ANEURYSMS OF THE CORONARY ARTERIES IN KAWASAKI DISEASE

AN ANGIOGRAPHIC STUDY OF 30 CASES

ZENSHIRO ONOUCHI, M.D., SHINICHIRO SHIMAZU, M.D., NOBUHIKO KIYOSAWA, M.D.
TETSURO TAKAMATSU, M.D., AND KENJI HAMAOKA, M.D.

SUMMARY
Thirty patients with coronary aneurysms associated with Kawasaki disease underwent coronary arteriography. Of 53 aneurysms, five were saccular, 24 sacculofusiform, 19 fusiform and five tubular. When tubular aneurysms were included in the fusiform type, the incidence of each configuration in the right coronary artery was almost the same as that in the left coronary artery. The left anterior descending coronary artery had the most aneurysms, followed by the right coronary, left main and circumflex arteries. Right coronary aneurysms always involved the bifurcation or the region from which a branch vessel arose; 13 of 31 left coronary aneurysms did not involve the bifurcation.

MATERIALS AND METHODS
Thirty patients with coronary artery aneurysms were studied. The patients (24 males and six females) were 4 months to 9 years old (mean 3 years) at the onset of illness. The mean interval between the onset of illness and angiography was 1 year (range 1 month to 7 years). Six of the 30 patients underwent repeat angiography 6 months to 6 years later. Left ventricular angiography was performed in all patients before coronary arteriography. Cine and large-cut films were obtained in the anteroposterior and lateral projections. If selective coronary arteriography was not possible, a semiselective injection was used. Coronary arteriograms were evaluated by three of the investigators independently, and coronary artery aneurysms were classified as saccular, sacculofusiform, fusiform or tubular. A saccular aneurysm is one in which the transverse dimension is greater than the longitudinal dimension, appearing as a pouch (fig. 1). A fusiform aneurysm has a dilatation along the axis of a vessel at least twice the diameter of the transverse dimension, appearing as a spindle. A sacculofusiform aneurysm is an intermediate form. A tubular aneurysm is a kind of fusiform aneurysm with an almost invariable transverse dimension for a certain distance. If an aneurysm was divided by a constricted segment less than the expected diameter of that section, it was counted as two aneurysms.

The distribution of aneurysms in the left main, left anterior descending, left circumflex and right coronary arteries was systematically analyzed (fig. 2). An aneurysm with the center located at the bifurcation was assessed arbitrarily, because the proximal segment was also involved when its longitudinal extent in the proximal direction from the center of the bifurcation exceeded the transverse dimension.

The 30 patients were selected from among 86 with Kawasaki disease on whom coronary angiography was performed at the Department of Pediatrics, Kyoto Prefectural University of Medicine and Kanazawa Medical University. The 56 not included had no aneurysm. Sixty-three of 86 patients were from a consecutive unselected series under our observation from the acute phase of the illness. The remainder were referred from other hospitals for cardiac evaluation because of prolonged and severe inflammatory reaction or presence of severe cardiovascular manifestations.

RESULTS
Fifty-three aneurysms were found in the coronary arteries of 30 patients: five saccular, 24 sacculofusiform, 19 fusiform and five tubular. Tubular aneurysms were seen only in the right coronary arteries. About the same incidence of each aneurysm configuration was found in the left and right coronary arteries (fig. 3). Because a tubular aneurysm may be regarded as a severe form of a fusiform aneurysm, they may be evaluated as of the same group.

The aneurysms were localized in the left coronary artery, with or without involvement of the right coronary artery, in 17 patients (87%) and in the right coronary artery in 13 patients (57%) (table 1). The left coronary artery was more often affected than the right one. The left anterior descending artery, alone or in combination with other arteries, was most often affect-
ed (25 patients); the right coronary artery was affected in 17 patients, the left main coronary artery in 16, and the left circumflex artery in eight. Eight patients (27%) had aneurysms of one vessel only: the right coronary artery in four patients, the left anterior descending in three and the left main coronary artery in one patient. No patient had involvement of the left circumflex artery alone. Aneurysms of two, three and four vessels were found in 11 (37%), seven (23%) and four patients (13%), respectively. Six patients had more than two aneurysms in the same vascular territory (fig. 4), especially in the right coronary artery.

Aneurysms were classified with respect to the segmental distribution of arteriographic lesions (figs. 5 and 6). The number of each type and the individual combinations of aneurysms in the left and the right coronary arteries are shown in figure 7. Of 53 aneurysms, 28 spread to an adjoining segment. Right coronary aneurysms always involved the bifurcation originating in the conus artery, acute marginal artery or the posterior descending artery, where their centers were usually located; 13 of 30 aneurysms in the left coronary artery did not involve the bifurcation. Aneurysms in the left main coronary artery or proximal portion of the right coronary artery, however, never spread to the coronary ostium. However, the proximal extent of the right coronary aneurysms from a point originating in the conus artery was longer in tubular aneurysms in R (1 + 2) than in localized aneurysms (i.e., R1 or R1 + R2) (fig. 6).

Table 2 shows the results of repeat angiography in six patients, who had a total of nine aneurysms at the time of the first angiogram. Five aneurysms did not

<table>
<thead>
<tr>
<th>No. of cases</th>
<th>5</th>
<th>10</th>
<th>15</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Left coronary aneurysms</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Saccular</td>
<td>2</td>
<td>(6)</td>
<td></td>
</tr>
<tr>
<td>Sacculofusiform</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fusiform</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Right coronary aneurysms</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Saccular</td>
<td>3</td>
<td>(12)</td>
<td></td>
</tr>
<tr>
<td>Sacculofusiform</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fusiform</td>
<td>5</td>
<td>(22)</td>
<td></td>
</tr>
<tr>
<td>Tubular</td>
<td>5</td>
<td>(22)</td>
<td></td>
</tr>
</tbody>
</table>

**FIGURE 1.** Configuration of the coronary artery aneurysm (A) Saccular aneurysm. (B) Sacculofusiform aneurysm. (C) Fusiform aneurysm. (D) Tubular aneurysm.

**FIGURE 2.** Arterial segments analyzed by coronary arteriography. LAD = left anterior descending coronary artery; LCX = left circumflex artery; C = conus artery; AM = acute marginal artery; PS = posterior descending artery.

**FIGURE 3.** The prevalence of each form of coronary artery aneurysm in 30 patients with Kawasaki disease. Numbers in parentheses are percentages.
change their configurations, but a small thrombosis was found within an aneurysm in case 4. Four aneurysms regressed into smaller ones (right coronary artery aneurysms in cases 1, 4 and 5) or a normal appearance (left coronary artery aneurysm in case 6).

**Discussion**

Coronary artery aneurysms were first reported by Bougon in 1812. Several case reports and a comprehensive review have since appeared. In 1963, Daoud et al. reported 10 cases and reviewed the literature,
which at that time contained only adult autopsy reports. In most reports, the patients had atherosclerosis. Aneurysms have been described as congenital, mycotic, embolic, dissecting, syphilitic, rheumatic and traumatic or associated with polyarteritis nodosa. Before the report by Kawasaki, aneurysms in patients 15 years of age and younger were very unusual and had been described as congenital or associated with polyarteritis nodosa. In reviewing the earlier cases reported as congenital aneurysms, we evaluated very carefully any etiologic diagnoses of aneurysm, especially for adult patients without pathologic examination.

Kusakawa and Asai reported the distribution of coronary artery aneurysms in 23 cases with Kawasaki disease in which there was no morphologic or segmental distribution data. The distribution of coronary artery aneurysms in their study was different from the distribution of atherosclerotic aneurysms (table 1). Involvement of two vessels was most common (37%), and the left anterior descending artery had the most aneurysms, followed by the right coronary, left main and left circumflex arteries. In atherosclerotic aneurysms, on the other hand, one-vessel involvement was most frequent. The right coronary artery had the most aneurysms, followed by the circumflex and the left anterior descending arteries. The left main coronary artery was not affected.

Lipton et al. proposed that the predilection of the right coronary involvement in atherosclerotic aneurysms may be related to this vessel’s mobility, to the fewer branch vessels arising from it compared with the left coronary artery, or both. This hypothesis may explain the pathogenesis of the tubular aneurysm in the coronary artery in Kawasaki disease. The distribution of the coronary obstruction, which should be the dominant and essential lesion in atherosclerosis, on the other hand, was similar to that presented in this study. Coronary aneurysms may be subset and an expression of mild atherosclerotic involvement. The territory of the left coronary artery, especially the left anterior descending branch, is much more extensively involved than is the right coronary artery, probably because of hemodynamic injury. Befeler et al. speculated that in atherosclerosis, the sequence of events may involve injury to the intima or about a plaque, which may only occlude the lumen minimally, with resulting ulceration and hemorrhage on a vessel with intrinsic abnormalities of the media, giving rise to dilatation and aneurysm.

However, this does not explain why atherosclerotic aneurysms occur more frequently in the right than in the left coronary artery. The distribution of coronary artery aneurysms with polyarteritis nodosa in infancy (table 3) was similar to the most severe cases in our series. This confirms our speculation on the pathogenesis of Kawasaki disease, i.e., that polyarteritis nodosa in infancy may be the most severe form of Kawasaki disease. Although coronary artery aneurysms associated with polyarteritis nodosa, either classic or infantile, most often occur at the bifurcation, 42% of the left coronary artery aneurysms in the present study did not involve the bifurcation. Aneurysm formation in Kawasaki disease is considered to be secondary to the destruction of the internal elastic membrane due to severe coronary angiitis. Why aneurysms are often located at the proximal portion of the coronary artery is unknown; we hypothesized that the vasa vasorum might have an important role in the pathogenesis of aneurysm formation because of their characteristic distribution.

Many investigators have tried to diagnose coronary artery aneurysms in patients with Kawasaki disease based upon the clinical picture, physical findings and laboratory examinations. The more severe the cardiac manifestations are during the acute phase of the disease, the higher the probability of an aneurysm formation. However, coronary artery aneurysms are occasionally found in patients without overt cardiovascular disease.

Weyman et al. reported the recording of the left main coronary artery by two-dimensional echocardiography. Matsuo and Yoshikawa et al. used two-dimensional echocardiography to detect the coro-

**Table 2. Repeat Coronary Angiograms**

<table>
<thead>
<tr>
<th>Case</th>
<th>Sex</th>
<th>Age (years)</th>
<th>Interval*</th>
<th>Site</th>
<th>Interval†</th>
<th>Site</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>3 yrs 3 mos</td>
<td>6 mos</td>
<td>L 2</td>
<td>19 mos</td>
<td>L 2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>R 1 + R (1 + 2)</td>
<td></td>
<td>R 1 + R (1 + 2)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>4</td>
<td>10 mos</td>
<td>L 2</td>
<td>7 mos</td>
<td>L 2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>R 1</td>
<td></td>
<td>R 1</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>1 yr 7 mos</td>
<td>8 mos</td>
<td>L 2</td>
<td>22 mos</td>
<td>L 2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>R 1 + R (1 + 2)</td>
<td></td>
<td>R 1 + R (1 + 2)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>5</td>
<td>3 mos</td>
<td>L 2</td>
<td>6 yrs 6 mos</td>
<td>L 2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>R 1 + R (1 + 2)</td>
<td></td>
<td>R 1</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>1 yr 2 mos</td>
<td>4 yrs 3 mos</td>
<td>L 2</td>
<td>5 yrs 9 mos</td>
<td>L 2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>R 1 + R (1 + 2)</td>
<td></td>
<td>R 2</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>4 yrs 11 mos</td>
<td>51 days</td>
<td>L 2</td>
<td>6 mos</td>
<td>L 2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>R 1</td>
<td></td>
<td>R 1</td>
<td></td>
</tr>
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</table>

*Interval between the onset of mucocutaneous lymph node syndrome and the first angiogram.
†Interval between the first and the second angiograms.
‡Small thrombus within an aneurysm.
Figure 5. Classification of left coronary artery aneurysms by segmental distribution. AP = anteroposterior projection; L (at the right lower corner) = lateral view. L (1 + 2) indicates that both segments L 1 and L 2 are involved continuously, forming a single aneurysm. LAD = left anterior descending coronary artery; LCC = left circumflex.
nary artery aneurysm associated with Kawasaki disease. Not all 86 patients in our series underwent two-dimensional echocardiography. Compared with coronary angiography, false-negative aneurysms in two-dimensional echocardiography revealed either a mild, fusiform configuration or their locations in the right coronary and the left circumflex arteries. Consequently, in our preliminary data from 18 patients with a total of 27 aneurysms, two-dimensional echocardiography for detecting the aneurysm with Kaw-

![Figure 6](http://circ.ahajournals.org/)

**Figure 6.** Classification of right coronary artery aneurysms by segmental distribution. AP = anteroposterior projection; L = lateral view; R (1+2) indicates that both segments R1 and R2 are involved continuously, forming a single aneurysm.
Table 3. Aneurysms of the Coronary Arteries Associated with Polyarteritis Nodosa

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Age</th>
<th>Sex</th>
<th>Diagnosis</th>
<th>Site</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scott and Rotondo</td>
<td>1944</td>
<td>9 mo</td>
<td>F</td>
<td>Pathologic</td>
<td>RCA, LM, LAD, LCx</td>
</tr>
<tr>
<td>Scott and Miller</td>
<td>1946</td>
<td>6 mo</td>
<td>F</td>
<td>Pathologic</td>
<td>RCA, LM, LAD, LCx</td>
</tr>
<tr>
<td>Pickard et al.</td>
<td>1947</td>
<td>1 yr</td>
<td>F</td>
<td>Pathologic</td>
<td>RCA, LAD</td>
</tr>
<tr>
<td>Sinclair and Nitsch</td>
<td>1949</td>
<td>9 mo</td>
<td>F</td>
<td>Pathologic</td>
<td>RCA, LM, LAD, LCx</td>
</tr>
<tr>
<td>Adelson et al.</td>
<td>1951</td>
<td>4 mo</td>
<td>M</td>
<td>Pathologic</td>
<td>RCA, LM, LAD, LCx</td>
</tr>
<tr>
<td>Fager et al.</td>
<td>1951</td>
<td>4 mo</td>
<td>M</td>
<td>Pathologic</td>
<td>RCA, LM, LAD, LCx</td>
</tr>
<tr>
<td>Mastelle</td>
<td>1955</td>
<td>5 mo</td>
<td>M</td>
<td>Pathologic</td>
<td>RCA, LM, LAD, LCx</td>
</tr>
<tr>
<td>Crocker et al.</td>
<td>1957</td>
<td>3 mo</td>
<td>M</td>
<td>Pathologic</td>
<td>RCA, LAD</td>
</tr>
<tr>
<td>Munro-Faure</td>
<td>1959</td>
<td>3 mo</td>
<td>M</td>
<td>Pathologic</td>
<td>RCA, LM, LAD, LCx</td>
</tr>
<tr>
<td>Savage and Smith</td>
<td>1960</td>
<td>3 mo</td>
<td>M</td>
<td>Pathologic</td>
<td>RCA, LAD</td>
</tr>
<tr>
<td>Roberts and Fetterman</td>
<td>1963</td>
<td>7 mo</td>
<td>M</td>
<td>Pathologic</td>
<td>RCA, LAD</td>
</tr>
<tr>
<td>Liddicoat et al.</td>
<td>1974</td>
<td>5 yr</td>
<td>F</td>
<td>Clinical</td>
<td>RCA, LM, LAD, LCx</td>
</tr>
<tr>
<td>McMartin et al.</td>
<td>1974</td>
<td>5 yr</td>
<td>F</td>
<td>Clinical</td>
<td>RCA, LM, LAD, LCx</td>
</tr>
</tbody>
</table>

Abbreviations: RCA = right coronary artery; LM = left main coronary artery; LAD = left anterior descending coronary artery; LCx = left circumflex artery.

Saki disease had specificities of 64% and 46% in the left and the right coronary arteries, respectively (table 4). Careful estimation by experienced persons may yield a sensitivity of 100%. Seventeen of 21 patients with right coronary aneurysms also had left coronary artery aneurysms that might be easily detected by two-dimensional echocardiography (fig. 7). The frequency of the fusiform aneurysms in the left coronary artery was 47%. Aneurysms in the left circumflex artery were always associated with the left main or the left anterior descending coronary arteries. One of four patients with only right coronary artery aneurysms had a small aneurysm at the origin of the conus artery that could not be visualized by two-dimensional echocardiography. The other three patients had aneurysms classified as R (1 + 2), one of which was a tubular aneurysm with proximal involvement extending to near the coronary ostium. It was easily detected by echocardiography. In four of 13 patients with only left coronary artery aneurysms, the main coronary arteries were intact; one of the aneurysms was located at the proximal portion of the left anterior descending coronary artery. Thus, it was easily visualized by two-dimensional echocardiography.

Although the natural history of aneurysms is not completely known, some aneurysms regress to the normal appearance. The interval between the onset of illness and the first angiogram in this study ranged from 6 months to 6 years (median 2 years) in six

Table 4. Two-dimensional Echocardiographic Detection of Coronary Artery Aneurysm in Comparison with Angiography

<table>
<thead>
<tr>
<th>Echocardiogram</th>
<th>Coronary angiogram</th>
<th>Normal</th>
<th>Abnormal</th>
</tr>
</thead>
<tbody>
<tr>
<td>LCA</td>
<td>Normal (n = 4)</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Abnormal (n = 14)</td>
<td>5</td>
<td>9</td>
</tr>
<tr>
<td>RCA</td>
<td>Normal (n = 5)</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Abnormal (n = 13)</td>
<td>7 (3)*</td>
<td>6</td>
</tr>
</tbody>
</table>

*Three of seven aneurysms were located at the region from which the marginal artery arises, an area usually difficult to detect by two-dimensional echocardiography. (Reprinted from Shimazu et al. with permission of Societas Pediatrica Japonica).
patients with repeat angiograms. One of these patients showed regression of an aneurysm 4–10 years after the onset of illness, although Kato43 pointed out the regression of aneurysms within 12 months after the onset of illness. The longer the interval between the onset of illness and the time angiography is performed, the more change occurs in the configuration and distribution of the aneurysm from those of the early period after onset.

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