The Oxidative Stress and Chronic Inflammatory Process in Chagas Disease: Role of Exosomes and Contributing Genetic Factors

- Maldonado E.[a]
- Rojas D.A.[b]
- Urbina F.[a]
- Solari A.[a]

Abstract

Chagas disease is a neglected tropical disease caused by the flagellated protozoa Trypanosoma cruzi that affects several million people mainly in Latin American countries. Chagas disease has two phases, which are acute and chronic, both separated by an indeterminate time period in which the infected individual is relatively asymptomatic. The acute phase extends for 40-60 days with atypical and mild symptoms; however, about 30% of the infected patients will develop a symptomatic chronic phase, which is characterized by either cardiac, digestive, neurological, or endocrine problems. Cardiomyopathy is the most important and severe result of Chagas disease, which leads to left ventricular systolic dysfunction, heart failure, and sudden cardiac death. Most deaths are due to heart failure (70%) and sudden death (30%) resulting from cardiomyopathy. During the chronic phase, T. cruzi-infected macrophages respond with the production of proinflammatory cytokines and production of superoxide and nitric oxide by the NADPH oxidase 2 (NOX2) and inducible nitric oxide synthase (iNOS) enzymes, respectively. During the chronic phase, myocardial changes are produced as a result of chronic inflammation, oxidative stress, fibrosis, and cell death. The cellular inflammatory response is mainly the result of activation of the NF-κB-dependent pathway, which activates gene expression of inflammatory cytokines, leading to progressive tissue damage. The persisting production of reactive oxygen species (ROS) is the result of mitochondrial dysfunction in the cardiomyocytes. In this review, we will discuss inflammation and oxidative damage which is produced in the heart during the chronic phase of Chagas disease and recent evidence on the role of macrophages and the production of proinflammatory cytokines during the acute phase and the origin of macrophages/monocytes during the chronic phase of Chagas disease. We will also discuss the contributing factors and mechanisms leading to the chronic inflammation of the cardiac tissue during the chronic phase of the disease as well as the innate and adaptive host immune response. The contribution of genetic factors to the progression of the chronic inflammatory cardiomyopathy of chronic Chagas disease is also discussed. The secreted extracellular vesicles (exosomes) produced for both T. cruzi and infected host cells can play key roles in the host immune response, and those roles are described. Lastly, we describe potential treatments to attenuate the chronic inflammation of the cardiac tissue, designed to improve heart function in chagasic patients.