Lymphocytic Myocarditis

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The term lymphocytic myocarditis refers to a heterogeneous group of disorders characterized by myocyte damage and interstitial infiltration of lymphocytes, which may be associated with variable numbers of macrophages, plasma cells, and eosinophils. Many etiological factors, including viral and parasitic infections, are linked with the morphological picture of lymphocytic myocarditis; however, the exact cause of the disease is very seldom established in the vast majority of patients diagnosed as having lymphocytic myocarditis. The mechanism by which lymphocytes induce myocardial damage has not been fully elucidated. During the course of morphological studies of myocardial biopsy specimens from patients with lymphocytic myocarditis, we have observed close contacts of lymphocytes with cardiac myocytes and endothelial cells. Such contacts are illustrated here. Similar contacts have been observed in experimentally induced coxsackie B viral myocarditis, Chagas' disease, and the myocarditis induced by interleukin-2. These contacts are characterized by the extremely close apposition of areas of the plasma membranes of the two cells. The basement membranes of the myocytes may show focal attenuations of lysis at the point of contact with the plasma membrane of the lymphocyte. We interpret these contacts as indicating a direct cytotoxic effect of the lymphocytes on the myocytes. Considerable evidence supports the concept that immune mechanisms mediate the release of toxic substances, such as perforin, from cytotoxic lymphocytes. Perforin, a powerful cytolytic agent, is localized in the cytoplasmic granules of cytotoxic lymphocytes, from which it is released upon recognition of and contact with the target cell. The released perforin molecules insert into the cell membrane, in which they induce the formation of porelike defects. This results in leakage of cytoplasmic constituents and entry of other cytotoxic products released from the lymphocytes. These lytic effects may lead to limited cell damage or to necrosis. The immunological activation of lymphocytes and the modulation of their cytotoxic effects constitute problems of critical relevance to our understanding of the processes that determine the severity and clinical course of lymphocytic myocarditis.

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Facing page: Light micrograph of 1-μm-thick, toluidine blue-stained section of plastic-embedded myocardial biopsy specimen from a young woman in whom the course of lymphocytic myocarditis had been followed by serial biopsies. This specimen was obtained at a time of marked increase in clinical symptoms. Severe myocyte damage is associated with marked interstitial infiltration of lymphocytes and smaller numbers of macrophages and plasma cells. Close contacts between lymphocytes and myocytes are evident (arrows) in several areas (magnification, ×630). Above: Electron micrograph of same specimen. Portions of two myocytes are shown, together with one granular lymphocyte, two agranular lymphocytes, and two connective tissue cells. The granular lymphocyte, in which several cytoplasmic granules (G) are present, has penetrated through the basement membrane (BM) of the myocyte and is in close contact with its plasma membrane. The myocyte shows hypercontraction and edema but is not necrotic (magnification, ×8000).
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