

The Prolongation of the QT Interval in the Acute Rheumatic Carditis: an Enigma

Lurildo R. Saraiva, Cleusa Lapa Santos, Inês Remígio de Aguiar

Universidade Federal de Pernambuco, Instituto Materno-Infantil Professor Fernando Figueira - Recife, PE, Brazil

In 1949, in his professorship thesis entitled "The Electric Ventricular Systole", Professor Luiz V. Décourt¹ by using Bazett's formula to calculate QT corrected to heart rate (QTc), drew a series of conclusions after a meticulous analysis of electrocardiograms (ECGs) from 60 patients suffering with active rheumatism, among them 35 with "primitive" rheumatic carditis. He stated that:

a) the duration of ventricular electric systole showed no correlation with the severity of the condition, although - and this he accepted as being another truth - it tended to increase significantly during the time of the rheumatic process. The enlargement was very clear in less than 50% of cases;

b) during the evolution of the process, the duration of the QT interval seemed to follow a persisting activity of the disease;

c) probably, the most significant finding were the mean QTc values in rheumatic active patients ($\bar{X} = 0.424$) were higher than was found for a group of normal individuals of the same gender and age distribution ($= 0.389$, $p < 0.05$).

In this original paper, the author for the first time in literature suggested, the possibility of a unique peculiarity in rheumatic patients as the QT interval duration, possibly an innate tendency toward this prolongation, which would later trigger acute rheumatic disease in the heart, in the presence of an immune mechanism.

One example of this behavior is in the ECG shown in Figure 1, which obtained from a three-year-old boy with acute rheumatic carditis, significant mitral insufficiency and congestive heart failure. On the tracing, where there is low QRS voltage in the frontal plane, first-degree AV block ($PR_i = 180$ ms) and signs of left atrial overload, it can be observed an elongated QTc (mean value $D2 = 0.441$, maximum for age and gender, 0.420^1), and, more than this, the increase of this prolongation after extrasystoles, with depressed T waves. Such elevated QTc values for the superior limit of normality of QTc, such as 0.450, admitted by English authors², are in no way a consensual fact among us.

If rheumatic carditis can induce elongated QTc, it can also be complicated with "torsade des pointes" (TdP). This possibility was demonstrated by Liberman et al³, in 2001, in a teenager with severe acute mitro-aortic valve disease, that subsequently

died from cardiac arrested and severe cerebral dysfunction. Deep inside the myocardium - that had shown a depressed function in a previous echocardiographic study - active Aschoff nodules were identified. The ECG prior to the TdP episode exhibited a QTc with 0.570 and T-wave alternans.

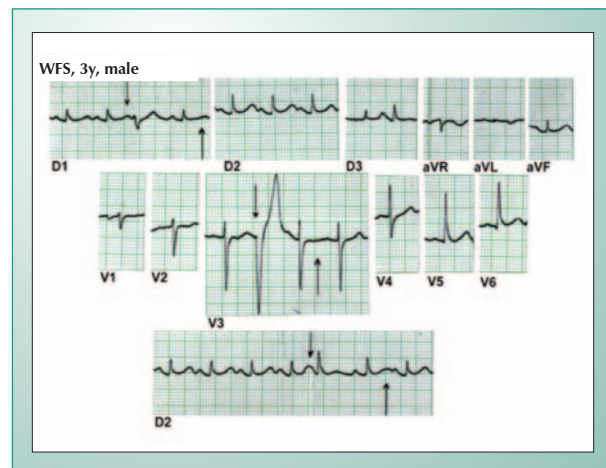


Fig. 1 - Electrocardiogram of a three-year-old boy in an initial rheumatic fever crisis. Besides low voltage in the frontal plane and the first-degree AV block, note the prolonged QT (QTc = 0.441 in D2), that is accentuated after supraventricular and ventricular extra-systoles (arrows).

New acquisitions in understanding QTc elongation in acute rheumatic fever: studies in Pernambuco

Some authors have proposed a multifactorial origin for QT prolongation and TdP⁴. An increase in the QT interval may be reached by multiple mechanisms that in conjunction alter the normal capacity or repolarization reserve with subsequent arrhythmias. The acting mechanisms for the abnormal increase of QT may be related to genetic factors, drugs, and heart diseases such as cardiac failure and cardiomyopathy, or even non-cardiac conditions, such as hepatic disease, brain hemorrhage and intense malnutrition^{4,5}. In this way, patients suffering ventricular arrhythmias related to drug use would have a slightly prolonged basal QTc interval, especially women,

Key words

Rheumatic fever, myocarditis, long QT syndrome, heart valve diseases.

Mailing Address: Lurildo R. Saraiva •

Avenida Prof. Moraes Rego, SN - Hospital das Clínicas - Cidade Universitária - 50670-901 - Recife, PE, Brazil

E-mail: lurildocleano@hotmail.com

Manuscript received April 18, 2006; revised manuscript received May 18, 2006; accepted May 18, 2006.

as consequence of the increase of the potential action⁴.

Although malignant ventricular arrhythmias seem rare in acute rheumatic disease^{3,6}, would old observations that acute rheumatic patients, regardless of the presence of carditis or not, have an innate tendency toward an increased QT when compared to normal individuals still be true? Moreover, as a corollary, what would the QT dispersion (dQT) be in this population?

Recent studies carried out in Pernambuco provided an extraordinary contribution to the understanding of this problem. The Master's degree thesis of Lapa Santos⁷ surprisingly revealed a prolongation of the QTc interval in eight children with subclinical carditis, out of 27 male and female patients with arthritis/chorea, by using the Décourt table for QTc values¹. *There was no QTc enlargement in all cases studied but there was subclinical valvitis in the ones with enlarged QTc.* Nonetheless, as the author emphasized, if there was no cavity increase seen on the Doppler echocardiographic study of these patients, if there was no mitral valve prolapse detected, if there was no evidence of myocarditis, or even changes in the contractile capacity of the organ, to what could the QTc prolongation be attributed? Did these children have an inadequate clinical progression relative to the others?

Another surprise came when we compare the mean value of QTc of the 27 patients with or without valvitis (mean value 0.412) with 26 normal children (mean value 0.391), coming from the same environment, and there was significant difference ($p < 0.01$). In Décourt's thesis, the corresponding means were, respectively, 0.424 and 0.383 ($p < 0.05$), but it is necessary to consider that at the time, electrocardiographic tracings showed gross T wave tracings, hindering a precise analysis of its termination.

On the other hand, in a earlier study, a Master's degree thesis by Aguiar⁸, in 2004, another unique feature was also perceived: *in acute rheumatic carditis the dQT ($\bar{X} = 42.03$ ms) is significantly increased ($p < 0.0001$) compared to the values to a group of normal children ($\bar{X} = 25.55$ ms).* Additionally, *in our context, dQT values over 40 ms may represent a predictor of the presence of carditis, habitually more severe with a specificity rate of 94%.* This interesting observation came as an answer to a question that Décourt himself had raised years ago in a personal communication: what would be the behavior of dQT in acute rheumatic carditis, especially in those patients who did not present a prolonged QTc? In the mentioned study, about 80% of the rheumatic subjects had normal QTc values.

Recently, a study from Turkey⁹ shown an increase of dQT in rheumatic carditis. Values above 55 ms for dQT would have high specificity and a lower sensitivity in predicting the occurrence of carditis, and if this value were equal to or greater than 65 ms, it would allow us to suppose the presence of severe valvulopathy. Fundamentally, the finding reproduces what we have observed. Nevertheless, the inclusion of patients with congestive heart failure could constitute an important

bias in the Turkish results. Although Polat et al⁹ accept some type of participation of the myocardium in the genesis of an increased dQT, the concept of true rheumatic myocarditis may suffer a deep review^{10,11}, although the description even though several studies have demonstrated a myocardial component in the disease, as exemplified in the very description by Liberman et al³.

If we are before a scientific fact, why are reports of malignant arrhythmias in acute rheumatic carditis habitually so scarce? In a personal communication, Lapa Santos reported a case resistant to conventional therapy with an inexorable progression of the child to frequent ventricular extrasystoles, ventricular tachycardia, and ventricular fibrillation. These cases seem to be rare as stated before⁶. Is this scarcity a result of the poor clinical-echocardiographic expression of rheumatic myocarditis, since the other possible cause for speculation, rheumatic coronary arthritis perhaps has been extinguished?⁶ We don't have the answer.

The tendency to the enlargements of QTc interval as a possible "marker" of acute rheumatic individuals

Many studies have demonstrated the existence of immune markers for rheumatic disease, starting from the original observation of Patarroyo et al, 1979, in Columbia^{12,13}. Papers by Swedo et al¹⁴ expanded the concept of rheumatic chorea, considered benign until then. Thus, it is now considered by many the probable extreme of a syndromic *continuum* that would include "tics" disturbances, Tourette's syndrome and real obsessive-compulsive disorders, as a possible consequence of the initial oro-pharyngeal streptococcal infection. Hounie et al¹⁵, in Sao Paulo, observed that rheumatic patients, even when out from the acute onset of the disease, presented a relative of over eight times greater for disorders of the obsessive-compulsive spectrum as if an inherited vulnerability would exist related to rheumatic fever and these manifestations¹⁶.

In face of the data collected in Pernambuco, could be an "electrical stigma" admitted in rheumatic patients? Undoubtedly, it is a real possibility. The observation of the great master in his last book is so pertinent¹⁷: "The fall in the incidence of rheumatic fever nowadays ... has brought some negligence from doctors, and perhaps ignorance concerning the care provide by many of them to these patients. An example of this is the incomplete ECG evaluation in the acute phase of rheumatic fever, characterized by the lack of clinical progress determination of the QT interval. This is usually increased, and progresses in parallel to the condition of the myocardium."

References

1. Décourt LV. A sístole elétrica ventricular: métodos de apreciação, valores normais e desvios em estados patológicos. [tese de cátedra]. São Paulo: Faculdade de Medicina. Universidade de São Paulo; 1949. 178 pp.
2. Dickinson DF. The normal ECG in childhood and adolescence. *Heart*. 2005; 91: 1626-30.
3. Liberman L, Hordof AJ, Alfayyadh M, Salafia CM. Torsade de pointes in a child with acute rheumatic fever. *J Pediatr*. 2001; 138: 280-2.
4. Schulze-Bahr E, Denjoy I, Haverkamp W, Breithardt G, Guicheney P. Genetic aspects in acquired long QT syndrome. In: Oto A, Breithardt G. (eds). *Myocardial repolarization: from gene to bedside*. Nova York: Futura PC; 2001. p. 333-41.
5. Aytemir K, Oto A. Evidence of repolarization abnormalities in various clinical conditions. In: Oto A, Breithardt G. (eds). *Myocardial repolarization: from gene to bedside*. Nova York: Futura PC; 2001. p. 365-82.
6. Krishnan SC, Kushwaha SS, Josephson ME. Electrocardiographic abnormalities and arrhythmias in patients with acute rheumatic fever. In: Narula J, Virmani R, Reddy KS, Tandon R. (eds). *Rheumatic fever*. Washington: American Registry of Pathology, 1999, Cap. 16, pp. 287-98.
7. Santos, CCL. Aspectos clínicos e ecodopplecardiográficos de uma série de crianças em primeiro surto de febre reumática sem sinais clínicos de cardite. [dissertação de mestrado]. Recife (PE): Universidade Federal de Pernambuco; 2006. 80 pp.
8. Aguiar, MIR. Dispersão do intervalo QT na cardite reumática. [dissertação de mestrado]. Recife (PE): Universidade Federal de Pernambuco; 2004. 49 pp.
9. Polat TB, Yalcin Y, Akdeniz C, Zeybek C, Erdem A, Celebi A. QT dispersion in acute rheumatic fever. *Cardiol Young*. 2006; 16: 141-6.
10. Essop MR, Wisenbaugh T, Sareli P. Evidence against a myocardial factor as the cause of left ventricular dilation in active rheumatic carditis. *J Am Coll Cardiol*. 1993; 22: 286-9.
11. Williams RV, Minich LL, Shaddy RE, Veasy G, Tani LY. Evidence for lack of myocardial injury in children with acute rheumatic carditis. *Cardiol Young*. 2002; 12: 519-23.
12. Patarroyo ME, Winchester RJ, Vejerano A, Gibofsky A, Chalem F, Zabriskie JB, et al. Association of a B cell alloantigen with susceptibility to rheumatic fever. *Nature*. 1979; 278: 173-4.
13. Guilherme L, Kalil J. Rheumatic fever: the T cell response leading to autoimmune aggression in the heart. *Autoimmun Rev*. 2002; 1: 261-6.
14. Swedo SE. Pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS). *Mol Psychiatry*. 2002; 7: S24-S25.
15. Hounie, AC, Pauls DL, Mercadante MT, Rosario-Campos MC, Shavitt RC, Mathis MA, et al. Obsessive-compulsive spectrum disorders in rheumatic fever with and without Sydenham's chorea. *J Clin Psychiatry*. 2004; 65: 994-9.
16. Dale RC. Autoimmunity and the basal ganglia: new insights into old diseases. *QJM*. 2003; 96: 183-91.
17. Ramires JAF, Lemos PC. A didática humanista do Professor Luiz Venere Décourt. São Paulo: Atheneu, 2005, p.188.