Clinical Diagnosis of Cardiac Involvement in Systemic Lupus Erythematosus

A Correlation of Clinical and Autopsy Findings in Thirty Patients

By Thomas Q. Kong, M.D., Robert E. Kellum, M.D., and John R. Haserick, M.D.

Systemic lupus erythematosus according to Harvey and associates was first described in 1872 by Kaposi, but it was not until 1924 that Libman and Sacks reported the specific lesion of verrucous endocarditis. They described the hearts in four patients who had not only verrucous endocarditis, but also myocarditis and pericarditis. Since that time many reports have been published concerning the cardiac involvement of systemic lupus erythematosus. The pathologic lesions have been well described, but the clinical features remain ill defined. The purpose of the present study has been to review the case histories of a series of patients who had systemic lupus erythematosus, in order to correlate the clinical manifestations of cardiovascular involvement with the pathologic findings at necropsy.

Materials and Methods

Between 1949 and 1960, 373 patients with systemic lupus erythematosus were examined at the Cleveland Clinic. Of the 373 patients, 191 had hypertension or clinical evidence of cardiovascular involvement as indicated by one or more of the following: cardiac enlargement, murmurs, pericarditis, myocarditis, pericardial effusion, gallop rhythm, cardiac arrhythmia, or myocardial infarction. Of these 191 patients, 130 are still living. Postmortem examination was performed on 30 of the 61 patients who died. A detailed clinicopathologic study was made on these 30 patients, and only these results are being reported. The diagnosis of systemic lupus erythematosus was established by the usual clinical findings and laboratory tests. All 30 patients had positive LE tests. Twenty-eight of the patients were treated with steroids, 14 with nitrogen mustard, and eight received antimalarial agents.

Results

The age and sex distribution of the 30 patients are recorded in table 1.

The initial systemic complaints leading to the diagnosis of systemic lupus erythematosus are summarized in table 2. Cardiovascular involvement occurred rarely as a first manifestation of the disease, and never occurred as the sole initial complaint. One patient had congestive heart failure as the initial manifestation, but this was accompanied by arthritis.

It is recognized that the time of onset of the disease and the actual time of onset of cardiovascular involvement are, at best, poorly defined. However, cardiovascular involvement (table 3) was first suspected at a median interval of 24 months (range: initially to 34 years) after the initial subjective complaints. The most common initial cardiovascular manifestation (13 patients) was the presence of a murmur. A murmur was noted at the time of first examination in four patients. Systolic murmurs at the apex or over the pulmonic area were present in 22 patients. No diastolic murmurs were heard in these 30 patients. There was no correlation between the occurrence of a murmur and the presence of anemia or increased pulse rate. There was no constant correlation between the appearance of a murmur and the presence of Libman-Sacks valvulitis at autopsy. Of the four patients with Libman-Sacks valvulitis, an apical systolic murmur was heard in each of two patients, and no murmurs were heard in two. Endocarditis was not suspected clini-
Verrucose endocarditis of the Libman-Sacks type was found in four patients (13.4 per cent); it occurred only on the mitral valves and was not so severe as to produce stenosis. One patient had significant aortic and mitral valvulitis due to rheumatic fever.

Fourteen patients had pericarditis during the course of their disease. In each of six of these the blood urea concentration was normal throughout the entire period of illness, and the pericarditis can be attributed primarily to systemic lupus erythematosus. In the other eight, pericarditis could have been either primary to systemic lupus erythematosus or secondary to uremia. All these patients were receiving steroids at the time the pericarditis occurred. Two patients suffered from pericarditis 7 years and 16 years before death. Neither patient had signs of constrictive pericarditis during life, although necropsy revealed obliteration of the pericardial cavity by dense fibrous adhesions.

Pericardial effusion was present in 12 patients, in 10 of whom it was clinically suspected. In the two patients in whom effusion was not suspected, only 50 ml. and 150 ml. of clear yellow fluid were found at autopsy and were thought to have been agonal. All patients except one were receiving steroids at the time the effusion occurred. Four patients had cardiac tamponade that required pericardiocentesis. The effusion was bloody in two patients. Improvement followed after removal of the fluid in three patients; in the fourth, at pericardiocentesis, the needle punctured the left anterior descending coronary artery, and resulted in death from acute cardiac tamponade. An erroneous diagnosis of the presence of pericardial fluid was made in one patient. This patient had a rapidly enlarging heart, pericardial friction rub, paradoxic pulse, and evidence of cardiac failure. Two pericardiocenteses were unsuccessful. The fluid was believed to be loculated, and an operation was performed; it revealed no fluid but a hemorrhagic pericarditis with an edematous, flabby heart.

Gallop rhythm was heard in 16 patients. Myocarditis of varying severity, as indicated by fibrinoid and collagenous degeneration, interstitial edema, necrosis, or cellular infiltration, was present in 15 of these patients at necropsy. In one patient who had had gallop rhythm, postmortem examination revealed a normal myocardium, but showed bilateral necrotizing staphylococcal pneumonia.

Enlargement of the heart was demonstrated by roentgenograms in 17 cases. Fifteen of the patients had myocarditis, pericardial effusion, or left ventricular hypertrophy, singly or in combination, at necropsy. All 15 had myocarditis of varying severity. Two had entirely normal hearts.

Cardiac arrhythmias were present in four patients. Two had multiple premature ventricular beats; one had atrial fibrillation; and one had atrial flutter. In no instance did the arrhythmia contribute to myocardial failure.

Hypertension was present in 16 patients, all of whom had nephropathy at autopsy. An additional nine patients with LE renal involvement had normal blood pressures. Four of the patients were not receiving steroids at the time hypertension was discovered, but all had increased concentration of blood urea. In three patients, hypertension appeared to be secondary to administration of steroids.

Table 1

<table>
<thead>
<tr>
<th>Sex</th>
<th>Total no. of patients</th>
<th>0-9</th>
<th>10-19</th>
<th>20-29</th>
<th>30-39</th>
<th>40-49</th>
<th>50-59</th>
<th>60-69</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>22</td>
<td>1</td>
<td>1</td>
<td>10</td>
<td>7</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Male</td>
<td>8</td>
<td>0</td>
<td>0</td>
<td>4</td>
<td>0</td>
<td>3</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>
creasing the dosage of steroids reduced the hypertension, but also resulted in an exacerbation of the manifestations of systemic lupus erythematosus. These three patients were treated subsequently with low-salt diet, rauwolfia, ganglion-blocking agents, and bed rest, with fair response of the blood pressure in two patients. One patient was not benefited, and died of a subarachnoid hemorrhage.

Renal failure was the cause of death of 18 of the 30 patients; infection was the cause of the death of five patients. Pulmonary edema and fever developed in two of these terminally, and autopsy revealed infiltration of the myocardium by aspergillosis in one patient, and staphyloccoc abscesses studding the myocardium in the other. Two patients died of cardiac failure due to systemic lupus erythematosus. Autopsy revealed severe myocarditis and pronounced pulmonary congestion, and in one patient they were accompanied by severe arteritis of the left anterior descending coronary artery. Acute myocardial infarction secondary to atherosclerotic heart disease was the cause of one death. At postmortem examination of two patients, severe bilateral necrotizing staphyloccocal pneumonia was present, which had produced the clinical findings of rales at the lung bases, dyspnea, tachycardia, and gallop rhythm. Four patients died after severe convulsions, and one patient died of Laennec’s cirrhosis.

An abnormal electrocardiogram was recorded of each of 21 patients. Eighteen of these had abnormal cardiac findings at autopsy. Low voltage in the standard and unipolar limb leads was noted in 10 patients; cardiac abnormalities were found at postmortem examination in nine of these; i.e., pericarditis in five, myocarditis in three, and pericardial effusion in one.

Nonspecific T-wave changes and RST depression interpreted as indicative of myocardial changes were recorded for five patients. Cardiac abnormalities were found in four; pericarditis was present in one patient, myocarditis in two patients, and left ventricular hypertrophy in one patient.

The electrocardiogram showed the changes of hyperpotassemia in two patients. In one of these the serum potassium value was 7.5 mg. per 100 ml., and in the other 9.3 mg. per 100 ml. at the time the electrocardiograms were taken.

Left ventricular hypertrophy was found at postmortem examination in eight patients, but had been recorded electrocardiographically for only three. In four of the nondiagnosed cases, myocarditis also was present, and it is possible that the myocarditis obscured the electrocardiographic diagnosis of left ventricular hypertrophy.

Myocardial infarction occurred twice in the series, once in a 42-year-old white woman and once in a 46-year-old white man. Both infarctions were secondary to atherosclerotic heart disease. An electrocardiogram of one of these patients was obtained, and presented the features of a remote anteroseptal infarction; this was confirmed at necropsy. The patient, however, died of renal failure.
Table 3
Initial Cardiovascular Manifestations in 30 Autopsied Patients with Systemic Lupus Erythematosus

<table>
<thead>
<tr>
<th>Initial cardiovascular manifestations</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Murmurs</td>
<td>(13)</td>
</tr>
<tr>
<td>Apical systolic</td>
<td>9</td>
</tr>
<tr>
<td>Pulmonic systolic</td>
<td>4</td>
</tr>
<tr>
<td>Heart failure</td>
<td>6</td>
</tr>
<tr>
<td>Friction rub</td>
<td>(5)</td>
</tr>
<tr>
<td>Symptomatic</td>
<td>2</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>3</td>
</tr>
<tr>
<td>Enlarged heart</td>
<td>3</td>
</tr>
<tr>
<td>Cardiac tamponade</td>
<td>2</td>
</tr>
<tr>
<td>Pericarditis, myocarditis, failure</td>
<td>1</td>
</tr>
</tbody>
</table>

There were nine patients with normal electrocardiograms, four of whom had abnormal hearts at postmortem examination. Old adhesive pericarditis was present in one patient; mild focal myocarditis was present in two patients, and left ventricular hypertrophy in one patient. Changing axis was not seen.

Discussion

The results of the study indicate that roentgen evidence of an enlarged heart, or a gallop rhythm in patients with systemic lupus erythematosus is strongly suggestive of myocardial involvement. On the other hand, an abnormal electrocardiogram is not pathognomonic of systemic lupus erythematosus, but may be due to myocardial or pericardial involvement or organic disease from unrelated causes. The detection of a systolic murmur cannot be interpreted as evidence for the presence of Libman-Sacks valvulitis. Systolic murmurs were present in 22 patients, but valvulitis was found in only two. In two other patients with valvulitis no murmurs were heard. Diastolic murmurs associated with systemic lupus erythematosus valvulitis have been reported, but they were not present in these 30 patients.* In patients with diastolic murmurs, the possible coincidental presence of rheumatic heart disease must be considered. The incidence of verrucous endocarditis was 13.4 per cent in this series, and is lower than previously reported by other investigators, who noted endocarditis in about 33 per cent of their autopsied patients.

Signs and symptoms referable to the heart as initial manifestations are unusual, evidenced by the fact that they occurred in only one patient. It is believed that no comment can be made in regard to the subsequent natural history of cardiac involvement with systemic lupus erythematosus, since the majority of patients received suppression treatment. Even though the clinical course may have been altered by chemotherapy, several interesting facts are noted. In these 30 patients, there was a median interval of 24 months between the initial subjective complaints of systemic lupus erythematosus and the clinical diagnosis of suggested cardiac involvement. In one third of this group, initial cardiac involvement was suggested by the presence of a murmur. However, since murmurs had no consistent pathologic significance, actual LE cardiac involvement may have occurred even later than 24 months.

Although the median survival in this group was only 12 months (range: 3 days to 84 months) from the time of positive diagnosis of systemic lupus erythematosus, heart failure accounted for the death of only two patients (6 per cent). This suggests that myocardial involvement does not further worsen the prognosis. When sudden cardiac failure occurs, the presence of superimposed complications as myocardial infarction or infection should be considered. The presence or absence of bronchopneumonia simulating cardiac failure must be established. Myocardial failure from arrhythmias or constrictive pericarditis did not occur.

Summary

A review was made of the case histories and autopsy reports of 30 patients with systemic lupus erythematosus who had clinical cardiovascular involvement. The presence of an enlarged heart or of gallop rhythm

*In the group of patients with systemic lupus erythematosus who are alive, diastolic murmurs that were heard have disappeared during steroid therapy.
strongly suggests myocardial involvement, but the electrocardiogram is not specific. Signs and symptoms referable to the heart are unusual as a first manifestation of systemic lupus erythematosus, and in patients receiving suppressive chemotherapy they do not further worsen the prognosis. Systolic murmurs cannot be interpreted as conclusive evidence of Libman-Sacks valvulitis.

Acknowledgment

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References


Galvani and the Electrophysiology of Muscular Contraction

Luigi Galvani was born on September 9, 1737, in a house which may still be seen on Via Mareoni, 25, in the center of Bologna, into a family which had produced several illustrious men. Upon the completion of his collegiate studies he attended medical classes with some famous teachers of his time: Jacopo Bartolomeo Becari and Domenico Maria Gusmano Galeazzi. He obtained his degree in medicine and philosophy on July 15, 1759 and on May 13, 1761 he was appointed alunno (student) at the Academy of Sciences of the Istituto. He practiced medicine and surgery in Bologna hospitals soon after but also found time for anatomical research. He was appointed lecturer de Rebus medici at the Archiginnasio he had attended, and on April 28, 1763 was made honorary lecturer. In the years which followed he taught surgery and theoretical anatomy. On June 22, 1768 he became a Lectura stipendaria (paid lecturer) and taught medical practice. He became Galeazzi’s adjunct in anatomy on December 12, 1775, under whom he taught practical anatomy. He held that office until the year of his death.

On February 26, 1782, that same Senate appointed him Professor of Obstetric Arts at the Istituto, a title which he held for sixteen years. In addition to these duties, he taught classes in his home on pathological anatomy and was thus kept busy teaching, investigating, and practicing medicine and obstetrics.

His moral greatness was in complete harmony with his intellectual stature. Contemporary writers and first biographers describe Galvani as an honest, mild, modest, polite, charitable to the unfortunate and always a noble and generous friend. Even in trying moments he showed unshakable strength of character.—Giulio Pupilli. Commentary on the Effect of Electricity on Muscular Motion. By Luigi Galvani. Translated by Robert Montraville Green, M.D. Cambridge, Massachusetts, Elizabeth Licht, Publisher, 1953, p. xvii.
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