1 Overview on Chronic Viral Cardiomyopathy/Chronic Myocarditis

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Abstract. Myocarditis is most often induced by cardiotropic viruses and often resolves with minimal cardiac remodelling and without discernable prognostic impact. Acute myocarditis has a highly diverse clinical presentation (asymptomatic, infarct-like presentation, atrioventricular (AV)-block, atrial fibrillation, sudden death due to ventricular tachycardia, fulminant myocarditis with severely depressed contractility). Progression of myocarditis to its sequela, dilated cardiomyopathy (DCM), has been documented in 20% of cases and is pathogenically linked to chronic inflammation and viral persistence. Persistence of cardiotropic viruses (enterovirus, adenovirus) constitutes one of the predominant aetiological factors in DCM. Additionally, circulating autoantibodies to distinct cardiac autoantigens have been described in patients with DCM, providing evidence for autoimmune involvement. Since clinical com-
plaints of myocarditis and DCM are unspecific, a positive effect of any specific therapy depends on an accurate biopsy-based diagnosis and characterization of the patients with histological, immunohistological and molecular biological methods (PCR), which have developed into sensitive tools for the detection of different viruses, active viral replication, and myocardial inflammation. The immunohistochemical characterization of infiltrates has supported a new era in the diagnosis of myocardial inflammation compared with the Dallas criteria, which has led to a new entity of secondary cardiomyopathies acknowledged by the WHO, the inflammatory cardiomyopathies (DCMi). Immunohistochemically quantified lymphocytes significantly better reflect troponin levels and correlate with findings by anti-myosin scintigraphy compared with the histological analysis. Furthermore, the orchestrated induction of endothelial cell adhesion molecules (CAMs) in 65% of DCM patients has confirmed that CAM induction is a prerequisite for lymphocytic infiltration in DCMi. The combination of these immunohistological with molecular biological diagnostic techniques of virus analysis allows a further classification of dilated cardiomyopathy by differentiating the disease entity in subgroups of virus-positive and virus-negative patients with or without cardiac inflammation. Further analysis of the predominant Th1-/Th2-immune response may provide additional prognostic information on the natural course of the disease. This differential analysis improves the clinical management of patients and is an indispensable prerequisite for the development of specific antiviral or immunomodulatory treatment strategies.

1.1 Introduction

Cardiomyopathies are diseases of the heart characterized by ventricular dysfunction that is not caused by primary heart diseases, e.g. hypertension or congenital, valvular, coronary, arterial or pericardial abnormalities. They are classified as primary cardiomyopathies if the origin of contractile dysfunction is unknown (dilated cardiomyopathy, hypertrophic cardiomyopathy) and as secondary or specific cardiomyopathies if the heart is affected in association with specific infectious, immunological, metabolic, neuromuscular or toxic diseases.

Dilated cardiomyopathy (DCM) is one of the most common cardiomyopathy entities. Its yearly incidence is 5–8 cases per 100,000, the age-corrected prevalence is 36 cases with 17 hospitalizations, and 3.8 deaths per 100,000 per year are due to DCM. DCM affects males most