Natural Course of Peripartum Cardiomyopathy

By John G. Demakis, M.D., Shahbudin H. Rahimtoola, M.B., M.R.C.P.E.,
George C. Sutton, M.D., W. Robert Meadows, M.D.,
Paul B. Szanto, M.D., John R. Tobin, M.D.,
and Rolf M. Gunnar, M.S., M.D.

SUMMARY
Twenty-seven patients presented in the puerperium with cardiomegaly, abnormal ECG, and congestive cardiac failure and were considered to have peripartum cardiomyopathy (PPCM). The incidence of PPCM was significantly higher in women over 30 years of age, in women in their third or subsequent pregnancy, and in the presence of twins or toxemia. Within 6 months, 14 patients had normal sized hearts (group A), and 13 patients maintained cardiomegaly (group B).

The 14 patients in group A have been followed for 3 to 21 years (average 10.7 years). Two have died of unrelated causes. Of the remaining 12, eight are functional class I and four are functional class II. Eight patients had 21 subsequent pregnancies, with no permanent deterioration of cardiac function. Of 13 patients in group B, 11 (85%) have died of congestive cardiac failure. Their average survival was 4.7 years; six of 11 were dead in 3 years. Their clinical course was punctuated by repeated admissions for congestive cardiac failure. Six had pulmonary emboli, one had a systemic embolus, and three of six patients with subsequent pregnancies deteriorated in the puerperium. Of the two surviving patients, one is functional class I and the other is functional class II.

Therefore, in those patients in whom cardiomegaly persisted, the prognosis was poor, and subsequent pregnancies were likely to lead to permanent deterioration. In those in whom the heart size returned to normal the prognosis was excellent.

Additional Indexing Words:
Primary myocardial disease
Pregnancy Cardiac failure
Myocardial fibrosis Myocardial biopsy
Postpartum cardiomyopathy

CARDIOMYOPATHY presenting initially in the postpartum period is well known, but the etiology and subsequent course of the disorder remain unclear. Since some of the reported patients developed cardiac failure in the last month of pregnancy, it is probably more appropriate to use the term “peripartum cardiomyopathy” (PPCM). This study presents data on 27 women with cardiomyopathy recognized for the first time in the puerperal period. The patients have been followed periodically for up to 21 years. Major emphasis will be placed on the clinical course in order to shed light on the natural history.

Criteria for Diagnosis. The criteria for the diagnosis of PPCM were (1) development of cardiac failure in the last month of pregnancy.

From the Department of Adult Cardiology, Division of Medicine, and the Hektoen Institute for Medical Research, Cook County Hospital; the Department of Medicine, Abraham Lincoln School of Medicine, University of Illinois College of Medicine, Northwestern University Medical School, and Chicago Medical School, Chicago, Illinois, and Loyola University Stritch School of Medicine, Maywood, Illinois.

Supported in part by grant RN-63-24 from the Chicago Heart Association, grant HE-9666 from the National Heart and Lung Institute, U. S. Public Health Service, and the Preble Laboratory Research Fund.

Address for reprints: John G. Demakis, M.D., Department of Adult Cardiology, Cook County Hospital, 1825 Harrison Street, Chicago, Illinois 60612.

Received May 20, 1971; revision accepted for publication August 6, 1971.
or within 5 months of delivery, (2) absence of a determinable etiology for the cardiac failure, and (3) absence of demonstrable heart disease prior to the last month of pregnancy.

**Material and Methods**

Observations are based on 27 patients, 15 of whom were reported in 1957. The patients were all seen at Cook County Hospital over a 20-year period (1947-1967) by one or more of the authors during the first episode of cardiac failure. These patients were seen in consultation because of the presence of cardiac failure. They have been followed for 3 to 21 years (average 7.6 years).

In addition to a complete history and physical examination, a more detailed dietary history included special emphasis on alcoholic intake. All patients had an electrocardiogram (ECG) and chest X-rays. The last 12 patients had vectorcardiograms (VCG). In addition, all patients had hematological, biochemical, and serological tests to rule out other forms of heart disease as previously described. Complement fixation titers for 15 agents, including coxsackie B2, B3, B5, adenovirus, influenza A and B, and chlamydia, were done on five patients during the initial episode of congestive cardiac failure and were repeated at 6 weeks and then serially every 3 months. Upon discharge from the hospital, all patients were followed in a "special" clinic. They were seen at 3-month intervals or more frequently if deemed necessary.

Five patients had thoracotomy for myocardial biopsy. The tissue obtained by biopsy weighed about 50 mg and included epicardium, myocardium, and endocardium. The biopsy specimens were fixed in 10% buffered formalin and were sectioned serially and stained. Necropsies were performed on seven patients.

Five of these patients had toxemia (increased blood pressure and proteinuria). In each patient, the blood pressure returned to normal, and the proteinuria disappeared before the onset of cardiac failure. Guidelines for excluding other forms of heart disease have been previously outlined.

**Results**

None of the patients had a previous history of heart disease. Seventeen of the 27 patients had a normal chest X-ray or cardiac examination, or both, during or just prior to pregnancy. None of the patients had clinical evidence of protein or vitamin deficiencies, and none overindulged in alcohol. Signs and symptoms of acute viremia were not present. Five patients had serial complement fixation titers but none showed a fourfold increase in titers.

In table 1, the incidence of five variables in the 27 patients with PPCM is compared with the same variables in all women who delivered at Cook County Hospital from 1952 through 1965 (226,878 women). The incidence of PPCM is significantly higher in older and multiparous women and in the presence of twins and toxemia.

The onset of heart failure occurred during the first 3 postpartum months in 22 patients (81%), in the fourth and fifth postpartum

**Table 1**

**Incidence of Certain Variables**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Patients with peripartum cardiomyopathy</th>
<th>Percent of all women who delivered at Cook County Hospital from 1952 - 1965 (226,878 women)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negro</td>
<td>25</td>
<td>93</td>
<td>84</td>
</tr>
<tr>
<td>Caucasian</td>
<td>2</td>
<td>7</td>
<td>16</td>
</tr>
<tr>
<td>Age at time of delivery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;30 years</td>
<td>14</td>
<td>52</td>
<td>77</td>
</tr>
<tr>
<td>≥ 30 years</td>
<td>13</td>
<td>48</td>
<td>23</td>
</tr>
<tr>
<td>Parity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1st and 2nd pregnancy</td>
<td>8</td>
<td>29</td>
<td>52</td>
</tr>
<tr>
<td>3 or more pregnancies</td>
<td>19</td>
<td>71</td>
<td>48</td>
</tr>
<tr>
<td>Toxemia</td>
<td>6</td>
<td>22</td>
<td>5</td>
</tr>
<tr>
<td>Twins</td>
<td>2</td>
<td>7</td>
<td>1</td>
</tr>
</tbody>
</table>

*Not significant.
months respectively in two other patients, and in two additional patients the symptoms started 1 month antepartum.

All patients presented with signs and symptoms of left ventricular failure. Table 2 lists the various clinical manifestations.

Cardiomegaly was present in all cases, and many had pulmonary venous congestion on the chest X-ray. The initial ECG was abnormal in each patient (table 3). One patient had Q-waves in V1-V3 that could be read as the pattern of an anteroseptal myocardial infarct. However, this woman, aged 43 at the time of her episode of peripartum cardiac failure, had never experienced cardiac pain. There were no biochemical or familial factors predisposing to the development of premature coronary artery disease. This patient has been followed for 5 years and remains asymptomatic. The ancillary laboratory investigations showed no significant abnormalities.

All patients were treated with conventional therapy for cardiac failure, including bed rest, digitalis, and diuretics. Prolonged bed rest was attempted in two patients whose heart size had not returned to normal with conventional therapy. However, prolonged bed rest was unsuccessful because of lack of patient cooperation. Initially, all patients made a satisfactory clinical response.

**Follow-Up Studies**

The patients were divided into two groups on the basis of the size of the heart (as assessed by clinical and radiological criteria) at the end of 6 months: Group A included patients whose heart size had returned to normal; group B included patients with persistent cardiomegaly. There was no difference between these two groups with respect to race, age, time of onset of symptoms, parity, incidence of twins, presence of toxemia, their initial clinical presentation, or mode of initial therapy. The follow-up data on these patients are summarized in table 4.

**Group A Patients**

In 14 patients the heart size returned to normal within 6 months, and all were free from symptoms at the time of discharge from the hospital (fig. 1). They have been followed for 3 to 21 years (average 10.7).

Eight patients had 21 subsequent pregnancies. Two patients developed postpartum cardiac failure with subsequent pregnancies and another developed cardiac failure due to systemic hypertension 20 years after her episode of peripartum cardiomyopathy. None of the other patients has developed cardiomegaly or gallop rhythm, nor has anyone experienced further episodes of heart failure. Two patients in this group have died, one of carcinoma of the cervix and the other of renal disease.

**Group B Patients**

Thirteen patients maintained cardiomegaly at the end of 6 months (fig. 2). They have been followed for 1 to 16 years (average 5.4 years). All 13 patients continued to have gallop rhythm and cardiomegaly. Eleven have
Table 4

Follow-up Data

<table>
<thead>
<tr>
<th>Patients</th>
<th>Group A</th>
<th>Group B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>14</td>
<td>13</td>
</tr>
<tr>
<td>Follow-up</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average (range), years</td>
<td>10.7 (3-21)</td>
<td>5.4 (1-16)</td>
</tr>
</tbody>
</table>

Clinical features

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiomegaly</td>
<td>0</td>
<td>13</td>
</tr>
<tr>
<td>Gallop rhythm</td>
<td>0</td>
<td>13</td>
</tr>
<tr>
<td>Chronic CCF*</td>
<td>0</td>
<td>11</td>
</tr>
<tr>
<td>Pulmonary emboli</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>Systemic emboli</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

Electrocardiogram

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>9</td>
<td>0</td>
</tr>
<tr>
<td>Abnormal</td>
<td>5</td>
<td>13</td>
</tr>
</tbody>
</table>

Other disorders

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Systemic hypertension</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Minimal aortic insufficiency</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

Subsequent pregnancies

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
</tr>
</thead>
<tbody>
<tr>
<td>No change</td>
<td>18 (6 pts†)</td>
<td>3</td>
</tr>
<tr>
<td>Deterioration — temporary permanent</td>
<td>3 (2 pts)</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>3</td>
</tr>
</tbody>
</table>

Deaths

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2 (14%)</td>
<td>11 (85%)</td>
</tr>
</tbody>
</table>

  1 Ca cervix, 6 years later
  1 Renal failure, 16 years later

Functional status of survivors (N.Y.H.A. Class.‡)

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>8</td>
<td>1</td>
</tr>
<tr>
<td>II</td>
<td>4</td>
<td>1</td>
</tr>
</tbody>
</table>

*CCF = Congestive cardiac failure.
†pts = patients.
‡(N.Y.H.A. Class.) = (New York Heart Association Classification).

had chronic cardiac failure, six have had pulmonary emboli, and one had an embolic cerebral vascular episode 6 months after onset of her illness.

All 13 patients have maintained ECG abnormalities (fig. 3). One developed atrial flutter. One patient, aged 35, with no history of chest pain and no discernible cause for premature coronary artery disease, developed ECG and VCG patterns consistent with inferior myocardial infarction 13 years after her initial episode of cardiac failure.

Six patients had subsequent pregnancies. Three had no change in cardiac status, and three experienced permanent deterioration of cardiac function that resulted in death. One patient developed sustained diastolic hypertension 2 years after onset of her cardiac symptoms.

Eleven patients (85%) died of cardiac failure in an average time of 4.7 years. Three patients died following an exacerbation of cardiac failure associated with another pregnancy, and eight have had repeated episodes of congestive cardiac failure terminating in death. Ten of the 11 patients died within 8 years, and seven within the first 5 years. One patient died 16 years after the onset of her disease.

Pathology

Five patients (two in group A and three in group B) had thoracotomy for myocardial and pericardial biopsy. In four of the five
patients the myocardial biopsies were performed within 3 months of the onset of PPCM. Grossly, the pericardium appeared normal in all. When the pericardium was opened, the heart was found to be enlarged in each case. The two patients in group A had slight cardiac enlargement; areas of fibrosis were not seen, and the contractions appeared normal. In the other three patients (group B) the heart was much larger and appeared flabby with poor contractions. (In one of the patients in group B, diffuse discolored areas were seen and interpreted as areas of fibrosis.)

Myocardial biopsies were taken from the outflow tract of the right ventricle. The most prominent findings were hypertrophy of myocardial fibers and varying degrees of fibrosis (fig. 4). There appeared to be no significant histological differences between the patients in the two groups—A and B.

Autopsies were performed in seven patients.

One of the patients was in group A and died of chronic renal failure secondary to bilateral stag-horn calculi and chronic pyelonephritis. The patient’s heart weighed 300 g. There was minimal coronary atherosclerosis without narrowing or occlusion of the lumen of the coronary arteries. There was no evidence of pericardial or valvular disease. There were an organized thrombus in the left ventricle and a recent mural thrombus in the right ventricle. The myocardium was brown, with grayish streaks of myocardial fibrosis. Endocardial fibrosis was marked at the sites of the mural thrombi. Sections revealed moderate focal fibrosis in both the free wall and the septum. In the posterior wall of the left ventricle subjacent to the mural thrombus there was replacement fibrosis. There was no significant hypertrophy of the myocardial fibers.

The six patients in group B had enlarged hearts (500 to 700 g) with hypertrophy and dilatation of all four chambers. There were

Figure 1

Chest roentgenograms of patient in group A. The admission chest X-ray (left) shows cardiomegaly. On right, chest roentgenogram of same patient 6 months later, showing a normal heart size.
mural thrombi in the left ventricle in all six patients, and four had mural thrombi in one or more of the other chambers. The endocardium showed fibrous thickening (focal to diffuse). Strands of connective tissue extended from the patchy areas of subendocardial

Figure 2

Left. Admission chest roentgenogram of patient in group B showing cardiomegaly. Right. Chest roentgenogram of same patient 1 year later, showing further increase in heart size.

Figure 3

Admission electrocardiogram of a patient in group B showing left ventricular hypertrophy with inverted T waves. The electrocardiogram remained unchanged until the patient’s demise 2 years later.
PERIPARTUM CARDIOMYOPATHY

fibrosis into the myocardium. There was no evidence of valvular or pericardial disease, and no evidence of significant coronary artery disease. Histologically, the myocardium showed varying degrees of hypertrophy of muscle fibers, fibrosis, interstitial edema, hypertrophy, and occasional focal accumulations of lymphocytes. Six of the patients had pulmonary and systemic infarcts (usually in the kidney and spleen). None of the patients had vascular changes of systemic hypertension.

Discussion

The diagnosis of PPCM is based on the recognition of primary myocardial disease (PMD) that presents for the first time toward the end of pregnancy or in the early puerperium. It has been suggested that this disorder may be a form of idiopathic PMD coincidentally associated with the pregnant state. However, the patients in this study were not alcoholic, had good nutrition, and viral titers on five patients revealed no evidence of acute viremia. Myocardial biopsy in five patients showed no evidence of acute inflammatory myocarditis. In addition, 17 of our patients were seen antepartum, and there was no evidence of heart disease at that time. This study has focused on the natural history of patients with cardiac failure of unknown etiology presenting for the first time in the puerperal period.

The incidence of PPCM is more common in the older, multiparous woman and is more frequently associated with twins and toxemia. Similar observations were made by Seftel and Susser. The significance of these associations is unknown.

The clinical presentations of the patients in this series and the initial satisfactory response to conventional therapy for cardiac failure did not differ in any respect from previous reports.

In half of our patients the cardiac size returned to normal within 6 months. However, only 20% (3 out of 15) of patients reported by Walsh and associates exhibited a return of heart size to normal. These patients showed "extremely deficient nutrition," whereas our patients were well nourished and did not show any clinical evidence of protein or vitamin deficiencies. The dietary state appears to be the only difference between the patients reported by Walsh and associates and those presented in our study. In Seftel and Susser's series nine of 20 patients had a return of cardiac size to normal, and none of their patients was malnourished.

This study has shown that the clinical course of PPCM is related to the return of heart size to normal within 6 months. The mortality of patients whose heart size returned to normal was 14% (no death was related to myocardial disease). Of those who maintained cardiomegaly beyond 6 months, 85% have died, all as a result of myocardial failure. Analysis of data reported by Walsh's group shows that of their 12 patients whose heart size did not return to normal, nine died.

Figure 4

Histological section of myocardial biopsy specimen taken from the outflow tract of the right ventricle during exploratory thoracotomy from a patient in group B. There is extensive myocardial fibrosis. Mallory stain ×105.
(mortality rate of 75%) in an average time of 29 months (range, 4 to 58 months). This is similar to the mortality rate of our group B. Of the 11 patients in Seftel and Susser’s series who maintained cardiomegaly, five died (45%), but the six survivors were followed for less than 14 months and thus cannot be compared to the patients in group B of our study. Of the 11 deceased in our group B, one died in the first year, seven died within the first 5 years, and 10 of the 11 were dead within 8 years.

The group A patients have been followed for an average of 10.7 years. Ten of the 12 surviving patients still have some cardiovascular disorder or limitations. Five have residual ECG abnormalities, two have had a recurrence of cardiac failure in subsequent pregnancies, two had focal myocardial fibrosis on myocardial biopsy, and four patients are in functional class II.

It has been observed that patients who have had PPCM are more prone to develop peripartum cardiac failure with a subsequent pregnancy. In our experience, the influence of a subsequent pregnancy was related to whether the heart size had returned to normal. Twenty-one subsequent pregnancies occurred in eight patients whose heart size had returned to normal (group A). There was a temporary recurrence of postpartum cardiac failure following three pregnancies in two of these patients. In each case, the patient responded promptly to therapy and was asymptomatic when discharged from the hospital. Six patients whose heart size did not return to normal (group B) had subsequent pregnancies. Although these six patients maintained cardiomegaly, they were not in clinical cardiac failure before onset of the subsequent pregnancy. In three there was no change in cardiac function. The other three patients experienced marked increase in cardiac symptoms in the last trimester or in the early postpartal period. In each case this initiated a permanent deterioration in cardiac function that resulted in death. This experience would strongly suggest that patients whose heart size has not returned to normal should avoid becoming pregnant.

The gross findings in the heart at autopsy and the histological findings of the myocardium (from biopsy specimens and at autopsy) do not differ from those seen in other forms of primary myocardial disease as reported from this institution and from the findings reported by other investigators. Although the clinical course of patients in groups A and B was considerably different, the pathological findings in the myocardium were indistinguishable.

Acknowledgment

We would like to thank Dr. A. Webster for making available the obstetrical charts, M. Patel, M.Sc. (Math.), M.Sc. (Stat.), Biostatistician, University of Illinois, for his help with the statistical analysis, and Mrs. J. L. Price for her secretarial assistance.

References


Circulation, Volume XLIV, December 1971
Natural Course of Peripartum Cardiomyopathy
JOHN G. DEMAKIS, SHAHBUDIN H. RAHIMTOOLA, GEORGE C. SUTTON,
W. ROBERT MEADOWS, PAUL B. SZANTO, JOHN R. TOBIN and ROLF M.
GUNNAR

Circulation. 1971;44:1053-1061
doi: 10.1161/01.CIR.44.6.1053
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX
75231
Copyright © 1971 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/44/6/1053

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/