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Importance of Autoantibodies at Eliciting Arrhythmias in Chagas cardiomyopathy

Jiménez MA, Nascimento JH, Monnerat G, Maciel L, Paiva CN, Pedrosa RC, et al. Autoantibodies with beta-adrenergic activity from chronic chagasic patients induce cardiac arrhythmias and early afterdepolarization in a drug-induced LQT2 rabbit hearts. **Int J Cardiol. 2017;240:354-9. http://doi.org/gbpdvp**

It is estimated that chronic Chagas disease causes approximately 12,500 deaths per year in Latin America and that arrhythmias due chronic Chagas cardiomyopathy are mainly responsible for these deaths. Once the acute phase is over, nearly 30-40% of patients infected with Chagas disease will develop clinical manifestations in the next 10 to 30 years, especially in the heart. The earliest signs of chronic cardiomyopathy are frequently conduction system disturbances and multiform ventricular arrhythmias. The chagasic heart is strongly arrhythmogenic, and has the characteristic of presenting with severe ventricular arrhythmias in subjects with relatively preserved global left ventricular systolic function, i.e. electric disorders precede structural ventricular remodeling and are an early manifestation of disease progression. The importance of autonomic regulation involvement is well known in Chagas cardiomyopathy. In the same sense, autoantibodies present functional activity as membrane receptor agonists coupled to G protein in patients with chronic infections. Specifically, anti-β-adrenergic receptor immunoglobulins are associated to arrhythmia triggering, though the mechanisms of action are not clearly understood.

Because the administration of serum with anti-β-adrenergic receptor autoantibodies of chagasic patients to normal rabbit hearts was unable to induce arrhythmias, in this interesting work, Vidal Jiménez et al. postulated that these antibodies need a favorable electrical environment as basis to elicit arrhythmias. They tested this hypothesis in isolated rabbit hearts with pharmacologically-induced long QT syndrome via potassium channel blockage. After these animals received serum from patients with chronic Chagas cardiomyopathy inducing severe arrhythmias, important electrical disturbances were observed, which were significantly greater than those in the control group treated without functional β-receptor antibodies. To confirm these results, atenolol completely blocked ventricular arrhythmias.

The authors concluded that anti-β-adrenergic receptors autoantibodies are able to promote cardiac arrhythmias in the favorable context of a microenvironment of electrical instability, as the experimental type-2 long-QT syndrome.

The first description of serum anti-β1-adrenergic receptor autoantibodies in patients with chagasic cardiomyopathy was made by research groups led by Rosembaum, Elizari and Chiale in 1994 and 1995. These last authors demonstrated an increase in the frequency of contraction and AMPc levels in isolated myocyte cultures from mice treated with anti-β1 and β2-receptor antibodies of patients with ventricular arrhythmias due to chagasic cardiomyopathy. They thus established an association between these immunoglobulins and arrhythmias of the chagasic heart. Later studies confirmed these findings and also that autoantibodies activating β1-receptors modify membrane ion channels as those of calcium and potassium, promoting arrhythmias due to increased intracellular calcium and reentry mechanisms.

Ventricular arrhythmias are very common in chagasic cardiomyopathy, and are frequently severe and associated with sudden cardiac death. Dysautonomia in Chagas disease contributes to the development of complex ventricular arrhythmias and sudden death independently of the degree of cardiac pump dysfunction or structural changes in left ventricular remodeling. The presence of agonist autoantibodies against G-protein-coupled receptors, as antibodies versus β-adrenergic receptors found in almost all chagasic patients, have been well characterized and demonstrated their ability to modulate electrogenesis and conduction of the cardiac electric impulse. Strategies aimed at eliminating these antibodies could be a possible future treatment in patients with refractory severe arrhythmias.