Relation of the Postcommissurotomy Syndrome to the Rheumatic State

By Daniel L. Larson, M.D.

The postcommissurotomy syndrome is a frequent troublesome complication after mitral valve surgery, the etiology of which is still obscure. In this study of 137 patients who survived surgery the clinical features of this complication are carefully detailed, possible associated conditions are studied, and pathologic findings in the atrial appendages are analyzed. In particular, the relation of this syndrome to the rheumatic state is critically examined.

Since the introduction of a practical method for the surgical treatment of mitral stenosis, a large number of patients have undergone this procedure. Soloff and his colleagues described the onset of chest pain and fever in the second or third week after operation of 47 out of 179 individuals. Since that time several reports have appeared from other clinics describing similar complications following this operation. In most series, between 10 and 40 per cent of the patients develop this distressing disease known as the "postcommissurotomy syndrome."

Characteristically, the patient has a normal postoperative course until the second or third week. Then chest pain begins, which often radiates into the shoulders or neck. The pain does not necessarily involve the incisional area and may be pleuritic in nature. It is accompanied by an elevation in temperature, erythrocyte sedimentation rate, and white blood cell count. A pleural or pericardial friction rub may reappear, and x-ray evidence of inflammation of the pleura is often demonstrable. There is no serologic or bacteriologic evidence of a recent infection with group A hemolytic streptococcus. There is no electrocardiographic evidence of rheumatic carditis, and the peripheral joints are not involved.

The duration of the fever is variable, and the patients may have several such attacks over a long period of time. The presence or absence of the phenomenon apparently bears no relation to the ultimate functional result of the operation. It is the purpose of this report to present evidence to suggest that most attacks of this condition are probably not rheumatic activity.

Clinical Material

This report includes observations on 154 patients undergoing exploration of the left atrium, with or without mitral valve commissurotomy, at the Columbia-Presbyterian Medical Center in New York, during the period 1950 through 1955.

Seventeen patients died within the period of a few days after operation. Many of the deaths occurred in group IV patients, and before much operative experience had been accumulated. Since these patients did not live long enough to develop the postcommissurotomy syndrome, they are not included in the report. Nine died as a result of embolization, and all of these patients had a thrombus in the atrial appendage, calcification of the valve margins, or both; only 1 had normal sinus rhythm. Five patients died in severe congestive heart failure, and 3 died of ventricular fibrillation.

Of the 137 survivors, 51 individuals (37 per cent) had 78 attacks of delayed onset of unexplained chest pain, fever (rectal temperature 100.2 F. or more for 2 days in succession) and other evidence of inflammation. This rate of attack is undoubtedly falsely low because some of the patients had been followed for a relatively short time after operation. Furthermore, the 78 attacks were severe enough to require hospitalization, while other attacks occurred in patients who were treated at home and ran a milder clinical course. The postcommissurotomy syndrome usually appeared within 3 weeks after operation. In no case was there circumstantial evidence of rheumatic activity such as recovery of group A hemolytic streptococci from the throat, elevation in circulating antibody titer to one of the streptococcal antigens, or lengthening of the P-R interval on the electrocardiogram to values in excess of 0.20 sec. In this report the clinical findings of the patients who did and the patients who did not sustain attacks of this syndrome are compared.
RESULTS

Historical Data. Only half of the individuals in each group had a definite history of an acute attack of rheumatic fever, and about 5 per cent in each group had scarlet fever in childhood. Twenty per cent of those without the postcommissurotomy syndrome had chorea while only 4 per cent of those with it gave such, a history. The age at which heart murmurs were first documented is approximately the same in both groups—usually before the age of 30.

Of the 137 surviving patients, 79 per cent are women, an expected finding, since rheumatic mitral valvular disease is more common in women. It is of considerable interest that the postcommissurotomy syndrome was seen in women more than twice as often (44 per cent) as in men (16 per cent).

The symptoms of congestive heart failure first appeared in the second and third decade in both groups—often occurring in the last trimester of pregnancy. In those developing congestive heart failure during pregnancy, the symptoms often disappeared following delivery, only to reappear several years later in the form of progressive decrease in cardiac reserve. Three patients were operated upon while in the first trimester of pregnancy with an uneventful postoperative course. One of these patients has since had a normal full-term spontaneous delivery. Two other patients had developed congestive heart failure with previous pregnancies but, after mitral commissurotomy, were able to go through normal pregnancies without symptoms of cardiac failure. None of these individuals developed the postcommissurotomy syndrome.

Rheumatic Activity Before Operation. The possibility of rheumatic activity must be ruled out before operation in order to avoid a stormy postoperative course. Individuals suspected of having activity may have low-grade pains in the extremities, fever, elevation in the erythrocyte sedimentation rate, conduction changes in the electrocardiogram, and other evidence of acute rheumatic fever. The usual management of patients with these inflammatory changes was bed rest over a relatively long period of time until the values returned to normal or until there was no further improvement. Of the 137 patients, 21 (15 per cent) fell into this group. Eleven of them escaped the postcommissurotomy syndrome and 10 had 1 or more attacks (table 1). Since the over-all incidence of the postcommissurotomy syndrome in this series is at least 37 per cent, and its incidence in individuals suspected of rheumatic activity before operation was approximately 50 per cent, there is at most only a small increase in the risk of subsequent occurrence of the postcommissurotomy syndrome among those showing inflammatory changes prior to operation ($p = < 0.01$).

Seasonal Incidence. Attacks of rheumatic fever usually have their highest incidence during the spring and fall of the year. If the postcommissurotomy syndrome is associated with rheumatic activity, it is possible that such a seasonal incidence would be recognized. In this series, there was a slight increase in the incidence of the postcommissurotomy syndrome during the spring of the year, but this was also the period when the largest number of operations were performed. It would appear, therefore, that there is no seasonal variation demonstrable in the occurrence of the postcommissurotomy syndrome.

Rate of Ambulation. The time of mobilization of patients in the postoperative period conceivably might be related to the incidence of the postcommissurotomy syndrome. This factor is difficult to evaluate, since many of the patients were discharged from the hospital and were not under direct observation before the onset of the syndrome. Progressive mobilization was started on almost all patients before the tenth postoperative day, and the rate at which this proceeded was, in general, related to the degree of improvement in exercise tolerance. There was no difference in the rate of functional improvement among those who developed the syndrome and those who did not. Thus, the rate of mobilization was not implicated as a precipitating factor.

Effect of Prophylaxis. The majority of attacks of the postcommissurotomy syndrome began within 3 weeks after operation. All patients were maintained on large intramuscular doses of penicillin for a week to 10 days after opera-
Table 1.—Incidence of Possible Low-Grade Rheumatic Activity Immediately Before Operation

<table>
<thead>
<tr>
<th>Postcommissurotomy syndrome</th>
<th>Absent</th>
<th>Present</th>
</tr>
</thead>
<tbody>
<tr>
<td>&quot;Rheumatic activity&quot;...</td>
<td>11</td>
<td>13</td>
</tr>
<tr>
<td>P-R &gt; 0.20 sec.</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>Erythrocyte sedimentation rate, preoperative:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20–40 mm.</td>
<td>9</td>
<td>10</td>
</tr>
<tr>
<td>&gt;40 mm.</td>
<td>6</td>
<td>7</td>
</tr>
</tbody>
</table>

Of the 51 individuals with the postcommissurotomy syndrome, 18 patients (35 per cent) developed at least 1 episode while on large dosages of penicillin. Similarly, sulfadiazine in dosage of 1 Gm./day has been shown to prevent recurrences of acute rheumatic fever in the majority of individuals. In this series, 11 patients (22 per cent of those developing the syndrome) sustained their initial attack while on prophylactic sulfadiazine.

Effect of Salicylates and Prednisone. Salicylates in adequate dosage usually suppress evidence of the inflammatory component associated with rheumatic activity. In the group of patients with the postcommissurotomy syndrome, 27 first attacks and 14 recurrences were noted during salicylate therapy. It should be pointed out, however, that the dosages of salicylate were often lower than what may be considered optimal for the suppression of rheumatic activity. Only 8 attacks occurred in individuals receiving 3.6 Gm. or more of salicylate per day.

In this series, adrenal steroids were used as antiinflammatory agents only when the syndrome did not respond satisfactorily to salicylate therapy. There is suggestive evidence that the prophylactic use of adrenal steroids may prevent some attacks of this syndrome. In the present series, there were 3 recurrences in individuals who were being carried on 15 mg. of prednisone daily. These 3 patients had exhibited dramatic improvement when treated with prednisone during their previous attack.

Clinical Course of the Postcommissurotomy Syndrome. The clinical course of the patients who developed the postcommissurotomy syndrome was quite variable. All of the patients were given salicylates if they were not already receiving the drug prophylactically. Half of the patients had a normal temperature and a disappearance of the chest pain within 10 days of the onset of the postcommissurotomy syndrome. The remainder of the group continued to be intermittently febrile with chest pain and an elevated erythrocyte sedimentation rate for as long as 5 weeks. A prolonged course occurred in some patients in spite of therapy considered optimal for the treatment of rheumatic fever. Most of the recurrences of the postcommissurotomy syndrome took place within 2 months of the initial attack, but several patients had repeated episodes for as long as 18 months after the operation.

Subacute Bacterial Endocarditis. Four patients in the present series had a history of subacute bacterial endocarditis treated with antibiotics, from 3 months to 4 years before the operation. Three of these developed at least 1 attack of the postcommissurotomy syndrome in the absence of any clinical or laboratory evidence of subacute bacterial endocarditis. One patient whose postoperative course was complicated by what was thought to be the postcommissurotomy syndrome, developed splenomegaly, anemia, and a positive blood culture for Streplococcus viridans. After a course of antibiotics the abnormal findings disappeared. No other patient was shown to have a positive blood culture in the postoperative period.

Thromboembolic Disease. Another consideration in the differential diagnosis of an unexplained postoperative fever is the occurrence of thromboembolic phenomena. One of the factors that predisposes to embolization is an abnormal cardiac rhythm. In the group without the postcommissurotomy syndrome normal sinus rhythm and chronic atrial fibrillation were equal in frequency (table 2). Among those with the syndrome, however, the incidence of normal sinus rhythm was over twice that of chronic atrial fibrillation. There was a correspondingly higher incidence of transient atrial fibrillation in the postoperative period of patients with the postcommissurotomy syndrome than in those without it. It should
The Postcommissurotomy Syndrome

Table 2.—Cardiac Rhythm

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Postcommissurotomy Syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Absent</td>
</tr>
<tr>
<td>Normal sinus rhythm</td>
<td>42</td>
</tr>
<tr>
<td>Chronic atrial fibrillation</td>
<td>44</td>
</tr>
<tr>
<td>Paroxysmal atrial fibrillation, postoperative</td>
<td>11</td>
</tr>
</tbody>
</table>

Table 3.—Pathologic Findings in Atrial Appendages

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Postcommissurotomy Syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Absent</td>
</tr>
<tr>
<td>Normal</td>
<td>7</td>
</tr>
<tr>
<td>Aschoff bodies</td>
<td>12</td>
</tr>
<tr>
<td>Thrombus</td>
<td>26</td>
</tr>
<tr>
<td>Calcification of valves</td>
<td>13</td>
</tr>
<tr>
<td>Myocarditis</td>
<td>12</td>
</tr>
<tr>
<td>Endocarditis</td>
<td>44</td>
</tr>
<tr>
<td>Myocardial hypertrophy</td>
<td>53</td>
</tr>
</tbody>
</table>

be noted that thromboembolism was not demonstrated in any of the postoperative episodes of paroxysmal atrial fibrillation, although the incidence of the postcommissurotomy syndrome was much increased.

Calcification of the margins of the valve and thrombus in the atrial appendage increase the risk of embolization following operation. Among the 30 patients with recognized thromboembolic episodes, 9 patients died of this complication before they could go on to develop the postcommissurotomy syndrome. All of them had calcification of the valve margins, thromboses in the appendage, or both.

An episode of the postcommissurotomy syndrome appeared in about one-half the remaining 21 patients who developed embolic phenomena. As can be seen in table 3, calcification of the valve margins was more frequent in those who developed the postcommissurotomy syndrome than in those who escaped the disease. In all probability, some of the patients diagnosed as having the postcommissurotomy syndrome were in reality undergoing unrecognized thromboembolic disease. The higher frequency of auricular thrombi among those who escaped the postcommissurotomy syndrome probably reflects the increased incidence of chronic atrial fibrillation in this group.

Pathologic Findings. In table 3 it can be seen that 94 per cent of the atrial appendages showed at least 1 abnormal finding. Aschoff nodules, usually interpreted as evidence of rheumatic carditis, were observed in 15 per cent of the specimens, which is less than reported in some series but more than in another series. The incidence of Aschoff nodules is more or less directly related to the thoroughness with which a search is carried out. Aschoff nodules were not significantly more common in the group that developed the postcommissurotomy syndrome than in the group that did not.

Anemia. With few exceptions, the preoperative hemoglobin values of all patients were above 12 Gm. per cent. As can be seen in table 4, only 7 per cent of the patients with an uncomplicated postoperative course had significant depressions in hemoglobin levels following operation. In contrast, 46 per cent of patients with the postcommissurotomy syndrome showed a drop in hemoglobin of from 2 to 6 Gm. per cent while undergoing the acute phase. The anemia was hypochromic in character and in many cases the values returned to normal upon oral administration of ferrous sulfate. Reticulocytes, which were counted in only 3 of these patients, ranged from 5 to 10 per cent. The anemia was somewhat surprising, since it could not be explained on the basis of overt blood loss.

Postcommissurotomy Syndrome in the Nonrheumatic Subject. The syndrome of delayed onset of chest pain, unexplained fever, and elevated erythrocyte sedimentation rate has been observed in patients undergoing chest surgery for disease unrelated to rheumatic fever. This syndrome has been seen at the Columbia-Presbyterian Medical Center following valvulotomy for congenital pulmonic stenosis, repair of a coarctation of the aorta, ligation of a patent ductus arteriosus, repair of an interatrial septal defect, lobectomy, and mediastinal exploration for suspected subternal thyroid. None of these patients had any indication of rheumatic fever, past or present.
Table 4.—Postoperative Depression of Hemoglobin (Gm. %)

<table>
<thead>
<tr>
<th>Gm. % depression</th>
<th>Postcommissurotomy syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Absent</td>
</tr>
<tr>
<td>Number</td>
<td>Per cent</td>
</tr>
<tr>
<td>2.1-3</td>
<td>2 2</td>
</tr>
<tr>
<td>3.1-4</td>
<td>2 2</td>
</tr>
<tr>
<td>4.1-5</td>
<td>2 2</td>
</tr>
<tr>
<td>&gt;5</td>
<td>1 1</td>
</tr>
</tbody>
</table>

Postoperative Rheumatic Activity. Occasionally, patients may have a classical reactivation of rheumatic activity in the postcommissurotomy period. In 1 reported series, 2 patients developed rheumatic fever following commissurotomy, 1 of whom developed definite aortic valvular damage. In our series, 3 patients had exacerbations of rheumatic activity with peripheral joint pains, fever, high erythrocyte sedimentation rate, and prolongation of the P-R interval.

Discussion

Since all the patients operated upon for mitral stenosis have had rheumatic activity in the past, it was reasonable to suspect that the postcommissurotomy syndrome represents an exacerbation of rheumatic fever. In the light of additional clinical experience, however, this position is becoming increasingly difficult to defend. At the present time there is serious doubt that rheumatic activity is responsible for the clinical manifestations of the syndrome in the majority of instances.

Half of the patients coming to commissurotomy give no history of an acute attack of rheumatic fever, and there is no relation between the natural history of the disease process in the preoperative period and the development of the postcommissurotomy syndrome. The risk of this complication in patients with nonspecific low-grade inflammatory reaction in the preoperative period is only slightly increased. Nonspecific inflammatory changes were seen in almost all amputated auricles, but the incidence of the postcommissurotomy syndrome was not significantly increased in those whose auricles showed Aschoff nodules.

Association of trauma with the onset of acute rheumatic fever has been observed many times. In a recent review it was apparent that many patients had a definite antecedent pharyngitis, and, in some cases, the injured area was simply the first one to be involved or was the area involved most severely. Other nonspecific stimuli associated with an exacerbation of rheumatic activity have usually been noted in patients with chronic low-grade activity, and they developed the other indications of the full blown disease such as joint pains and carditis. Trauma or nonspecific stimulation does not explain the variable delay in onset of the syndrome after operation, as well as the multiple recurrences in the absence of such stimuli.

Patients with the postcommissurotomy syndrome do not exhibit any epidemiologic, bacteriologic, or serologic evidence of a group A hemolytic streptococcus infection; furthermore, the complication occurs despite adequate prophylaxis with penicillin or sulfadiazine. An exacerbation of acute rheumatic fever under these circumstances would appear to be most unlikely. Some patients developed the syndrome while on full suppressive dosages of salicylates or prednisone and evidence of inflammatory response could be detected in some individuals for several weeks after institution of a regimen considered optimal for the treatment of rheumatic activity.

If rheumatic fever were the basis for the postcommissurotomy syndrome, some additional residual cardiac damage would be likely after 1 or more severe episodes. Despite several attacks, however, the patients with this complication had just as good a functional result as those who escaped it.

The possibility of subacute bacterial endocarditis must be ruled out in any patient with unexplained fever in the postcommissurotomy period. Several instances of this complication have been reported. One patient in our series developed a classical clinical picture of endocarditis. It must be remembered that patients receive antibiotics in large dosage in the postoperative period, which may alter the usual clinical picture of subacute bacterial endocarditis.

A group of signs and symptoms, indis-
tinguishable from the postcommissurotomy syndrome, has been observed in patients undergoing chest surgery in whom rheumatic activity would appear to be excluded. The procedures were done for a variety of congenital cardiovascular lesions and for exploration of the mediastinum. It is apparent then that simple operative disturbance of the contents of the mediastinum may occasionally be associated with an inflammatory response of the delayed type.

It is established that an occasional patient may have an easily recognizable exacerbation of rheumatic fever in the postoperative period. Even though there may be striking improvement of exercise tolerance after operation, there is therefore no justification for elimination of measures to prevent recurrences of rheumatic fever or subacute bacterial endocarditis.

Among other causes of postoperative fever that may be considered are drug sensitivity, idiopathic pericarditis, and thromboembolic disease. In our series, the patient most likely to develop the postcommissurotomy syndrome is a woman with a normal sinus rhythm before operation, calcification of the margins of the valves, and an auricular thrombus, who has an episode of atrial fibrillation.

SUMMARY

Of 137 patients surviving mitral commissurotomy, 51 patients sustained 78 attacks of the postcommissurotomy syndrome. None of the patients had evidence of a recent group A hemolytic streptococcus infection, and the attacks were not prevented by the administration of sulfadiazine, penicillin, salicylates, or prednisone. In this series, female patients with normal sinus rhythm before operation and with a bout of atrial fibrillation in the postoperative period were the most likely to develop this complication. An unexplained hypochromic anemia occurred in almost half of the patients during an episode of the postcommissurotomy syndrome. Subacute bacterial endocarditis occurred in 1 patient, and easily recognized acute rheumatic fever developed in 3 patients during the postoperative period. A disorder indistinguishable from this syndrome may occur in patients following chest surgery for a variety of congenital or acquired diseases that are unrelated to rheumatic fever. Although typical rheumatic fever may occasionally recur in the postoperative period, it is concluded that the majority of individuals with the postcommissurotomy syndrome are probably not undergoing an exacerbation of rheumatic activity.

SUMMARIO IN INTERLINGUA

Inter 137 patientes supervivente a commissurotoma mitral, 51 suffrevan attaccos del syndrome post-commissurotomic. Nulle de iste 51 patientes exhibiva signos de un recente infection per streptococcus hemolytic grupo A, e le attaccos non esseva prevenite per le administration de sulfadiazina, penicillina, salicylato, o prednisone. In le serie hic repor-
tate, patientes feminin con normal rhythmos sinusal ante le operation o con un episodio de fibrillation atrial durante le periodo post-operatori se monstrava le plus susceptibile a disvellopar le syndrome post-commissurotomic. Un inexplican anemia hypochro-
mie occurreva in quasi un medietate del patientes durante episodios de iste compi-
lication. Subacute endocarditis bacterial occurreva in 1 patiente, e febre rheumatic in formas facilmente recognoscibile se disveloppava in 3 patientes—ambes durante le periodo post-operatori. Un ordine non distinguibile ab le syndrome post-commissurotomic pote occurrer in patientes subjicite a operationes thoracic pro varie congenite o acquiritie morbos non connectite con febre rheumatic. Ben que typic febre rheumatic pote recurrer in certe casos durante le periodo post-operatori, nostre datos supporta le conclusion que le majoritate de individuos con le syndrome post-commissurotomic non suffre un exacerbation del activitate rheumatic.

REFERENCES


Legal Judgments and Clinical Diagnosis

General propositions do not decide concrete cases. The decision will depend on a judgment or intuition more subtle than any articulate major premise.—O. W. Holmes, Jr., 1905.
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