

Myocarditis is a disease leading to cardiomyocytes damage due to inflammation and may result in inflammatory cardiomyopathy/dilated cardiomyopathy and consequently heart failure. It also carries a risk of dangerous arrhythmias, need for a heart transplantation and sudden cardiac death. Unfortunately, myocarditis occurs mostly in children and young adults who lead active family life and either receive education or work. Therefore, the disease impacts the life of entire families and generates high and long-term treatment costs which indicates an urgent need for improvement of diagnostics and therapy of myocarditis. The symptoms of myocarditis are diverse and untypical (e.g., shortness of breath, chest pain, palpitations, fatigue, limb swelling, accompanying signs of infection), which makes the diagnostic process difficult and complex. The only method that allows for a definite diagnosis of myocarditis is endomyocardial biopsy (EMB) or autopsy – in other words the collection of a myocardial tissue for further tests from an alive or deceased patient.

Myocarditis can be caused by infectious and non-infectious factors (e.g., autoimmune diseases, prescribed drugs), however viruses are considered to be the most common cause of myocarditis. The most frequently detected viruses in the EMBs of patients with myocarditis are parvovirus B19 (B19V), coxsackievirus type B and other enteroviruses, human herpesvirus type 6 (HHV-6) and adenoviruses. Recently, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) responsible for the coronavirus disease 2019 (COVID-19) pandemic has been widely proclaimed to be the cause of myocarditis. However, the mechanisms behind myocardial injury caused by the virus remain unknown.

Currently, treatment of myocarditis is usually limited only to reducing physical activity for prolonged periods of time and treatment of arising complications (e.g., heart failure, arrhythmias, thromboembolic events). According to current guidelines, the exclusion of the presence of viral genome in the myocardium (collected using EMB) is crucial for the initiation of targeted treatment (i.e., immunosuppressive therapy) which was shown to improve patient's prognosis. Starting immunosuppression is contraindicated when a viral genome is detected in EMB, due to the increased risk of exacerbation of the viral infection. On the other hand, antiviral treatment is not routinely recommended due to the lack of evidence of its efficacy.

However, the role of the viruses in the pathogenesis of myocarditis is now a subject of debate. It is suggested that the presence of viruses in the myocardium may not play a significant role in the pathogenesis of myocarditis and may be an accidental finding without correlation with past or active disease, especially when the amount of viral genetic material (viral load) is low and it belongs to a particular species (i.e., B19V, HHV-6). This hypothesis is backed by the fact, that sometimes particular viral genomes can be found in the heart of patients with no history of myocarditis or cardiomyopathy. In order to achieve a better understanding of the mechanism driving myocarditis, more data on virus prevalence and viral load in the myocardium as well as their correlation with markers of inflammatory processes in patients without history of myocarditis or cardiomyopathy are of very high interest. The described project aims to provide these data by performing EMBs intraoperatively during cardiac surgery in patients without history of myocarditis or cardiomyopathy.

Additionally, data regarding other factors that could potentially play a role in the pathogenesis/diagnosis of myocarditis will be gathered. These include: specific serum anti-heart autoantibodies (AHA) – presence of which alongside concomitant inflammatory cell infiltration in the heart muscle, may indicate an immune-mediated form of myocarditis; cytokines - small proteins involved in the immune response an increased level of which was found in the serum of patients with EMB-proven myocarditis; microRNA (miRNA) - small, non-coding RNA molecules which control gene expression; and changes in the expression of selected genes in EMB material. Data regarding the presence of viruses (and the viral load) in the heart muscle and their correlation with changed expression of selected genes, as well as presence of novel biomarkers found in blood serum or heart tissue of patients without a history of myocarditis or cardiomyopathy are highly needed in order to improve diagnostics and design effective therapeutic strategies.

This project aims to (1) assess the prevalence and amount of genetic material of selected viral species in EMB among 100 patients without a history of myocarditis and/or cardiomyopathies as well as to (2) correlate them with the histological and immunohistochemical features of active or past myocarditis. The third main goal of the study is (3) identification/validation of novel biomarkers in serum or heart tissue and analysis of their relationship with the EMB findings (active/past myocarditis, viral presence). The study will also (4) correlate the above-mentioned results with serum and EMB findings from 20 patients with confirmed myocarditis.

The results of our study will increase the knowledge and challenge the paradigm regarding the clinical significance of presence of cardiotropic viruses in EMB through investigating their prevalence and load in patients without history of myocarditis or cardiomyopathies. Moreover, prevalence of AHA, changes in levels of particular cytokines, miRNA and changes in expression of selected genes in the same group of patients will be investigated. These results will drastically impact the knowledge regarding the clinical role of these parameters, as well as their role in the pathogenesis and diagnosis of myocarditis.