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CLINICAL STUDIES

Clinicopathologic Description of Myocarditis

ERIC B. LIEBERMAN, MD, GROVER M. HUTCHINS, MD, AHVIE HERSKOWITZ, MD, NOEL R. ROSE, MD, PhD, KENNETH L. BAUGHMAN, MD, FACC

Baltimore, Maryland

Histologic evidence of myocarditis was demonstrated in 35 of 348 patients submitted to endomyocardial biopsy over 5 years. Analysis of the histologic findings and clinical course of these patients resulted in a new clinicopathologic classification of myocarditis in which four distinct subgroups are identified. Patients with fulminant myocarditis become acutely ill after a distinct viral prodrome, have severe cardiovascular compromise, multiple foci of active myocarditis by histologic study and ventricular dysfunction that either resolves spontaneously or results in death. Patients with acute, chronic active and chronic persistent myocarditis have a less distinct onset of illness.

Patients with acute myocarditis present with established ventricular dysfunction and may respond to immunosuppressive therapy or their condition may progress to dilated cardiomyopathy. Those with chronic active myocarditis initially respond to immunosuppressive therapy, but they have clinical and histologic relapses and develop ventricular dysfunction associated with chronic inflammatory changes including giant cells on histologic study. Chronic persistent myocarditis is characterized by a persistent histologic infiltrate, often with foci of myocyte necrosis but without ventricular dysfunction despite other cardiovascular symptoms such as chest pain or palpitation.

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Idiopathic myocarditis is an inflammatory disease of the myocardium of unknown etiology. Although the clinical (1–5) and histopathologic (4–10) features of the disease have been extensively studied, a unifying characterization of the disease has failed to emerge. Historically, cases of subclinical (11), lethal (4,5,11) and progressive (1,4–6) myocarditis have been observed and the disease has been variously described utilizing electrocardiography (2), echocardiography (2,12), serologic studies (13,14) or endomyocardial biopsy (4,8,13,15). In an effort to provide uniform criteria for the pathologic diagnosis of myocarditis, a panel of cardiac pathologists developed a classification of this disease based on histologic features of endomyocardial biopsy specimens. Known as the Dallas criteria (16), this system has been criticized for interobserver variability (17) and may be subject to sampling error (1,18). The failure to develop a clinical description of myocarditis to accompany the pathologic classification has impaired the development of therapeutic trials and fostered controversy as to the very existence of the disease (18).

The purpose of this study was to identify the clinical spectrum of myocarditis and to categorize this disease into four subgroups. This classification is supported by animal models and in humans by clinical and pathologic experience and, in addition, is analogous to the accepted classification of viral hepatitis (19,20). It is hoped that recognition of the clinical substrata of histologically documented myocarditis will allow a better understanding of the anticipated course of patients with this disease. Then, as in hepatitis (20), we may better define an individual patient's suitability for immunosuppressive therapy.

Methods

Study patients. Between December 1, 1983 and July 1, 1988, 348 patients underwent diagnostic endomyocardial biopsy to evaluate cardiac dysfunction. On histologic analysis, 60 patients (17.2%) exhibited active or borderline myocarditis as defined by the Dallas criteria (16):

Two separate classifications are used for the first and subsequent biopsies. On the first biopsy, *active myocarditis* is defined by myocyte necrosis or degeneration, or both, associated with an inflammatory infiltrate adjacent to the degenerating or necrotic myocytes. *Borderline myocarditis* is diagnosed when the inflammatory infiltrate is too sparse or when damage to myocytes is not demonstrable. *No myocarditis* implies that the myocardium is either entirely normal or shows nonspecific changes.

On subsequent biopsies, *ongoing myocarditis* means that myocyte damage or necrosis in association with inflammatory infiltrate persists. In *resolving myocarditis*, the inflammatory infiltrate is substantially reduced and is not inti-

From the Division of Cardiology, the Department of Pathology and the Department of Immunology & Infectious Diseases, The Johns Hopkins Medical Institutions, Baltimore, Maryland.

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Address for reprints: Kenneth L. Baughman, MD, Clayton Heart Disease, The Johns Hopkins Hospital, 600 North Wolfe Street, Baltimore, Maryland 21205.

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