TREATMENT OF UNSTABLE ANGINA WITH CHOLESTEROL EMBOLIZATION AS A COMPLICATION OF LEFT HEART CATHETERIZATION

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We describe 3 patients with cholesterol embolization after left heart catheterization via the femoral route. The left catheterizations were performed via the femoral route in all reported cases in which cholesterol embolization occurred as a complication of left catheterization. Postmortem examinations reveal that PTCA, using the right brachial approach, is the safest method for treatment of intractable angina in patients with evidence of cholesterol embolization.

CHOLESTEROL crystals from atherosclerotic lesions with ulcerated plaques can cause distal emboli of varying sizes. Cholesterol embolization has been reported as a complication of angioplasty and angiography. The clinical features of cholesterol embolization are widespread; in some patients there is only a moderate loss of renal function, with subsequent impairment; in others there is renal failure, confusion, and ultimately death. We describe 3 cases with cholesterol embolization after left heart catheterization and discuss the treatment of intractable angina with cholesterol embolization as a complication of catheterization.

Case 1
On January 10, 1982, a 64-year-old male with a history of essential hypertension and diabetes mellitus came to our hospital complaining of chest pains. Laboratory data revealed a white blood cell count of 8000/mm³, 2% eosinophils; creatinine 2.3 mg/dl; BUN 18.6 mg/dl. Left heart catheterization was performed using the right femoral route with Judkins catheters (Cordis 7F R4 and L4) and a pig-tail catheter (Cordis 7F). Heparin, 3000 units, was administered intravenously at the commencement of the procedure, which was performed without difficulty. Coronary angiography revealed stenosis of the left main trunk. At the end of the procedure he complained of abdominal pain which was due to an ileus. The femoral and dorsalis pedis pulses were equal. 3 weeks later, an ileotomy was done for the mechanical ileus and a diagnosis of cholesterol embolism was made on the basis of the specimen of the ileum (Fig. 1). Laboratory data showed a white blood cell count of 9600/mm³, 13% eosinophils; creatinine 5.0 mg/dl; BUN 41.2 mg/dl. Despite dialysis, he died of multiorgan failure 3 months after the heart catheterization. A postmortem examination revealed widespread cholesterol embolization in the small arteries and arterioles of the kidneys, liver, spleen, pancreas, stomach, intestines, bone marrow, adrenal glands, and testes. The aortic arch, descending aorta, and abdominal aorta showed severe atherosclerosis with ulcerated plaques.

Key words:
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Japanese Circulation Journal Vol. 34, May 1990 487
Case 2

On October 16, 1985, a 57-year-old man with a history of diabetes mellitus, hypercholesterolemia, and an old myocardial infarction came to our hospital complaining of chest pains. A left heart catheterization was performed via the right femoral route with use of Judkins catheters (Cordis 7F R4 and L4) and a pig-tail catheter (Cordis 7F). Heparin, 3000 units, was administered intravenously at the commencement of the procedure, which was performed without difficulty. A coronary angiogram showed severe stenosis of the right coronary artery and left anterior descending artery. Although he complained of right leg pain 2 days later, the dorsalis pedis pulses were equal. Laboratory data revealed a white blood cell count of 7100/mm³, 11% eosinophils; creatinine 1.5 mg/dl; blood urea nitrogen (BUN) 15.0 mg/dl; total cholesterol 265 mg/dl; triglyceride 144 mg/dl. The 2 weeks later, percutaneous transluminal coronary angioplasty (PTCA) via the right femoral route was performed on the stenosis of the right coronary artery and left anterior descending artery with a 3.5 mm/20 mm Simpson-Roberts ACS balloon dilatation system using a left 4.0 cm Judkins guiding catheter. The manipulation of catheter presented no difficulties. Heparin, 5000 units, was administered intravenously at the commencement of the procedure. He complained of abdominal pain and loss of appetite after the procedure. Gastroendoscopy revealed acute gastritis. Creatinine and BUN levels increased gradually and he eventually required hemodialysis. Despite dialysis, he died of multiorgan failure 2 months after the PTCA. A postmortem examination revealed widespread cholesterol embolization in the small arteries and arterioles of the kidneys, liver, spleen, pancreas, stomach, intestines, bone marrow, adrenal glands, bladder,
prostate, testes, and skeletal muscle. The acute gastritis was found to be due to cholesterol embolization of the arterioles of the stomach (Fig. 2). The aortic arch, descending aorta and abdominal aorta had severe atherosclerosis with ulcerated plaques.

Case 3

On October 17, 1988, a 66-year-old male with a history of cerebral infarction and diabetes mellitus came to hospital with progressive angina which had increased in frequency. Laboratory data revealed a white blood cell count of 6900/mm³, 3% eosinophils; creatinine 2.1mg/dl; BUN 30mg/dl. The next day, he suffered prolonged and severe chest pain, and an electrocardiogram revealed ST depressions and negative U waves in V₅₋₆. On the basis of these findings, a coronary angiogram was performed. The left femoral artery was used because of the tight stenosis of the right femoral artery. The coronary angiography revealed severe stenosis of the left circumflex artery (99%) and the diagonal branch (90%). Intracoronary thrombolysis (Urokinase 96×10⁴ unit administered to the left coronary artery) reduced the stenosis of the left circumflex artery to 90% and normalized his electrocardiogram. The aortogram revealed a significant stenosis of the right external iliac artery and wall-irregularities of the abdominal aorta, the left common iliac artery, and the bilateral internal iliac and left external iliac arteries (Fig. 3). Heparin, 5000 units, was administered intravenously at the beginning of the procedure which used Judkins catheters (Cordis 7F R4 and L4) and a pig-tail catheter (Cordis 7F). The patient received antianginal therapy with nifedipine, nicorandil, propranolol, and ISDN, and his angina was brought under control. 2 weeks later, he underwent coronary angiography utilizing the same catheter system, and the coronary angiographic findings were similar to the initial ones. He experienced severe and prolonged attacks of angina, however, and on November 9, he was transferred to our hospital for intractable angina pectoris. His cardiac state was NYHA functional class 4. His left toes were purple, and left dorsalis pedis pulse was weak. Laboratory data revealed a white blood cell count of 9500/mm³, 16% eosinophils; creatinine 3.6mg/dl; BUN 47 mg/dl. Arterial blood gases showed pH 7.51, pCO₂ 28.7 mmHg, pO₂ 33.8 mmHg, and bicarbonate of 22.8 mEq/L. The 2 dimensional echocardiogram (2 DE) revealed proportional hypokinesia of the left ventricle. There was concern over the possibility of cholesterol embolization in view of the eosinophils level and the increases in creatinine and BUN that were seen after the second left heart catheterization. This resulted in hesitation to proceed with the intervention (e.g. intra-aortic balloon pumping, coronary- aorto bypass grafts, and PTCA). Heparin, 12000 units/day, was intravenously administered for 4 days. The administration of diuretics improved his heart condition. Renal failure had progressed to such an advanced stage that hemodialysis was required. His angina continued to be intractable. We thought a renal biopsy to diagnose the cholesterol embolization was indicated even in his intractable stage if the intervention would be performed, because the cholesterol embolism as a complication of the intervention could be lethal. The cholesterol embolism was diagnosed by an open renal biopsy (Fig. 4). At the same time, a grade 2/6 holosystolic murmur was heard at the left lower sternal border. A 2 DE-color Doppler study showed hypokinesis of

Japanese Circulation Journal Vol. 54, May 1990
Fig. 4. Case 3. Renal biopsy specimen demonstrating an arteriolar with needle- shaped clefts of cholesterol embolization (Hematoxylin/ Eosin staining).

the posterior, lateral, and inferior walls and severe mitral regurgitation due to papillary muscle dysfunction. Through a right brachial artery cutdown, a PTCA was performed using USCI Profile Plus 2.0 mm/20 mm and 3.5 mm/ 20 mm balloon dilatation system and Angiomedics Amplatz L1 8F guiding catheter just at the take-off of the left circumflex artery for the lesion. The stenosis was reduced to 50% after the PTCA. Heparin, 5000 units, was administered intravenously during the manipulation, which was performed without difficulty. He was free of angina and the grade of the mitral regurgitation decreased. He exhibited no clinical signs of embolic episodes during or after the PTCA. He was discharged but continued to undergo hemodialysis every other day.

Comment
Cholesterol embolization is not widely recognized as a complication of angiography or angioplasty. The catheter manipulation dislodges cholesterol crystals from the wall of severely atherosclerotic vessels. The diagnosis of cholesterol embolization is extremely difficult because its clinical features are variable depending on the extent and speed of embolization. The increased erythrocyte sedimentation rate, eosinophils, hypocomplementemia, and thrombocytopenia were reported to be important diagnostic clues of cholesterol embolization. All our cases had increased eosinophil counts, which appeared after the left heart catheterization. The kidney is most frequently involved and creatinine increase is slowly progressive (e.g., our cases), but, in radiocontrast-induced renal failure, the renal failure occurs early and recovery is within ten to fourteen days. Antemortem diagnosis depends exactly on the biopsy of the embolized organ (e.g., ileum in case 1, kidney in case 3). Until now, there has been no treatment which has been proven effective against cholesterol embolization, with the exception of steroids in a small number of cases. Anticoagulants may aggravate the embolization and promote further embolization by preventing thrombus formation over eroded atheromas. Thrombolytic agents may have the same effect. In case 3, intracoronary thrombolysis with urokinase did not appear to promote cholesterol embolization because the increase in creatinine and eosinophils occurred after the second catheterization. Furthermore, anticoagulant therapy with heparin was prescribed for the unstable angina and the renal failure was progressive. It was not clear, however, if heparin aggravated the renal embolization or if the renal failure became progressively worse as a part of the course of the cholesterol embolization. Ramirez reported an incidence of cholesterol embolization of 30% and 25.5% in necropsy specimens from patients dying within 6

months of angiography. It was reported that 5 deaths were due to cholesterol embolization out of a total 8300 patients that had undergone catheterization. In our hospital, 2 deaths that occurred within 3 months of catheterization were attributed to cholesterol embolization out of a total 3000 left heart catheterizations. The catheterizations were performed by the femoral route in all cases in which cholesterol embolization was reported. There has been no report, to date, of cholesterol embolization in left catheterization using the brachial route so far as we are aware. All of reported cases had no difficulty with catheter manipulation. In case 3, aortographic finding failed to reveal the severe stenosis in the aorta and arteries through which the catheter was easily manipulated using the left femoral route. It would appear, therefore, that an aortogram cannot be used to determine the severity of atherosclerosis in the walls of the aorta or arteries. Thus, it seems to be impossible to predict the occurrence of cholesterol embolization with existing techniques. Perdue reported that most cholesterol emboli originated from the infra-abdominal aorta, iliac and femoral arteries. In the postmortem examinations of cases 1 and 2, severe atherosclerosis with ulcerated plaques was seen in the aortic arch, descending aorta, and abdominal aorta, but was not seen in the subclavian and brachial arteries or in the ascending aorta. The risk of cholesterol embolization, therefore, appears to be higher with the femoral approach than with the brachial approach and this may be partially explained by the fact that with left heart catheterization using the femoral route, the catheter touches the arch after passage into the abdominal aorta. No clinical evidence of cholesterol emboli during or after the PTCA by the right brachial approach was seen in case 3. The brachial approach, while better than the femoral approach, is not totally safe if there is severe atherosclerosis in the aortic arch. Systemic cholesterol embolization was reported as a complication of coronary-aorto bypass grafts and intra-aortic balloon pumping for treatment of intractable angina pectoris. These procedures should, therefore, be considered hazardous in patients with evidence of cholesterol embolization (e.g. case 3). PTCA by the right brachial approach, however, can be the safest option for treatment of intractable angina in patients with evidence of cholesterol embolization. All angiographers should manipulate the catheters very carefully to avoid the rare but dangerous side effects of left heart catheterizations.

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