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Stimulated Cellular Immune System in Patients with Congestive Heart Failure[1])

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Summary: In this cross-sectional study, we analysed serum concentrations of soluble markers of cellular immune activation, namely, interferon-γ, neopterin (a product of activated macrophages), soluble interleukin-2 receptor, and soluble CD8, in 25 patients with congestive heart failure. Ten (40%) patients showed increased concentrations (i. e. above the reference ranges of healthy controls) of neopterin, 14 (56%) showed increased soluble interleukin-2 receptor, and 6 (24%) showed increased soluble CD8. Endogenous interferon-γ was detectable in 10 patients (40%). In addition, we found significant correlations between neopterin and interferon-γ ($rs = 0.417$, $p < 0.05$), and between neopterin and soluble CD8 concentrations ($rs = 0.430$, $p < 0.05$). All patients with increased soluble CD8 also had increased soluble interleukin-2 receptor. However, no significant correlations of soluble interleukin-2 receptor with soluble CD8 or any of the other quantities were observed.

Increased concentrations of soluble interleukin-2 receptors, soluble CD8 and neopterin indicate that cellular immunity is stimulated in patients with congestive heart failure. Activated CD8-positive T-lymphocytes may represent the source of increased soluble CD8. Endogenous interferon-γ, which is derived from activated T-cells, may induce neopterin release by monocytes/macrophages.

Introduction

Patients with congestive heart failure often present with immunological abnormalities (1–3). Viral infections or autoimmune phenomena appear to be involved in the pathogenesis of the disorder (4, 5). Serologic evidence of persistent enterovirus infection and enterovirus-specific RNA sequences can be found in myocardial biopsies of patients with myocarditis and dilated cardiomyopathy (6, 7).

Recently we described increased concentrations of serum neopterin in patients with chronic myocarditis and dilated cardiomyopathy (8, 9). Large amounts of neopterin, which is a pyrazino-pyrimidine-derivative derived biosynthetically from guanosine triphosphate, are released from human macrophages on stimulation with interferon-γ (10). Increased neopterin concentrations were observed earlier in patients suffering from diseases which involve activation of the cellular immune system, such as viral infections, allograft rejection, and autoimmune diseases (10, 11). Also, in these clinical conditions, increased neopterin may indicate the increased endogenous formation of interferon-γ, because significant correlations between the concentrations of those two compounds are frequently found (12, 13).

In this study, we tried to gain further evidence for cellular immune activation in patients with congestive heart failure. We examined serum concentrations of interferon-γ, neopterin, and additional immune activation markers, such as soluble interleukin-2 receptor and soluble CD8 in the serum of patients.

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