The evolution of Chagas’ disease (CD) from its “indeterminate” form towards chronic cardiomyopathy remains a controversial subject and several pathogenic mechanisms seem to be involved: the neurogenic component, microvascular alterations, Trypanosoma cruzi \((T. cruzi)\) direct action, and immunological processes being among them. The latter mechanism includes, in turn, antigen \(\text{(Ag)}\) immune response to the parasite, autoimmune phenomena and the inflammatory component, coexisting with cell-mediated immunity development.

Since cardiopathy appears many years after primary infection by \(T. cruzi\) and several factors related to the etiologic agent and its strains, reinfections and host immune factors take part, it is possible that conventional cardiovascular risk factors (CRFs) might have some kind of involvement in this evolution. A possible way to approach the analysis of these concerns consists in trying to determine a possible association between the profile of known pathogenic antibodies, the coexistence of CRFs and their connection to the presence chronic chagasic cardiomyopathy (CCC). Many parasite structures and self-antigens seem to be involved in the pathogenesis of chronic chagasic cardiomyopathy. Antibodies against \(T cruzi\), ribosomal proteins \(\text{(P)}\) and cruzipain \(\text{(Cz)}\), capable of inducing electrocardiographic alterations (ECGA) in noninfected hearts of immunized mice, have been demonstrated in experiments with animals; which suggests a crossreactivity immune mechanism. Also, antibody levels against different \(\text{Cz}\) epitopes, the most important \(T. cruzi\) cysteine proteinase, seem to be related to the CD patient’s clinical status. It is also known that \(T. cruzi\) antigens and antigens released by host cell lysis show a marked homologous structure, which further reinforces the development of autoimmune reactions.

Within the varied list of self-antigens, there are neural antigens such as cerebroside 3-sulphates or sulphatides \(\text{(S)}\). The latter are specific lipid components of peripheral nerve myelin sheaths and are also present in \(T. cruzi\) epimastigotes. Patients with CCC or other cardiomyopathies present a significant number of antisulphatide antibodies, which has also been observed in experimentally infected rats, in which these antibodies were found to bind homologous neural structures.

On these grounds, it is admissible to assume that the presence of CRFs during \(T. cruzi\) infection might contribute to reinforce the physiopathogenic mechanisms involved in myocardial damage. As a result, modifications as to the severity of cardiac involvement and the circulating levels of antibodies against \(\text{Cz, P, and S}\) in CD patients’ sera might be expected in association with the presence or absence of CRF.

In order to analyze this question, \(T. cruzi\) seropositive patients attending the Servicio de Cardiología del Hospital Provincial del Centenario on a regular basis were studied following a standardized protocol approved by the Comité de Ética of the Facultad de Ciencias Médicas of the UNR (Universidad Nacional de Rosario). Participants were stratified in two arms defined by the presence or absence of CRFs such as nicotine poisoning, alcoholism and high blood pressure. A cardiovascular clinical examination was performed on every one of them: frontal chest X-ray \(\text{(Rx)}\) and 12-lead electrocardiogram \(\text{(ECG)}\) at rest. Serological diagnosis was performed by means of three conventional reactions: indirect
immunofluorescence (II), direct agglutination test (DAT) and indirect haemagglutination (IH). The required parameter was having two tests of the three positive. From the cardiovascular point of view they were classified in three groups, following Storino classification: group 1 (G1), asymptomatic, with normal Rx and ECG; group 2 (G2), with ECGA and group 3 (G3) with cardiac failure and, of course, abnormal Rx and ECG. Immunoglobulins G anti-Cz, anti-S and anti-P levels were determined by enzyme-immunoanalysis. Four groups of individuals were conformed according to serology and the presence or absence of CRFs: reactive with CRFs (PosCRF), non reactive with CRFs (NegCRF), reactive without CRFs (Pos) and non reactive without CRFs (Neg). 118 patients of whom 71 were CD seropositive were analysed. Mean age was approximately 50 years, and residence time in the highly endemic area between 21 and 26 years approximately.

CCC development is a process that occurs many years after T. cruzi infection. Due to this prolonged latent period, it is possible that other factors’ involvement could contribute in establishing and determining the presence and extension of cardiac chronic involvement. In this direction, the findings indicated suggest that CRFs presence is related to different profiles of immune responses and CCC stage. Thus, the PosRCF group presented the highest anti-S antibody values, and the most severe CCC cases showed higher concentrations of such antibodies. As a whole, seropositive individuals showed a greater reactivity to S, which might be associated with not only molecular mimicry but also with the reported release of glycolipids that takes place after destruction of autonomic ganglia caused by T. cruzi infection. Notably, seronegative heart disease patients also presented a greater anti-S seroreactivity, which gives evidence to assume that concomitant non infectious stimuli might also be capable of facilitating antibody production and, consequently, heart damage. Anti-Cz and anti-P antibody presence was apparent only in the seropositive group and among them, most notably in those who also presented CRFs (PosCRF). As it was mentioned, anti-P antibodies may provoke ECGA in non infected animals probably through parasite ribosomal proteins and host structure crossreactivity.

Data from other laboratories indicate that chronic chagasic patients show a strong anti-Cz antibody response. Besides Cz deposits have been found in the myocardial tissue of CCC patients, which suggests a pathogenic role of this glycoprotein, although other experimental studies have not demonstrated a relationship between anti-Cz antibody levels and myocardial damage extent. Nevertheless, the findings seem to suggest that CRFs and their relationship to potentially pathogenic antibodies would express their involvement in CCC development. In an attempt to produce a comprehensive interpretation of the results commented and the context of CCC genesis, it can be considered that the infection produced by the parasite unleashes an immune response which is potentially harmful for the myocardium, be it by molecular mimicry, host cryptic antigen release or by the appearance of neoantigens. Regardless of the intimate triggering mechanism, it is very likely that exposure to additional events capable of damaging cardiac tissue even more should occur for CCC to emerge. Infection reactivation, like other non infectious pathological processes that operate in association, might in turn exacerbate the basic mechanisms involved in tissue damage. That is, anti- T. cruzi immune response, autoimmune reactions and immunity mediated inflammation. As a result of such complex interrelation, a series of molecular abnormalities associated to tissue damage would emerge, as our results seem to indicate; that is, modifications in anti-P and anti-S antibody levels.

Although it is difficult to differentiate cause and result in cross sectional studies, because they are both evaluated at the same time, our findings favour the supposition that the CRFs studied might have a contributing role in the development of CCC. This supposition is based on the fact that in a great proportion of the cases, cardiac disease had a relatively recent diagnosis so, exposure to these CRFs must have been present before cardiac damage manifestation and, in addition, CCC is an unremitting disease. Anyway, the possibility that of study population individuals presented a higher exposure-event relationship might not be completely discarded.

Bibliografía


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