Serial cardiac function tests in myocarditis

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Summary: Sixteen patients (mean age 27 years, range 16 to 39 years) with the diagnosis of myopericarditis established by strict clinical criteria were evaluated following recovery 0.7 to 4.0 years (mean 2.7 years) later. Evidence of an acute viral infection was present in 44%. During the acute illness, the major clinical manifestations consisted of pericarditis in 10 patients, acute myocardial infarction in 5, right ventricular dysfunction in 5, bundle branch or hemiblock in 4, ventricular arrhythmias in 3, congestive heart failure in 3 and cardiogenic shock and inappropriate sinus tachycardia in one patient each. Holter monitoring, echophonocardiography and radionuclide ventriculography results were abnormal in 57, 67 and 64% of patients respectively. At follow-up, these tests were abnormal in 67, 7 and 73%. Focal wall motion abnormalities were present in five. Seventy-five percent of patients had one or more abnormal tests at last follow-up. Although 8 patients had improved by a scoring system, 5 patients had an increase in the number of abnormal tests, including one who died. These findings indicate that persistent abnormalities following recovery from myopericarditis are not rare and support the hypothesis that the syndrome of dilated cardiomyopathy may be a sequel of myopericarditis.

Introduction

The syndrome of dilated cardiomyopathy has been suggested by many to be a late complication of acute viral myocarditis (Smith, 1970; Sainani *et al.*, 1975; Bengtsson & Lamberger, 1966). Advances in the non-invasive technology used to evaluate cardiac function have made study of this postulate feasible.

In 1979, we undertook a 5 year clinical prospective study based on this hypothesis. Our goal was to determine if cardiac function deteriorated over time following clinical recovery from myopericarditis. We identified 16 patients using strict criteria for the diagnosis of myopericarditis and studied them at periodic follow-up intervals with a wide array of non-invasive tests of cardiac function. We have already presented earlier follow-up results from these patients (Miklozek *et al.*, 1984). We now present the latest results.

Materials and methods

Criteria for the diagnosis of myopericarditis

Myopericarditis was diagnosed if the patient de-

veloped new cardiac abnormalities during symptoms of an acute viral infection and had no known cardiac disease, cardiac risk factors, history of alcohol abuse, and did not have endocarditis or another systemic disease. In order to be eligible, patients had to be less than 55 years of age.

Acute illness

A careful history and physical examination were obtained in each patient. Non-invasive studies consisted of standard 12 lead electrocardiograms, M-mode echocardiograms, phonocardiograms, Holter monitoring for 24 hours and radionuclide ventriculograms. A Holter monitor was considered abnormal if one of the following was present: (1) intraventricular conduction disturbance, (2) A-V block, (3) multiform or frequent premature ventricular or atrial beats, or (4) supraventricular tachycardia. The echocardiographic left ventricular ejection fraction was calculated from the formula of Teichholz *et al.* (1976); an ejection fraction less than 55% was considered abnormal. The mean velocity of circumferential fibre shortening (mVcf) was measured according to Cooper *et al.* (1972); a mVcf less than 0.83 circ/s was abnormal. The PEP/LVET ratio was calculated from systolic time intervals obtained from the phonocardiograms as

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described by Tavel (1979); a PEP/LVET ratio greater than 0.420 was considered abnormal. Radionuclide ventriculograms were performed in most patients by intravenous injection of pertechnetate 99m labelled red blood cells; left ventricular ejection fraction was calculated by the count method of Parker *et al.* (1977).

Viral studies

Urine, stool, and throat specimens from each patient were inoculated into continuous cell line cultures maintained in the Virology Laboratory at Beth Israel Hospital. Sera were collected during the acute illness and at least 2 weeks later for determination of microneutralization antibodies. In some patients, sera were sent to the State Board of Health and to Dr John V. Sullivan at the University of Massachusetts for measurement of antibodies to cytomegalovirus and Epstein-Barr virus, respectively.

Follow-up studies

Patients were seen by either CLM or WHA or the primary care physician at various intervals in time following clinical recovery. Whenever possible, electrocardiograms, M-mode echophonocardiograms, radionuclide ventriculograms, 24 hour ambulatory Holter monitoring and symptom limited exercise tests were performed. Exercise tests were performed in conjunction with radionuclide ventriculography using a bicycle ergometer in most patients. Endpoints for the exercise test consisted of (1) onset of cardiac symptoms, (2) significant depression of the S-T segments and/or inversion of the T waves, (3) dysrhythmias, (4) attainment of 85% of the age predicted maximal heart rate, or (5) hypotension.

Results

Sixteen patients with the clinical diagnosis of acute myopericarditis and with available follow-up studies were enrolled from 1979 to 1981. The duration of follow-up ranged from 0.7 to 4.0 years with a mean of 2.7 years. Twelve were males. The mean age was 27 years and ranged from 16 to 39 years. All patients survived the acute illness. One patient died 8.3 months later. There were no other deaths.

Acute illness

Seven patients (44%) had evidence of an acute viral infection by culture or antibody titre. Echovirus 11 was isolated from 5 patients. Another, although culture negative, had stable but elevated titres (1:40) to echovirus 11. In one of these patients, Coxsackievirus B-3 was also isolated during a subsequent

episode of myopericarditis. A seventh patient had both a fourfold rise in titre to cytomegalovirus and reactivation of an Epstein-Barr virus infection.

At the time of diagnosis, the following major cardiac abnormalities were present with overlap in the individual patient of myocardial and pericardial manifestations. Ten patients had pericarditis based on either history, electrocardiogram, presence of a pericardial rub, or effusion by echocardiography. Five presented with evidence of an acute myocardial infarction. Five had clinical right ventricular dysfunction with elevated venous pressure and a right ventricular heave. A bundle branch or hemiblock was present in four patients, while ventricular arrhythmias occurred in three patients. One patient had an inappropriate sinus tachycardia. Congestive heart failure developed in three patients, one of whom had cardiogenic shock.

Abnormalities were commonly detected by all methods used. Cardiac symptoms were elicited from 88% (14/16), and the examination was abnormal in 94% (15/16). Electrocardiograms, Holter monitoring, echophonocardiograms, and radionuclide ventriculograms were abnormal in 88% (14/16), 57% (8/14), 67% (10/15) and 64% (9/14), respectively. A broader definition of abnormalities by Holter monitor was used in this report and explains the larger number of abnormalities when compared to our initial report (Miklozek *et al.*, 1984). Focal wall motion abnormalities by radionuclide ventriculograms were present in 3 patients.

Follow-up

At follow-up, 44% (7/16) still had cardiac symptoms, while the physical examination was abnormal in 63% (10/16). Electrocardiograms, Holter monitoring, echophonocardiograms, radionuclide ventriculograms, and exercise tests were abnormal in 60% (9/15), 67% (6/9), 7% (1/14), 73% (11/15), and 8% (1/13), respectively. Regional wall motion abnormalities were present in five by radionuclide ventriculography. The ejection fraction by echocardiography had increased from $58 \pm 2.7\%$ (s.e.m.) to $69 \pm 1.8\%$ (s.e.m.) ($P < 0.005$), while mean Vcf increased from 1.18 ± 0.9 circ/s (s.e.m.) to 1.31 ± 0.5 circ/s (s.e.m.) (not significant) in 13 of the group. The PEP/LVET ratio calculated from the phonocardiogram decreased from 0.400 ± 0.2 to 0.310 ± 0.05 (s.e.m.) (not significant) in 12 of the group. Ejection fraction by radionuclide ventriculography decreased from $62 \pm 3.8\%$ (s.e.m.) to $55 \pm 3.9\%$ (s.e.m.) (not significant) in 13 of the group. Only 10 of these were also included in the echocardiographic group above.

Since all tests could not be performed in all patients, we attempted to compare the patients by the following method. A scoring system was devised in which each patient received one point for each abnormal category.

The number of points was then summed and divided by the total number of categories and expressed as a percentage. The categories consisted of (1) symptoms of myocardial dysfunction, (2) ventricular enlargement by physical examination, and (3) conduction disturbances or dysrhythmias by electrocardiogram or (4) by Holter monitoring, (5) echophonocardiogram and (6) resting radionuclide ventriculograms. The maximum score possible was 6 points per visit, or 100%. By this system, 8 patients improved, 3 patients showed no change, and 5 patients deteriorated.

Discussion

We have followed 16 patients with myopericarditis for a mean period of 2.7 years following clinical recovery using a wide variety of non-invasive tests of cardiac function. The diagnosis of myopericarditis was based on strict clinical criteria. Patients were less than 55 years of age, did not have known prior cardiac disease or alcoholism, and had new cardiac abnormalities during symptoms of an acute viral infection. Evidence of a viral infection was found in 44%. The large prevalence of cardiac symptoms and abnormalities by examination and by electrocardiograms is explained by the strict criteria used in identifying patients with myopericarditis. Holter monitoring, echophonocardiograms, and radionuclide ventriculograms identified abnormalities in 57, 67, and 64%, respectively.

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