Valvular, Myocardial, Pericardial, Pulmonary, Congenital Heart Disease – Myocardial Disease, Clinical, Dilated Cardiomyopathy

Interleukin-17 and interferon-gamma in patients with different forms of non-ischemic cardiomyopathies

V. Zach¹, C. Plappert¹, G. Aleshcheva², C. Baumeier², L. Alasfar³, H.P. Schultheiss², F. Escher¹

¹Deutsches Herzzentrum der Charité (DHZC), Klinik für Kardiologie, Angiologie und Intensivmedizin CVK, Berlin, Germany
²Institute of Cardiac Diagnostics and Therapy (IKDT), Berlin, Germany
³Charité - University Medicine Berlin, Berlin, Germany

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Introduction: Dilated cardiomyopathy (DCM) characterized by left ventricular dilation and impaired left ventricular function represents a common and severe cause of heart failure (HF). Predominantly affecting younger patients, it is considered a leading cause for sudden cardiac death and heart transplantation. Several studies identified myocarditis as a substantive precursor and potential cause of DCM. Inflammatory cardiomyopathy (DCMi) can lead to cardiomyocytal damage and exposure of cardiac myosin and other heart proteins. This cascade can in susceptible individuals trigger an altered immune response consecutively leading to autoimmunity and chronic inflammation. A variety of inflammatory and immunologic agents are discussed to be involved in the pathophysiology of myocardial inflammation. Several studies suggested a role of Interleukin -17 (IL-17) and Interferon-γ (IFN-γ) in chronic HF, myocardial infarction and other cardiovascular diseases. Underlying pathomechanisms, however, are poorly understood.

Methods: In this study we measured IL-17 and IFN-γ levels in serum by ELISA in patients in which an endomyocardial biopsy (EMB) was performed due to chronic unexplained heart failure symptoms after exclusion of ischemic or valvular heart disease at our center. All patients underwent transthoracic echocardiography prior to EMB sampling. Patients were classified according to the histological presence of inflammation into DCMi, DCM and patients with preserved left ventricular ejection fraction (LVEF) without inflammation. EMB specimens were analyzed including histology, immunohistochemistry and molecular virology.

Results: A total of 289 patients were included into the final analysis. Mean age was 47 years and 71% were male. Mean LVEF was 50% and mean left ventricular end-diastolic diameter (LVEDD) was 57 mm. Based on EMB results, 71 (25%) samples were categorized as DCMi and 113 (39%) as DCM. 105 (36%) samples were assigned to the group without myocardial inflammation and normal LVEF. The groups differed significantly in their inflammatory profiles. Levels of IL-17 (p < 0.001) and IFN-γ (p < 0.01) were significantly higher in patients with DCMi compared to the DCM as well as the normal LVEF group (Figure 1, Figure 2). Therefore, this effect is not specific for heart failure, but seems to be an important mediator in inflammatory cardiomyopathy.

Conclusion: Our data showed a significant elevation of IL-17 and IFN-γ in patients with inflammatory dilated cardiomyopathy. These findings suggest that these agents play an important role in the disease entity development and progression that remains poorly understood. So far treatment strategies in DCMi are unspecific. Therefore, blocking IL-17 expression could be an interesting potential therapeutic target in future (personalized) treatment for a wide group of patients with heart failure generated by inflammatory causes.
Serum IL-17 levels.
t-SNE analysis of the different groups.