Introduction

Cardiogenic shock (CS) is one of the most serious complications of acute myocardial infarction (AMI). In spite of great progress in its therapy (early revascularisation, use of intra-aortic balloon contra-pulsation etc.), there are some questions concerning its pathophysiology which remain to be elucidated. One of them is immune system activation and its role in the myocardial ischemia-reperfusion process in the course of AMI complicated with cardiogenic shock.

The activated neutrophils and their interaction with endothelial cells and myocytes are believed to play the key role in the pathophysiology of the ischemia and reperfusion process by producing free oxygen radicals, arachidonic acid derivatives and proteolytic enzymes (5,6,8). Emmanu et al. (5) showed that cytokines and adhesion molecules are involved in this process. In his hypothesis the injured myocardial cells initially release the products that promote chemotaxis, neutrophil shape change, enhanced neutrophil surface expression of CD11/CD18 adhesion heterodimers, and upon adherence, release of granular contents and production of oxygen free radicals. The secretary and migratory functions of neutrophils require adherence of CD11/CD18 to the intercellular adhesion molecule-1 (ICAM-1). At least one additional ligand (E-selectin, CD62E) is suggested to be involved in this process. E-selectin is expressed on the cell surface over a period of 2-6 h after stimulation of the endothelial cells with interleukin-1 and TNFα. Once neutrophils are bound to the endothelium in the capillary venules, they can migrate into the extracellular space. Previous studies have shown that the effect of neutrophil on the cardiac myocyte also requires expression of the adherence complex of CD11/CD18 and ICAM 1, and that these processes are mediated by cytokines (12). We have shown the elevation of plasma interleukin and adhesion molecules levels in the course of AMI in our previous studies (9,10). Furthermore, the negative haemodynamic effects of cytokines, IL-1β and TNFα, have been described in previous studies in patients with chronic heart failure. But little is known about the impact of CS on the plasma cytokine and adhesion molecule levels in the course of AMI.

The aim of this observation is to evaluate the plasma interleukin and adhesion molecule levels in the patient with AMI, complicated by fatal cardiogenic shock.

Report of a Case

A 60 year old man with no previous history of coronary artery disease was admitted for typical chest pain 3 h after onset of the symptoms. Physical examination revealed dys-
Recent studies (4-6,8,9,10,12) have shown that immune shock (normal value of ICAM 1 189.05 ng/ml, SD 42.32ng/ml, E-selectin 29.1-63.4 ng/ml).

Plasma ICAM 1 and E-selectin levels in cardiogenic shock (normal value of IL 6 <10 pg/ml, normal value of IL 8 <30pg/ml).

The plasma IL 8 level was elevated throughout the time period of observation because of cardiogenic shock (the last TNF α level was 204.1 pg/ml) - Fig. 1.

The soluble adhesion molecule levels (E-selectin and ICAM 1) were elevated throughout the period of observation without any significant peak - Fig. 3.

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**Discussion**

Recent studies (4-6,8,9,10,12) have shown that immune system activation, and the accumulation of activated neutrophils at the site of infarction are regulated by cytokines, and that neutrophil-endothelium, and neutrophil-myocyte interactions require the expression of adherence molecules (ICAM 1, E-selectin etc.).

Our observation showed the elevation of proinflamma-
tory cytokines during the course of AMI, and, after a short period of decrease, the second elevation of TNF α, IL 6 and IL 8, which is very likely to be caused by CS. Two pe-
aks of TNF α plasma concentration were noticed. The first elevation was caused by AMI and the second one was caus-
ed by cardiogenic shock. Although TNF α cytokine has a pleiotropic effect, it is also known to have cardio-depres-
sant properties. The mechanism of TNF α elevation is not yet clear, but Brunkhorst et al. (3) showed, that expression to bacterial endotoxin, perhaps due to bowel congestion or in-
flammation, and thereby endotoxin release, which may result in immune activation that is characteristic for patients with severe heart failure. Also Anker et al. (1,2) hypothesized that in patients with heart failure mesenteric venous congestion leads to increased bowel permeability, bacterial transloca-
tion, and thereby endotoxin release, which is responsible for immune system activation and increased TNF α pro-
duction. However, these observations have been found in groups of patients with chronic heart failure. The study of Riemsdijk et al. (11) showed local myocardial production of these cytokines by myocytes and endothelium (7), and that the TNFcs system is deregulated in the course of acute left ventricular failure. A positive correlation is found between the severity of heart failure and TNF α levels in patients with chronic heart failure. In contrast to these observations, our results could sup-
port the hypothesis that elevated plasma TNF α level could be a marker of acute left ventricular dysfunction and cardi-
ogenic shock.

**Conclusion**

This study confirms the excessive overproduction of in-
terleukins with a predominantly negative effect on the car-
diovascular system in the course of CS.

This observation also reveals a possible target for future therapeutic interventions with the aim of improving the sur-
vival of patients with cardiogenic shock.
system, and the accumulation of activated neutrophils at the site of infarction are regulated by cytokines, and that neutrophil-endothelium, and neutrophil-myocyte interactions require the expression of adhesion molecules (ICAM 1, E-selection etc.).

Our observation showed the elevation of proinflammatory cytokines during the course of AMI, and, after a short period of decrease, the second elevation of TNF α, IL 6 and IL 8, which is very likely to be caused by CS. Two peaks of TNF α plasma concentration were noticed. The first elevation was caused by AMI and the second one was caused by cardiogenic shock. Although TNF α cytokine has a pleiotropic effect, it is also known to have cardio-depressant properties. The mechanism of TNF α elevation is not yet clear, but Brunkhorst et al. (3) showed, that exposure to bacterial endotoxin, perhaps due to bowel congestion or bacterial translocation, and thereby endotoxin release, which may result in ineffective circulation of patients with severe heart failure. Also Anker et al. (12) hypothesized that in patients with heart failure mesenteric venous congestion leads to increased bowel permeability, bacterial translocation, and thereby endotoxin release, which is responsible for immune system activation and increased TNF α production. However, these observations have been found in groups of patients with chronic heart failure. The study of Ryensdijk et al. (11) showed local myocardial production of these cytokines by myocytes and endothelium (7), and that the TNF α system is deregulated in the course of acute left ventricular failure. A positive correlation is found between the severity of heart failure and TNF α levels in patients with chronic heart failure. In contrast to these observations, our results could support the hypothesis that elevated plasma TNF α level could be a marker of acute left ventricular dysfunction and cardiogenic shock.

Conclusion

This study confirms the excessive overproduction of interleukins with a predominantly negative effect on the cardiovascular system in the course of CS.

This observation also reveals a possible target for future therapeutic interventions with the aim of improving the survival of patients with cardiogenic shock.

References