The role of autoimmune inflammation in the pathogenesis of arrhythmogenic right ventricular cardiomyopathy

Arrhythmogenic right ventricular cardiomyopathy (ARVC) is a progressive heart muscle disease, which is associated with the risk of sudden cardiac death and progressive heart failure. It is characterized by the replacement of the right ventricular myocardium with fibrous and fatty tissue, but the exact mechanism of this process has not yet been known. It is believed that the disease has a genetic basis with pathogenic mutations in genes encoding proteins composing structures responsible for cell-to-cell adhesion, called desmosomes. Abnormalities of desmosomes lead to cardiomyocyte detachment and death, and, consequently, fibrofatty replacement of the myocardium. Interestingly, dying myocytes are frequently observed in association with inflammatory infiltrates, suggesting that the fibrosis process may be immunologically mediated. Another observation in favor of the participation of the immune process in the pathogenesis of the disease is the recent finding of Canadian researchers, who detected autoantibodies against one of the proteins involved in the formation of desmosomes, desmoglein-2. However, the importance of this discovery remains unclear.

The aim of the study is to assess the role of autoimmune inflammation in the pathogenesis of arrhythmogenic right ventricular cardiomyopathy and verification of the hypothesis that the inflammatory process leads to progressive fibrosis and is responsible for the clinical outcome. Patients with ARVC involved in the study will be examined with positron-emission tomography (PET) to detect inflammation within the heart muscle. At the same time, blood levels of biomarkers of inflammation and fibrosis will be evaluated, as well as the levels of anti-desmoglein-2 autoantibodies. Genetic testing will also be performed to detect pathogenic mutations in genes encoding protein components of intercellular junctions. Patients with signs of inflammation in the heart muscle will be referred for endomyocardial biopsy. The material obtained in this way will undergo a histopathological and immunohistochemical assessment to determine the extent and severity of myocardial inflammation.

We believe that our study will significantly expand the current state of knowledge about the pathogenesis of ARVC and the role of inflammation in the disease progression. Particular emphasis will be placed on the importance of the autoimmune process, which is a new and poorly understood aspect of the disease pathogenesis. In the future, the study may lead to revolutionary changes in the management of ARVC patients, resulting in the administration of immunosuppressive therapy to stop inflammation, prevent disease progression, and lessen the severity of symptoms.