CASE REPORTS

ACUTE MYOCARDIAL INFARCTION IN A YOUNG ADULT AS POSSIBLE SEQUELA OF KAWASAKI DISEASE
— A Case Report of Successful Intracoronary Thrombolytic Therapy and Histological Study of an Aneurysm —

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Emergency coronary angiography in a 28-year-old male suffering an acute anteroseptal myocardial infarction revealed complete obstruction of the left anterior descending artery in association with multiple aneurysms of the 3 major coronary arteries. Successful intracoronary thrombolytic treatment with urokinase infusion directly into the infarct-related artery was performed 2 h after the onset. Follow-up left ventriculogram showed preservation of left ventricular wall motion. Fifty days after the infarction, he underwent aorto-coronary bypass surgery. Histological examination of the biopsy specimen obtained from the aneurysm of the distal portion of the right coronary artery revealed that the 3-layer architecture of the arterial wall had been completely lost. The wall was replaced by fibrotic tissue, with slight mononuclear cell infiltration around the small vessels, but no acute inflammatory reaction or atheromatous change was seen. In spite of the presence of the coronary risk factors of hypertension and hyperlipidemia, angiography revealed no evidence of atherosclerosis of systemic arteries. It is suggested that the coronary aneurysms in this case are possible sequelae of Kawasaki disease in childhood. (Jpn Circ J 1992; 56: 681—686)

More than 20 years have passed since Kawasaki disease (KD) was first reported; and the patients in whom it was studied have now entered adulthood. Thrombosis in multiple coronary artery aneurysms as sequel of KD is now well known to be one cause of the development of acute myocardial infarction (AMI) in young adult patients. There have been, however, no reports of successful intracoronary thrombolysis of AMI in young adults with a history of KD or of histopathological findings for the coronary aneurysms in KD patients who are now adults. We recently attempted coronary recanalization for AMI and had the opportunity to obtain in situ materials from the coronary aneurysm for histopathological study during the aorto-coronary bypass surgery in a patient with presumed KD.

Key words:
Myocardial infarction
Kawasaki disease
Adult sequelae
Histopathology of coronary aneurysm
Intracoronary thrombolysis

(Received July 20, 1991; accepted November 30, 1991)
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This work was supported in part by the JINSENKAI ALUMNI RESEARCH FUND, Osaka Medical College,
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Japanese Circulation Journal  Vol.56, July 1992  681
Fig. 1. Coronary arteriogram in the right (RAO) and left anterior oblique (LAO) projection. The left coronary artery was totally occluded in segment 7. Both right and left coronary arteries had localized stenosis of more than 90% at segments 2 and 12, and multiple aneurysms in segments 1, 2, 3, 5, 6, 7, 9, 11, 12, 13 and 15, while distal segments exhibited an apparently normal configuration.

CASE REPORT

A 28-year-old male who had been under medical treatment for hypertension (134-156/76-100 mmHg) and hyperlipidemia (Fredrickson type IIa, non-familial hypercholesterolemia) without any complaints for about 2 years and who had no history of apparent KD or fever of unknown origin with exanthema during childhood was awakened at 4:00 a.m. by anterior chest pain. The patient had never previously experienced this symptom. The pain was temporarily relieved by some medication prescribed by a family physician, but it gradually progressed beginning at 12:00 p.m., and he was referred to our hospital for evaluation of AMI. On physical examination, pulse rate was regular at 100/min and blood pressure was 140/90 mmHg. No xanthoma of the eyelids were found. The optic fundi was normal. The chest was clear upon auscultation. The heart was normal other than the presence of an S4 sound. The electrocardiogram showed acute anteroseptal infarction with ST-segment elevation in leads V1 to V5 and reciprocal ST-segment depression in leads II, III, and aVF. X-ray film of the chest showed cardiac enlargement, with a cardiothoracic ratio of 0.55; there was no pulmonary venous congestion. Laboratory examination on admission; peripheral white blood cell count was 13900/mm³, serum creatine kinase (CK) 325 U/ml, and CK-MB isozyme 7 U/ml. Total cholesterol was 362 mg/dl, HDL-cholesterol 47 mg/dl, \( \beta \)-lipoprotein 871 mg/dl, triglyceride 101 mg/dl, low density lipoprotein 664 mg/dl, and very low density lipoprotein 86 mg/dl. The serological test for syphilis was negative.

Coronary angiography (CAG): The patient underwent emergency CAG by Judkin's method which revealed total occlusion at segment 7 of the left anterior descending artery with evolving anteroseptal myocardial infarction, and a localized stenosis of more
Fig. 2. Coronary arteriogram after selective injection of urokinase (total, $9.6 \times 10^5$ IU in 40 min) into the left coronary artery. The infarct-affected artery was patent, and distal run-off of contrast medium was found to be good beyond the point of occlusion. The inset shows the aneurysm sac of the recanalized artery in the left cranial angulation view, in which remaining coronary thrombus shadows (arrow) are clearly seen as intraluminal filling defects.

9.6×10⁵ IU in 40 min Fig. 2). The clinical course thereafter was uneventful. Follow-up CAG and left ventriculography (LVG) were performed on the 22nd hospital day. CAG showed disappearance of residual thrombus in the aneurysm sac in segment 7 and regression of the stenosis to 50% in segment 2. The possible mechanism of the regression seemed to be partial resolution or organization of the thrombus in the vessel. LVG was normal except hypokinesia of regional wall motion in segments 3 and 6 (Fig. 3). Infarcting myocardial tissue in this patient had apparently been salvaged by early thrombolysis. In addition, angiography revealed no congenital cardiac malformation or arteriosclerotic findings in the thoracic and abdominal aorta, carotid, renal, and femoral arteries. Fifty days after the onset of AMI, the patient underwent aorto-coronary bypass graft surgery, at which time a specimen was obtained from the aneurysm sac in the distal right coronary artery. No atherosclerotic changes was noted at any site of anastomosis of the coronary artery to the arterial graft.

**Histopathological findings:** Examination of longitudinal consecutive sections revealed that the normal 3-layer architecture of the arterial wall had been replaced by a proliferation of collagen fibers within which no smooth muscle or elastic fiber was seen. Although a few mononuclear cells had infiltrated locally around the small vessels, there was neither acute inflammatory reaction nor the appearance of foam cells, cholesterol cleft or calcification in the fibrous tissues (Fig. 4).

**DISCUSSION**

Although aneurysms of the coronary artery have been described in the literature since the first case report by Bourgon in 1813 their exact incidence is not known. Swayne et al reviewed the total registry of patients in the Coronary Artery Surgery Study and noted that 4.9% of the registry population were identified by angiography as having coronary artery aneurysms. There are several causes of coronary artery aneurysms, including congenital abnormality, arteriosclerosis, inflammation, trauma, neoplasm, arteriovenous fistula, and coro-
The most frequent cause of coronary artery aneurysm found by angiography or at postmortem examination is atherosclerosis. In a study conducted by Daoud et al., the incidence of atherosclerosis among those with coronary artery aneurysm in the United States was 52%. Much attention has been paid to the sequelae of KD as a cause of multiple coronary aneurysms in young adults in Japan, because they constitute a risk factor for thrombotic coronary occlusion, which may lead to ischemic heart disease or sudden death.

The etiology of this patient's coronary aneurysms cannot be determined with certainty. It was, however, speculated that coronary arteritis had occurred based on the histological findings of scar formation with focal mononuclear cell infiltration in the artery. Therefore, differentiation between KD and other inflammatory vascular diseases would have to be made on the basis of histological changes at the healed stage of the vasculitis. The patient had no clinical symptoms of vascular Behcet disease, syphilitic vasculitis, periarthritis nodosa, or aortitis syndrome. It appeared that the pathological features of focal cell infiltration, disappearance of elastic fibers, and proliferation of collagen fibers were not specific, but were identical to those seen in KD. According to a pathological report of the acute stage of KD by Fujiwara et al., the characteristic features of stage IV are scar formation with calcification and recanalization and severe stenosis in the major coronary arteries. It is impossible, however, to deny KD in our adult case based only on there being no calcification within the aneurysm histologically or calcification of the coronary arteries by angiogram. The patient had risk factors for atherosclerosis, but he was unusually young to be among the portion of the Japanese population with arteriosclerotic disease of the coronary arteries resulting in myocardial infarction.

Coronary artery aneurysms that relate to atherosclerosis usually appear later in life than those of a congenital or inflammatory nature. Though it seems all the more difficult to distinguish the sequelae of KD from atherosclerosis on histological study because KD may lead to premature atherosclerosis, his coronary arteries exhibited no atheromatous changes of the intima upon observation at surgery, and the histological findings of a diffuse structural defect of the arterial wall did not appear to support these aneurysms being arteriosclerotic in origin. Unfortunately, there are no reports in the literature on the histological findings of coronary aneurysms that are the adult sequelae of KD with which we could compare to the findings in our case.

We suggest that the likely sequence of events in this patient was formation of coronary aneurysms after KD in childhood and subsequent thrombus formation within the sac of the left anterior descending artery aneurysm. Subsequent temporary occlusion of the artery at this point, or distal embolization from the thrombus, could have caused the myocardial infarction. Coronary aneurysms occur in the proximal segments of the major coronary arteries in the majority of cases. In our case, the aneurysms were also associated with the distal segments of, especially, the right coronary artery and the left circumflex artery. These arteries may be more prone to extensive aneurysm formation of the ectatic or segmented variety because of their courses within the atrioventricular grooves, where the walls are not embedded in the myocardium.

A serial angiographic follow-up study of patients with KD has revealed that coronary aneurysms may regress in 1 or 2 years in about half of the pediatric patients. The remaining patients are at risk for ischemic heart disease? However, the natural history, including the long-term fate of coronary aneurysms, is not known. Postmortem studies have shown that the most frequent cause of death is coronary artery aneurysm rupture. The next most frequent cause is myocardial infarction, due to sudden complete thrombotic occlusion of a major coronary artery at the site of the aneurysm or due to distal embolization from the aneurysmal sac, producing multiple occlusions. Because of these findings, coronary artery surgery is recommended.

Intracoronary thrombolytic therapy or percutaneous transluminal coronary revascu-
larization (PTCR) has been used for the treatment of AMI, and its efficacy reported. The goal of the therapy is reduction of infarct size. PTCR in KD patients was first attempted by Kato and his colleagues. In our case, PTCR was performed 2 h after the onset of AMI, and recanalization of the coronary artery was obtained. PTCR was assessed as successful on the basis of left ventricular function demonstrated on follow-up angiogram.

Coronary artery aneurysm as a sequelae of KD is an uncommon disease of the coronary artery system in young adults. As its clinical recognition and the number of case reports increase, its natural history, prognosis, and true etiology may be clarified. Finally, we recommend that biopsy specimens of the aneurysms be obtained if aorto-coronary bypass surgery is performed to better understand the nature of aneurysmal formation.

Acknowledgment

We are grateful to Akio Kurokawa, M.D., in the Department of Pathology, Osaka Medical College for his invaluable suggestion to the histological study, and to Mr. Daniel Mrozak for assistance with the preparation on this manuscript.

REFERENCE