Mitral Regurgitation Associated with Aortitis Syndrome

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SUMMARY

Three patients with mitral regurgitation (MR) associated with aortitis syndrome are presented. All had multiple lesions of the large sized arteries, calcification of the aorta, mild inflammatory findings, a chronic course, and congestive heart failure.

MR was observed by ventriculography in all 3 patients. Case 1 had mitral valve prolapse and secondary systemic hypertension. Case 2 showed mildly thickened mitral valve leaflets and had moderate aortic regurgitation (AR). Case 3 had massive AR. The grade of MR was moderate in Cases 1 and 2, and massive in Case 3. The left ventricle was moderately dilated in Cases 1 and 2 but contracted sufficiently and symmetrically in all 3 patients. Other than the prolapse, no significant mitral valve deformity or left ventricular asynergy was evident by ventriculography. The incidence of MR was 3.1% of 128 patients with aortitis syndrome observed in our clinic.

MR may be found in the late stage of aortitis syndrome. It may be caused by a mild valvular lesion related to aortitis syndrome and be exacerbated by increased hemodynamic loads such as those which occur in secondary hypertension and AR.

Additional Indexing Words:
Takayasu’s arteritis Mitral valve prolapse Aortic regurgitation Secondary hypertension

AORTITIS syndrome (Takayasu’s arteritis) is characterized by chronic inflammatory and multiple stenotic lesions of the aorta, main branch arteries, and pulmonary artery.1–9)

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In some cases the cardiac murmur of mitral regurgitation (MR) has been detected in patients with aortitis syndrome, but the clinical features of the MR have not been documented, and it is not clear in these cases whether the lesion had the same etiology as the aortitis syndrome.

In this paper, we report on 3 clinical cases with MR associated with aortitis syndrome.

**Case Reports**

The 3 Japanese patients reported on here were among the 128 with aortitis syndrome hospitalized in our clinic from 1945 to 1981. In these 3, MR was diagnosed by auscultation and was confirmed by cineventriculography. We had 1 additional case with MR that was evident by auscultation and phonocardiography, but not studied angiographically (Case YY). Therefore, in our series the incidence of MR was 3.1% (4/128).

Case 1 is a 48-year-old man who had consulted a doctor for fatigue 11 years before admission. At that time blood pressure was 210/110 mmHg (Systole/diastole) in the right arm and 160/72 mmHg in the left arm. He had chest pain, dyspnea and palpitation on exertion for the 3 months prior to admission.

On admission, the heart rate was 60/min. Blood pressure was 212/64 mmHg in the right arm, 168/72 mmHg in the left arm, and 148/84 mmHg in the right leg. Venous engorgement in the neck and hepatomegaly (3 finger breadths) were observed. An accentuated third heart sound at the apex, holosystolic murmur (4/6 in grade) at the apex, and vascular bruits on both sides of the neck, back, and epigastrium were audible.

Laboratory findings are listed in Table I. Erythrocyte sedimentation rate (ESR) was 39 mm at 1 hour and C-reactive protein (CRP) was positive (3+). Marked calcification of the aorta was seen on the chest X-ray. The short dimension of the left ventricular cavity was 57 mm at end-diastole and 45 mm at end-systole, and mitral valve prolapse was suspected by M-mode echocardiography. The left ventricle was moderately dilated but contracted sufficiently and symmetrically, and both MR (II in grade by Sellers' criteria) and mitral valve prolapse of the posterior leaflet were evident by ventriculography (Fig. 1a). However, the mitral valve was not stenosed or thickened.

Coronary angiography showed a mild stenosis (50%) in the left anterior descending branch. The aortic valve and the ascending aorta appeared normal by aortography. The left common carotid artery was occluded, and the left subclavian artery was stenosed (Fig. 1b). A coarctation (43%
MR ASSOCIATED WITH AORTITIS SYNDROME

Table I. Laboratory Data, Cardiac Hemodynamics and Angiographic Findings of the 3 Patients

<table>
<thead>
<tr>
<th>Laboratory Data</th>
<th>Case 1</th>
<th>Case 2</th>
<th>Case 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>ESR (mm at 1 hour)</td>
<td>39</td>
<td>25</td>
<td>5</td>
</tr>
<tr>
<td>C-reactive protein</td>
<td>(+)</td>
<td>(+)</td>
<td>(+)</td>
</tr>
<tr>
<td>STS</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>ASL-O</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Rheumatoid factor (RA)</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Serum total protein (Gm/100 ml)</td>
<td>7.7</td>
<td>6.4</td>
<td>6.6</td>
</tr>
<tr>
<td>Serum r-globulin (%)</td>
<td>17</td>
<td>22</td>
<td>22</td>
</tr>
<tr>
<td>ECG</td>
<td>LVH</td>
<td>LVH</td>
<td>LVH, af</td>
</tr>
<tr>
<td>Chest X-ray CTR (%)</td>
<td>52</td>
<td>60</td>
<td>67</td>
</tr>
<tr>
<td>Calcification of aorta</td>
<td>++</td>
<td>+</td>
<td>++</td>
</tr>
</tbody>
</table>

Hemodynamics

| Left ventricular pressure, Systole (mmHg) | 242 | 174 | 141 |
| End-diastole | 14 | 23 | 14 |
| Pulmonary capillary pressure, mean | 13 | 26 | 16 |
| Right ventricular pressure, Systole | 35 | 56 | 44 |
| End-diastole | 4 | 6 | 5 |
| Cardiac index (l/min/m²) | 8.1 | 2.5 | 1.9 |

Angiography

| Mitral regurgitation (grade) | II | II | IV |
| Mitral valve prolapse | + | — | — |
| Aortic regurgitation (grade) | — | II | IV |
| Left ventricular volume (ml/m²) | 203 | 258 | dilatation |
| End-diastole | 78 | 151 | |
| Coronary artery stenosis | mid LAD 50% | prox CX 50% | mid RCA 90% |
| Pulmonary artery stenosis | right lobe periphery | right lobe periphery |

Abbreviations: af=atrial fibrillation; ASL-O=antistreptolysin-o; CTR=cardio-thoracic ratio; ESR=erythrocyte sedimentation rate; LAD=left anterior descending branch; LVH=left ventricular hypertrophy; LX=circumflex branch; mid=mid portion; prox=proximal portion; RCA=right coronary artery; STS=serologic test for syphilis; —=negative or within normal range.

stenosis) of the abdominal aorta above the celiac trunk was seen and the aortic pressure was 164/64 mmHg above and 109/65 mmHg below the coarctation. Small sized aneurysms were observed in the abdominal aorta and the proximal portion of the left renal artery. Both renal arteries showed stenosis on the aortogram.

MR and mitral valve prolapse associated with aortitis syndrome were diagnosed.
Case 2 is a 64-year-old woman who had dyspnea for 8 years. Cough, sputum, and nocturnal dyspnea appeared 2 months before admission.

On admission, the heart rate was 54/min. Blood pressure was 150/90 mmHg in the right arm, 109/90 mmHg in the left arm, and 160/80 mmHg in the right leg. A holosystolic murmur (3/6) at the apex, a diastolic blowing murmur (3/6) at the lower left sternal edge, and moist rales in both lower lungs were audible.

Laboratory findings are listed in Table I. ESR was 25 mm at 1 hour and CRP was positive (1+). Calcification of the aortic arch and descending aorta was observed on the chest X-ray. The left ventricle was moderately dilated but contracted symmetrically on the ventriculogram. MR (grade II) was evident and the mitral valve was mildly thickened (Fig. 2a).
Aortic regurgitation (AR) (grade II), dilatation of the aortic valve ring and ascending aorta, and stenosis of the left subclavian artery were seen by aortography (Fig. 2b). A perfusion defect in the left lower lung was seen by pulmonary perfusion scintigraphy. A right coronary artery stenosis (90%) in the mid portion and a mild stenosis (50%) at the proximal portion of the left circumflex branch were seen on the coronary angiogram.

MR and AR associated with aortitis syndrome were diagnosed, and coronary artery disease was suspected. Her congestive heart failure responded well to treatment.
Fig. 3. Mitral valve and arterial lesions of Case 3.  a: The left atrium (arrow) and the left ventricle were opacified due to aortic regurgitation and mitral regurgitation on the aortogram. The aortic valve ring and ascending aorta were dilated, and the luminal surface of descending aorta was irregular. Both side subclavian arteries (thin arrows) were narrowed.  b: The luminal surface of the abdominal aorta was irregular and the lumen below the branching portion of renal arteries was mildly narrowed.
Case 3 is a 45-year-old woman. She felt fatigue, palpitation on exertion and numbness and pain in her left arm during the past 12 years. She was admitted at a hospital with dyspnea and chest pain 5 years previously, at which time absence of pulses in both arms, accelerated ESR (70 mm at 1 hour) and cardiomegaly were noticed.

She had paroxysmal dyspnea at rest and edema of the legs for 2 months prior to her most recent admission. She was severely ill on admission. The heart rate was 52/min. Blood pressure was 85/50 mmHg in the right arm, 84/76 mmHg in the left arm, and 196/20 mmHg in the left leg. Venous engorgement on the neck (205 mm H2O in venous pressure), hepatomegaly (3 finger breadths below the costal margin), and edema in the legs were evident. Increased second and third sounds, a holosystolic murmur (3/6) at the apex, a diastolic blowing murmur at the lower left sternal border (2/6), and vascular bruits on both sides of the neck and back were audible.

Laboratory findings are listed in Table I. ESR was normal but CRP was positive (1+). Marked calcification of the aorta was observed on the chest X-ray. The ECG showed atrial fibrillation and left ventricular hypertrophy. Elevated left atrial pressure was noted on cardiac catheterization. The MR was severe (Fig. 3a), and the left ventricle was dilated but contracted symmetrically on the ventriculogram.

AR (grade IV), dilatation of the aortic valve ring and ascending aorta, narrowing of the bilateral subclavian arteries and a mild coarctation of the abdominal aorta were seen by aortography (Fig. 3b). The main pulmonary artery was dilated and the peripheral pulmonary arteries in the upper and middle segments of the right lobe were narrow on the pulmonary arteriogram. Coronary arteriography was not performed. She responded well to treatment during hospitalization, but died suddenly at home 2 years later. Autopsy was not done.

**DISCUSSION**

Aortitis syndrome is characterized clinically by chronic inflammatory signs and multiple lesions of the large sized arteries, but the etiology is still unknown. Evidence of inflammation is not always apparent over the entire course of the disease, and clinical findings related to arterial stenosis are often evident in the late stage of aortitis syndrome.6)

The association of aortic regurgitation has been documented as a frequent complication and as a result of the aortic lesion, but the intrinsic relation of mitral regurgitation to aortitis syndrome may be open to question because the lesions are not continuous. The 3 cases reported here all re-
vealed multiple lesions of the aorta, main branch arteries, and pulmonary artery. They all showed positive CRP, normal or mildly accelerated ESR, calcification of the aorta and a course of more than 8 years from the initial onset of symptoms. Thus, these 3 patients seem to have been in the late stage of aortitis syndrome at admission. Case YY also had a 12 year course before admission and showed massive calcification of the aorta on the chest X-ray.

The incidence of mitral valve disease has been reported in some large series of aortitis syndrome, i.e. 3 of 48 patients by Pokrovsky and 2 of 48 patients by Teok. The incidence of MR in our study was 3.1% (4/128). The etiology of the MR, however, has not been clear. Rheumatic valve deformity or papillary muscle dysfunction due to left ventricular dilatation were possibilities, but there was no clear evidence to support these.

MR was evident in our 3 cases by ventriculography. Mitral valve prolapse in Case 1 and mild thickened leaflets in Case 2 were also observed. In Case 3, changes in the mitral valve could not be confirmed angiographically. Case YY showed fibrous and thickened mitral leaflets without verruca at autopsy. None of these 4 patients showed any specific findings of rheumatic fever in the clinical courses of their disease. In the Committee Report on autopsy patients with aortitis syndrome, mitral valve lesions were observed in 9 of 72 cases. The valve was thickened but without verruca or severe deformity in 8 of the 9. This suggests that a mild mitral valve lesion may occur primarily and that it may be of the same etiology as the aortitis syndrome.

The mitral valve prolapse seen in Case 1 may be, at least in part, a form of valvular lesion although its incidence has not been studied. Ruptured mitral valve chordae have not been reported in patients with aortitis syndrome, and an acute onset of MR was unlikely in any of the 3 cases studied.

Papillary muscle dysfunction with MR is usually associated with marked dilatation of left ventricle or asynergy of left ventricular contraction. In the 3 cases presented, however, the left ventricle contracted without asynergy. Case 2 had a significant stenosis of the right coronary artery but showed normal contraction of the posterior left ventricular wall on the ventriculogram. In addition, the left ventricle was dilated moderately but not severely in Cases 1 and 2. In Case 3, the massive MR and AR might have been a cause rather than a result of the ventricular dilatation. From these findings it seems unlikely that the MR was caused by papillary muscle dysfunction.

Case 1 had systemic hypertension secondary to coarctation of the aorta and renal artery stenosis. Cases 2 and 3 had hypertension, and both of these cases and Case YY had AR. Such increased hemodynamic loads to the mitral valve might be related to the MR in cases with injured mitral valves.
Cases 2, 3, and YY had AR which could be considered an aortic valve ring injury due to aortitis.\textsuperscript{11,12} But Case 1 did not show any abnormality of the aortic valve and ascending aorta. From these it appears that MR is not always associated with lesions of the ascending aorta. In our cases the MR was found in the late stage of aortitis syndrome. This suggests that the MR may have been related to a progressive degeneration of the mitral valve or to long term exposure to increased hemodynamic loads.

In aortitis syndrome, congestive heart failure, usually left heart failure due to AR and secondary hypertension, has been known to be the main cause of death.\textsuperscript{13–15} Our cases had symptoms not only of left heart failure, but also of right heart failure such as venous engorgement, hepatomegaly, and edema of the legs. Congestive heart failure seems to be observed frequently in patients with MR associated with aortitis syndrome.

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