Streptococcal Tonsillitis and Acute Nonrheumatic Myopericarditis

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Two young men with streptococcal tonsillitis had acute myopericarditis mimicking myocardial infarction. Subsequently, 264 consecutive army conscripts hospitalized with a fever and sore throat underwent throat cultures. Group A streptococci were found in 84 patients. When these patients were systematically screened by serial electrocardiography for myopericarditis, one case of probable asymptomatic myocarditis was diagnosed. None had signs of acute rheumatic fever. All three patients received penicillin therapy when the signs of myocarditis appeared. Their recovery was good. (Chest 1989; 85:389-83)

Today, viruses are usually incriminated in acute myopericarditis in developed countries since diphtheria and rheumatic fever have become rarities. However, streptococcal infections, especially tonsillitis¹ and scarlet fever,² may be related to acute nonrheumatic myocarditis during the acute stage of the disease.

A report was made previously of a consecutive series of acute infectious myocarditis patients in Finnish army conscripts during the period from 1977 to 1981.³ In the series, the most common infectious agents connected with clearcut clinical myopericarditis were vaccinia virus, adenovirus, infectious mononucleosis, Mycoplasma pneumoniae, and Coxsackie B virus.⁴ Since the completion of the study, two cases have been found of acute myopericarditis mimicking acute myocardial infarction during febrile streptococcal tonsillitis. The present paper reports these two cases. Further, to evaluate the current incidence of myocardial involvement in streptococcal tonsillitis, a prospective screening study was undertaken based on serial electrocardiographic recordings in consecutive patients.

Case Reports

Case 1

A 20-year-old conscript was healthy until he developed a sore throat and fever. Exudative tonsillitis was found on admission. A throat culture yielded group A beta-hemolytic streptococci. Oral penicillin therapy was started on the second day of the symptomatic disease. On the third and fourth days, the patient experienced oppression nonradiating left-sided chest pain, which was not influenced by respiration. No pericardial rub or gallop sounds were heard. An ECG on the third day showed a ST-segment elevation and peaked T waves in leads 1, 2, aVL, and V₄₄. The voltage on the R wave in lead 1 was reduced, but no Q waves appeared (Fig 1). Creatine kinase value rose to 742 U/L and its MB fraction to 36 U/L (normal values <220 and <5 U/L, respectively); aspartate aminotransferase level rose to 105 U/L (normal value <40 U/L). Enzyme levels normalized within three days. The antistreptolysin 0 titer rose to 400 U, but no increases in common viral antibodies between acute and convalescent sera were found. In the acute stage, echocardiography displayed increased left ventricular end-diastolic diameter of 88 mm. The apical part of the anterior wall had hypokinetik contraction, and no pericardial effusion was present. A ⁹⁹mTc myocardial scan on the fifth day was positive. The patient became asymptomatic on the fifth day and recovered quickly.

Serial ECGs displayed the typical evolutionary changes of acute myopericarditis. After the initial ST-segment elevations (day 1 in Fig 1), local early T-wave inversions appeared when the ST segment was still elevated (day 2 in Fig 1). Then after a transient intermediate stage of almost normal ECG (day 5 in Fig 1), deeper late T-wave inversions appeared (day 12 in Fig 1) until the ECG was normalized, usually after two months.⁸

Three months later, the echocardiogram and ECG were normal and no symptoms or ST-segment deviation appeared in a maximal exercise test.

Case 2

A 21-year-old conscript was hospitalized because of nausea and substernal pain which radiated to the left shoulder, elbow, and wrist. He had seen a doctor two days earlier for a sore throat and fever. Group A beta-hemolytic streptococci had been cultured from the throat, and oral penicillin therapy had been started one day before admission. A physical examination revealed exudative tonsillitis. On auscultation, S₄ and a loud S₃ were present, but no pericardial rub was heard. An ECG displayed ST-segment elevations in leads 2, 3, aVF, and V₄₄ (Fig 2). A chest roentgenogram showed that the left side of the heart was moderately enlarged and that there was slight pulmonary venous congestion (Fig 3). Creatine kinase value rose to 433 U/L and the MB fraction to 44 U/L.

The patient became asymptomatic two days after admission. Two weeks later, the chest roentgenogram was normal. An echocardiogram displayed a small amount of pericardial fluid apically. The left ventricular end-diastolic diameter was 40 mm, and the contraction of the left ventricular inferior wall was hypokinetic. A 24-hour ECG revealed no complex arrhythmias at this stage. Serial ECGs showed the evolutionary changes typical of myopericarditis (Fig 2). The antistreptolysin O titer rose to 400 U, but no increase in viral antibodies was found. After 2½ months, the patient had fully recovered. An ECG at rest was normal, and the patient had no symptoms during a maximal exercise test, where no ST-segment deviation was found.

Prospective Study

Patients and Methods

The patients were young men, Finnish army conscripts, with a mean age of 20 (range 18 to 26) years. All of the 264 consecutive
FIGURE 1. Serial ECGs, serum enzyme levels, and echocardiographic findings in case 1 with acute myopericarditis during streptococcal tonsillitis. CK is creatine kinase; LVEDD, left ventricular end diastolic diameter; EF, ejection fraction.

<table>
<thead>
<tr>
<th>DAY</th>
<th>LVEDD (mm)</th>
<th>EF (%)</th>
<th>CK U/l</th>
<th>CK - MB U/l</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>58</td>
<td>56</td>
<td>742</td>
<td>36</td>
</tr>
<tr>
<td>12</td>
<td>48</td>
<td>60</td>
<td>304</td>
<td>17</td>
</tr>
<tr>
<td>3</td>
<td>43</td>
<td>66</td>
<td>70</td>
<td>0</td>
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</tbody>
</table>

FIGURE 2. Serial electrocardiographic changes of acute myopericarditis in case 2.

patients admitted to the Central Military Hospital during a 14-month period for a sore throat and fever (over 37.5°C) underwent throat cultures for group A beta-hemolytic streptococci. If the throat culture was positive, the patient was included in the screening study. An ECG was recorded on the first and third days and two weeks thereafter. Further, to uncover any simultaneous viral infection, paired sera for virus antibody determinations were taken at the same time as the first and third ECG. Tests were done for adenovirus, influenza A and B, parainfluenza 1 and 3, herpes simplex, respiratory syncytial virus, enterovirus group antigen, Mycoplasma pneumoniae, Chlamydia group antigen, and infectious mononucleosis. Antistreptolysin O titer were measured.

The electrocardiographic diagnosis of myopericarditis or myocarditis based on serial recordings was presented in detail earlier. In short, myocarditis was considered to be definite if serial tracings showed the four stage ST-T-wave changes of "acute pericarditis" where the initial ST-segment elevations were later followed by T-wave inversions. Myocarditis was probable if a gradually changing pattern of negative T waves occurred in at least two leads where the T waves are normally positive and this T-wave inversion lasted at least four days before the ECG was eventually normalized. "Functional" T-wave changes were usually found in the inferoapical lead; they were vacillating and were normalized by beta blockade.

RESULTS

The initial throat culture was positive for group A streptococci in 84 conscripts (32 percent), while it remained negative in 180 patients. Fourteen (17 percent) of the conscripts with a positive throat culture also had at least a fourfold rise in some virus antibody
titer. Of these 14 patients, 11 had adenovirus infection, one had an influenza A infection, one had both influenza A and B infections, and one had infectious mononucleosis.

On the basis of serial electrocardiographic tracings, one patient (1.2 percent) with streptococcal tonsillitis had probable myocarditis. The first ECG, which was taken two days after penicillin therapy was started, showed upward curved ST segment in leads 1 and V3,6, where the T waves were also biphasic. The T wave was negative in leads 2, 3, and aVF. After two weeks, the ECG was otherwise normal but the T wave was still inverted in lead 3 (Fig 4). Heart involvement was asymptomatic. The patient made a rapid recovery from tonsillitis; his fever lasted two days and he was discharged from the hospital on the fourth day. The antistreptolysin O titer rose to 400 units, but virus antibody titers did not increase.

Three other patients with streptococcal sore throat had electrocardiographic changes which were not considered to be connected with myocardial involvement: two conscripts had vacillating T-wave changes in inferior leads and one had transient junctional rhythm.

In the third tracing taken during the convalescence, none of patients with streptococcal tonsillitis displayed new electrocardiographic changes possibly related to acute rheumatic fever carditis.

**DISCUSSION**

Streptococcal exudative tonsillitis is still complicated by acute myocarditis. This report describes two cases of acute myopericarditis mimicking acute myocardial infarction during the acute stage of streptococcal tonsillitis. These cases were the point of departure for a prospective study to screen myocarditis in 264 consecutive young men with a sore throat and fever. Serial electrocardiograms revealed one case of probable subclinical myocarditis among the 84 patients with a positive throat culture for group A streptococi. All three myocarditis patients were on penicillin therapy when the signs of myocarditis appeared.

There has been evidence for quite some time that myocarditis occurs during the acute stage (the third or the fourth day) of a streptococcal disease. In fact, Gore and Saphir reported fatal acute myocarditis in 12 young men with hemolytic streptococcal tonsillitis out of a total of 1402 autopsied myocarditis cases. Watson and co-workers found T-wave changes suggesting myocarditis in two of 110 scarlet fever patients during the five first days of the disease, while 19 patients developed electrocardiographic changes during convalescence indicating possible acute rheumatic fever.

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**FIGURE 3.** A moderately enlarged heart on admission was normalized in two weeks in case 2.

**FIGURE 4.** Electrocardiographic changes suggesting myocardial involvement found in the prospective study.
Six of the 55 myocarditis patients followed by Gerzen and co-workers⁵ had streptococcal pharyngotonsillitis simultaneously with the appearance of cardiac involvement. Corresponding figures in other Swedish series of myopericarditis patients are 0/15⁷ and 7/29.⁸

Streptococcal toxins have been implicated in nonrheumatic myocarditis which emerges without the latent period typical of acute rheumatic fever. Of the large number of extracellular products and cellular components of group A streptococci, only the pyrogenic exotoxins and hemolysins (eg, streptolysin O), and possibly streptococcal cell wall fragments, appear to have toxic properties.⁹ The direct myocardial invasion of bacteria is improbable: in fatal cases, the histologic findings in myocardium resemble those in viral or diphtheritic myocarditis, necrosis of the muscle fibers, and mononuclear inflammatory cell reaction being the principal features.¹⁰

The clinical picture of nonrheumatic myocarditis associated with streptococcal tonsillitis is similar to that of acute viral myopericarditis. Chest pain is the main symptom, either mimicking coronary pain or typically pericardial sharp pain aggravated by respiratory movements. On the other hand, heart involvement may be silent, and detected only if an ECG is recorded. The myocardium leaks enzymes during the first days that an ECG displays a myocardial injury current, an ST-segment elevation.⁹ In serial ECGs, early T-wave inversions occur as early as the ST-segment elevation stage (Fig 1 and 2), then after a “intermediate stage” with a normal looking ECG, longer lasting late T-wave inversions appear until the ECG is normal, usually after two months. In spite of the often dramatic onset of symptoms and signs of acute myopericarditis, the patients usually recover quickly and completely.⁹ Heart block is uncommon but has recently been described even in suspected nonrheumatic myocarditis during streptococcal tonsillitis.¹⁰ A later progression to chronic inflammatory myocarditis and dilated cardiomyopathy has not been proved conclusively.

All three myocarditis patients included in this report were receiving oral penicillin therapy when myocarditis appeared (Table 1). Penicillin is one of the drugs implicated in causing hypersensitivity myocarditis.¹¹ However, penicillin is a highly improbable cause of myocarditis in the present series since the patients recovered in spite of continued penicillin therapy. Further, the patients had no other signs of drug hypersensitivity. It is possible, however, that the initiation of penicillin therapy and emergence of myocarditis the following day was not a mere coincidence. Streptococci dying in large numbers may have released toxins that triggered the cardiac injury, although no clearcut Jarisch-Herxheimer reaction¹² was otherwise noted.

Myocarditis may be a concomitant of infections such as meningitis¹³ and pneumonia,¹⁴ but acute tonsillitis seems to be a special case in this respect. In addition to diphtheria and streptococcal tonsillitis, infectious mononucleosis, Mycoplasma pneumoniae infection, and adenovirus infection are possible causes of both tonsillitis and simultaneous myopericarditis.⁴ Also during the present prospective study, two patients were unexpectedly found to have clinical myopericarditis in the group of 180 patients with nonstreptococcal tonsillitis, one with adenovirus infection and the other with a peritonsillar abscess of obscure etiology. Myopericarditis connected with nonstreptococcal acute tonsillitis¹⁵ or peritonsillar abscess¹⁶ has been fatal. The pathogenesis of this tonsillitis-myocarditis connection is not known. Lymphatic channels between the tonsils and the heart have been shown to exist,¹⁷ but their significance has remained obscure.

In summary, streptococcal tonsillitis may be complicated by nonrheumatic myocarditis, which clinically resembles acute viral myopericarditis.

### Table 1—Summary of Clinical Findings in Patients with Myocarditis During Streptococcal Tonsillitis

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Interval, days*</th>
<th>Penicillin, days</th>
<th>AST, U/L</th>
<th>ESR, 10⁴/cu mm³</th>
<th>Leuc, U/L (%)</th>
<th>CK(CK-MB), U/L %</th>
<th>Chest pain</th>
<th>Diagnosis</th>
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<tr>
<td>1</td>
<td>2</td>
<td>1</td>
<td>400</td>
<td>12</td>
<td>13</td>
<td>742 (5)</td>
<td>++</td>
<td>Definite</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>1</td>
<td>400</td>
<td>25</td>
<td>11</td>
<td>433 (10)</td>
<td>++</td>
<td>Definite</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>2</td>
<td>400</td>
<td>35</td>
<td>12</td>
<td>. . .</td>
<td>0</td>
<td>Probable</td>
</tr>
</tbody>
</table>

*Interval from beginning of fever to first signs of myocardial involvement, AST is antistreptolysin O; ESR, erythrocyte sedimentation rate; CK, creatine kinase.

References

2. Watson RF, Rothbard S, Swift HF. The relationship of postarthritis and carditis to rheumatic fever. JAMA 1945; 128:1145-52
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