

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Key words > Long QT Syndrome - Drug Interactions

Abbreviations >

ECV Electric cardioversion	**PVT** Polymorphic ventricular tachycardia
VF Ventricular fibrillation	

BACKGROUND

The electrocardiogram is the cheapest and most useful non-invasive diagnostic tool in clinical cardiology practice, and rapidly available. Electrocardiographic waves, segments and intervals represent depolarization and repolarization of myocardial tissue Electrocardiographic waveforms are closely related to ionic currents, specially sodium and potassium, across the cell membranes of myocytes. Therefore, it seems reasonable to think that electrolyte disorders, as well as arrhythmic drugs that affect ionic transport across cell membranes, may be responsible for the electrocardiographic changes associated with high-risk ventricular arrhythmias.

The following case report deals with electrocardiographic changes in ventricular repolarization secondary both to electrolyte disturbances and amiodarone effects as a cause of malignant ventricular arrhythmias.

CASE REPORT

A 36-year old woman was admitted to the Intensive Care Unit located in her place of residence due to a sepsis originated in the right foot sole. She had neither prior personal nor family history of cardiovascular disease. Therapy with antibiotics - vancomycin and imipenem- was started, with favorable clinical response. No electrolyte disturbances were observed at admission. The patient evolved with functional class IV dyspnea due to congestive heart failure and therapy with intravenous loop diuretics was initiated. Twenty four hours after the administration of furosemide the patient presented cardiac arrest due to ventricular fibrillation (VF), which was successfully reverted by electrical cardioversion (ECV). However, due to the presence of very frequent isolated and multifocal ventricular premature beats, couplets and bursts of polymorphic ventricular tachycardia (PVT), amiodarone was administrated intravenously at an initial loading dose followed by a maintenance dose.

Thereafter, she was transferred to our institution. The results of lab tests at admission were as follows: hypokalemia (K^+ 2,7 mEq/L), hypomagnesemia (Mg^{++} 1,34 mEq/L) and hypocalcemia (Ca^{++} 7,65 mEq/L). The electrocardiogram showed a long QT interval greater than 600 milliseconds; however, its exact duration could not be precisely defined due to the presence of permanent ventricular bigeminy with fixed coupling interval and R-on-T phenomenon (Figure1) and multiple episodes of self-limited PVT (Figure 2). These findings were already present in the electrocardiogram taken in the other institution. Correction of internal environment was initiated and amiodarone infusion was stopped. Subsequently, and before achieving the therapeutic goal, the patient persisted presenting multiple episodes of PVT and VF (arrhythmic storm) which required ECV; for this reason a transient pacemaker was implanted to produce homogenization of ventricular repolarization until normalization of QT interval duration (Figure 3), and internal environment stabilization. The patient presented favorable progress and once electrolyte disorders were corrected, QT interval duration became normal; in addition, no ventricular premature beats with R-on-T phenomenon and bursts of PVT were recorded.

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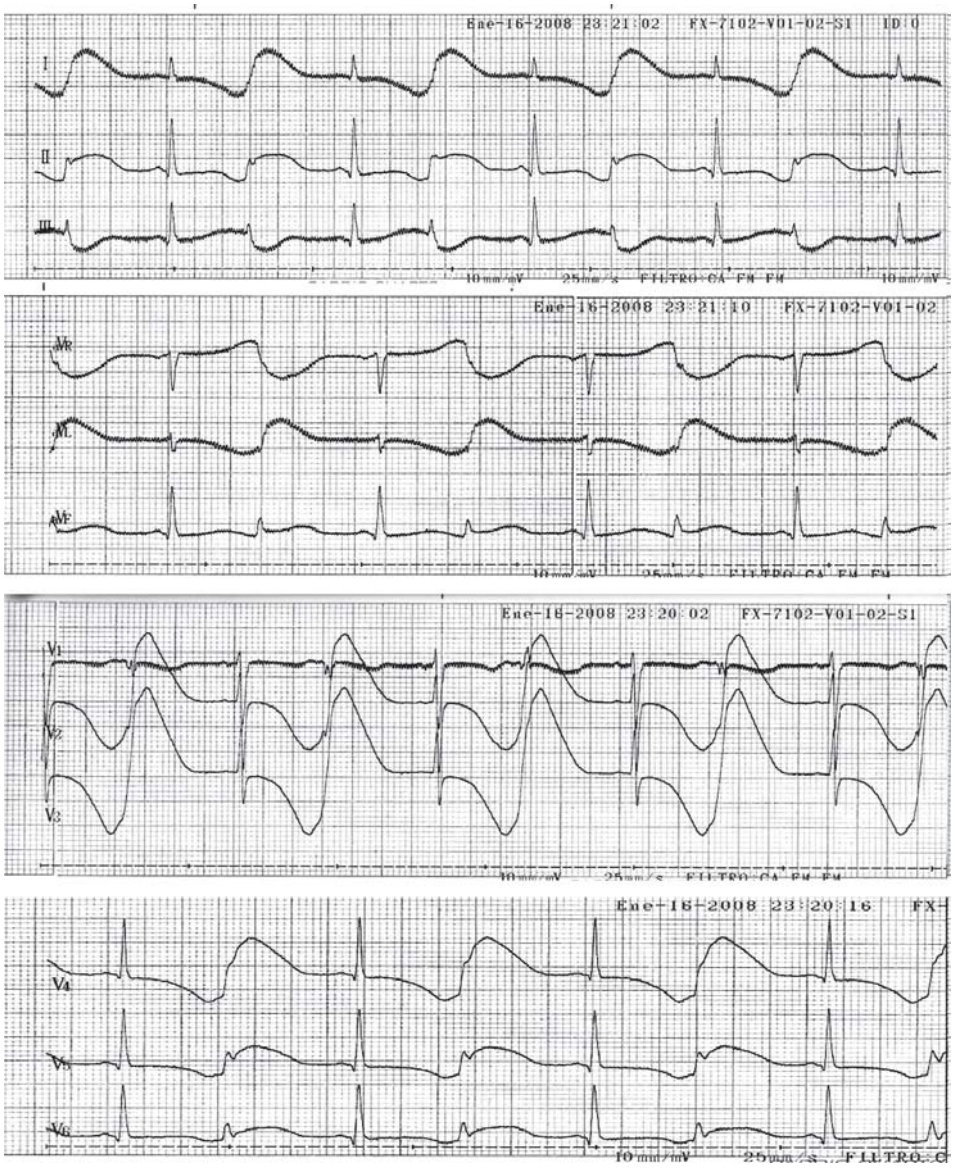

Fig. 1. Standard 12-lead electrocardiogram. Sinus rhythm, long QT interval, T wave inversion, ventricular bigeminy with R-on-T phenomenon.

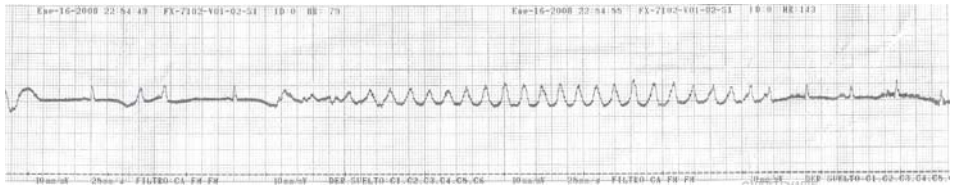

Fig. 2. Self-limited polymorphic ventricular tachycardia initiated by a ventricular premature beat with R-on-T phenomenon in presence of long QT interval. Amiodarone and electrolyte disturbances generate phase 2 early afterdepolarizations, which represent the physiopathologic mechanism of ventricular premature beats with R-on-T phenomenon.

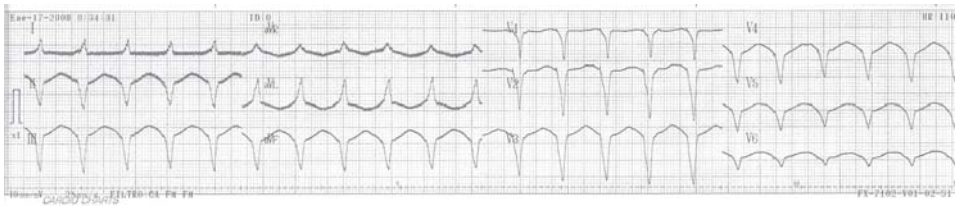

Fig. 3. Standard 12-lead electrocardiogram. Transient pacemaker stimulation for suppression of ventricular tachycardia.

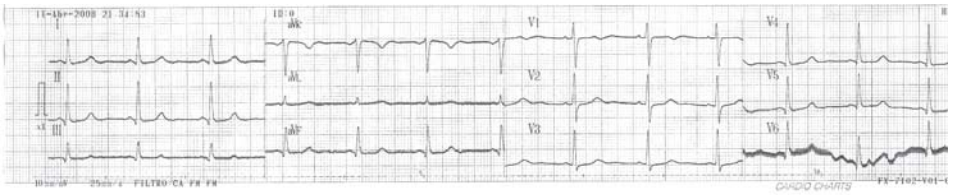

Fig. 4. Standard 12-lead electrocardiogram recorded during patient's follow-up. Similar findings to ECG before discharge. Normal QT interval.

Finally, the patient remained stable with good response to treatment and was discharged with normal electrocardiogram and internal environment; she would continue follow-up in the out-patient clinic.

DISCUSSION

Fluid and electrolyte disturbances are well known triggers of complex ventricular arrhythmias related to changes in ventricular repolarization. Amiodarone, a Vaughan Williams class III antiarrhythmic drug most frequently used in our country, modifies the action potential of cardiac myocytes. Both factors modify ventricular repolarization expressed by the QT interval and T wave, leading to malignant ventricular arrhythmias - polymorphic ventricular tachycardia (PVT) and ventricular fibrillation (VF). (1, 2)

This clinical case presents the association of both factors that modify ventricular repolarization, leading to ventricular arrhythmias; in addition, the electrocardiographic records serve for educational purposes.

Progress in basic and clinical research achieved in the last two decades related to electrical heterogeneity of ventricular myocardium has enabled the understanding of cellular and ionic basis of electrocardiographic waveforms that represent ventricular repolarization, as well as its clinical implications. Higuchi and Nakaya (3) demonstrated in the early eighties that electrocardiographic waveforms represent voltage gradients. They described the sequence of repolarization of ventricular myocardium and the difference in durations of the action potential in the epicardial and endocardial surfaces (40-60 msec greater in the epicardium). These findings certify the presence of a transmural voltage gradient between both layers due to different repolarization duration. Nevertheless, it was not until the beginning of the nineties that Antzelevich et al. (4) described the cellular and ionic basis of this transmural gradient. They demonstrated the presence of a subpopulation of cells with unique electrophysiological properties in the deep subepicardium, which the called M cells. These cells are capable of producing a greater duration of the action potential in response to fluid and electrolyte disturbances or in presence of antiarrhythmic drugs, and they play an important role in the development of acquired long QT syndrome. The morphology and the duration of QT interval and T wave are determined by the relationship between endocardial cells, epicardial cells and M cells during ventricular repolarization under normal or abnormal conditions. (5-8) Acquired long QT syndrome is mainly produced by the effects of drugs that prolong the duration of the action potential by an inhibition of sodium and/or potassium channels, or by fluid an electrolyte disorders, such as hypokalemia, hypomagnesemia and hypocalcemia. These conditions predispose to *torsade de pointes*, a polymorphic ventricular tachycardia closely related to prolonged repolarization of endocardial and subendocardial cells. (5, 7, 9, 10)

Few research articles have described the presence of subclinical mutations in cardiac ion channel genes that predispose to drug-induced long QT syndrome and malignant ventricular arrhythmias under conditions of electrolyte disturbances. (10, 11) These patients have normal or borderline QT intervals and they are considered frustrated forms of congenital long QT syndrome which are clinically expressed under the action of certain triggers (electrolyte disturbances and/or antiarrhythmic drugs) (12)

Torsades de pointes are triggered by phase 2 early afterdepolarizations and maintained by a functional reentrant substrate due to increase in dispersion of repolarization. (13, 14)

Any transmurally conducted electrical activity during phase 2 or 3 of the action potential can manifest as an R-on-T ventricular premature beat. T-wave downslope is the expression of both phases in the surface electrocardiogram and represents a vulnerable window for malignant ventricular arrhythmias due to heterogeneity of repolarization of ventricular myocytes. Therefore, any ventricular premature beat generated during this period can initiate PVT and VF. The physiopathologic mechanism involved with complex ventricular arrhythmias in acquired long QT syndrome is the presence of phase 2 early afterdepolarizations generated in the endocardium or subendocardium under drug effects or electrolyte disturbances that increase the duration of the action potential. (7)

This case report illustrates the complete scope of the electrocardiographic features of the two factors most frequently related to the development of acquired long QT syndrome, as well as their arrhythmic consequences.

RESUMEN

Síndrome de QT largo. El electrocardiograma de interacciones medicamentosas peligrosas

La repolarización ventricular no siempre se evalúa correctamente a la hora de adoptar una conducta médica determinada y sus consecuencias pueden ser fatales. Los trastornos electrolíticos del medio interno y la administración de drogas antiarrítmicas de clase III son asociaciones que se presentan con frecuencia en la práctica clínica diaria y constituyen dos factores de gran repercusión en la modificación de la repolarización ventricular y en la generación de arritmias ventriculares malignas.

En el caso clínico que se presenta se hace referencia a esta interacción, a su repercusión electrocardiográfica y a sus consecuencias arrítmicas.

Palabras clave > Síndrome de QT prolongado - Interacciones de drogas

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