10 The Roles of Immunity and Autoimmunity in Chronic Heart Failure

S. von Haehling, W. Doehner, S.D. Anker

Abstract. Chronic heart failure (CHF) represents a major public health burden in developed countries. The introduction of new treatments has helped to improve its prognosis in recent years. However, it is still not possible to directly target the immunological aspects of the disease. In fact, chronic immune activation with the up-regulation of pro-inflammatory substances in the plasma remains an important feature of the disease, independently of its aetiology. Autoimmune mechanisms play a significant role in a subgroup of patients with dilated cardiomyopathy. The interplay between the two systems has not been established so far. This review briefly summarizes immune and autoimmune mechanisms in CHF.

10.1 Introduction

Chronic heart failure (CHF) is a multisystem disorder that affects various bodily systems and not merely the cardiovascular system. Indeed, convincing evidence has accumulated over the last years to suggest that CHF represents a state of chronic inflammation (Anker and von Haehling 2004). The original discovery of elevated levels of tumour necrosis factor-α (TNF-α), a pro-inflammatory cytokine, in advanced stages of the disease (Levine et al. 1990) triggered an avalanche of research 15 years ago that has lasted to the present day. Thus, attention has mostly focussed on the role of TNF-α and other pro-inflammatory substances. However, the origin of pro-inflammatory activation remains enigmatic. Several hypotheses have been suggested to explain this phenomenon; there is only indirect evidence available to support these theories. However, it is clear that pro-inflammatory activation largely contributes to the progression of CHF and that it triggers the deterioration of the clinical status of the patients.

Pro-inflammatory cytokine activation occurs independently of CHF aetiology. A subgroup of approximately 25% of CHF patients present with dilated cardiomyopathy (DCM), a disorder associated with progressive dilatation of the (predominantly left) ventricle and loss of cardiac function in the absence of known causes. DCM represents the most important cause for severe CHF in younger adults in developed countries (Centers for Disease Control and Prevention 1998). A genetic background (mutations in genes encoding for myocyte structural proteins) is suspected in about 30% of these patients (Graham and Owens 1999; Seidman and Seidman 2001). In many other cases, myocarditis appears to be the underlying disorder that eventually yields DCM; however, in some patients the aetiology remains unclear. Autoantibodies also appear to play an important role. Current concepts regarding exogenous causes of DCM, therefore, comprise chronic myocarditis and primary abnormalities of the immune system (Kühl et al. 1996; Luppi et al. 1998). This, for example, is the case in giant-cell myocarditis, a rare disease associated with autoimmune disorders (Eriksson and Penninger 2005). The article will briefly summarize the roles of both immune and autoimmune mechanisms in CHF.