Histopathology of Giant Coronary Artery Aneurysm Associated with Coronary Artery Fistula

A Case Report

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Summary

Giant coronary artery aneurysms related to coronary fistula are rare, and the precise mechanisms by which they occur are unknown. We present a case of giant coronary artery aneurysm of the left coronary artery to the pulmonary artery fistula with a lack of internal and (or) external elastic lamina and medial degeneration.

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Coronary artery fistula (CAF) is a rare abnormal connection between a coronary artery and another coronary artery, major vessel, or cardiac chamber,¹⁾ and multiple coronary micro fistulae have also been reported.²⁾ The prevalence of CAF is reportedly 0.2% to 2% in patients who undergo coronary angiography.^{3,4)} Potential long-term complications caused by a large left-to-right shunt include right ventricular enlargement, pulmonary hypertension, congestive heart failure, and rupture or thrombosis of the fistula or associated arterial aneurysm.⁵⁾

Coronary artery aneurysm is seen in 0.3% to 5% of patients undergoing coronary angiography, and the prevalence of giant coronary artery aneurysms (defined as having a diameter ≥ 2 cm) is reportedly 0.02-0.2%.⁶⁾ Thus, giant coronary aneurysms associated with coronary fistulae are very rare, and their precise mechanism of formation is unknown. We present a case of a giant coronary artery aneurysm of fistula from the left coronary artery to the pulmonary artery with precise histological examination, and we also review previous reports of giant coronary artery aneurysm associated with coronary fistula.

Case Report

A 68-year-old asymptomatic Japanese woman was referred to our hospital for evaluation of an abnormal shadow that was detected on routine chest X-ray performed at her medical check-up. She had hypertension and was treated with 5 mg amlodipine once a day. Her past medical and surgical history was also notable for onset of hypothyroidism at 64 years and cholecystectomy due to gallstones at 67 years. She had no other diseases such as Kawasaki, inflammatory, or connective tissue dis-

ease.

Physical examination on admission revealed a blood pressure of 126/68 mmHg, a heart rate of 70 bpm, and a body temperature was 36.5°C. A continuous Levine grade II heart murmur was heard at the second intercostal space of the left sternal border.

Laboratory testing showed a white blood cell count of 5,140/mm³, hemoglobin of 13.4 g/dL, blood urea nitrogen of 13.2 mg/dL, creatinine of 0.70 mg/dL, aspartate aminotransferase of 26 IU/L, alanine aminotransferase of 33 IU/L, lactate dehydrogenase of 216 IU/L, creatine kinase of 117 IU/L, C-reactive protein of 0.06 mg/dL, and brain natriuretic peptide of 21.1 pg/mL.

A chest X-ray showed a bulge in the third arch of the left heart border that was not present on a comparison X-ray taken 7 years prior (Figure 1A, B). The electrocardiogram was almost normal and the transthoracic echocardiography was normal with a left ventricular ejection fraction of 73%. Three-dimensional coronary artery computed tomography (Figure 1C) and a coronary angiography (Figure 1D) showed a giant aneurysm (3 cm in diameter) of the left anterior descending artery segment 6 in the left coronary artery to main pulmonary artery fistula. Cardiac catheterization revealed that the left-to-right shunt was very small ($Q_p/Q_s = 1.02:1$). Exercise stress thallium-201 single-photon emission computed tomography myocardial perfusion imaging showed no myocardial ischemia.

After the diagnosis, surgery was recommended due to the risk of rupture. The aneurysmal wall was resected and closed after the openings of the three vessels to the aneurysm were closed with sutures.

The resected aneurysm contained a fistula conduit from the left anterior descending (LAD) of the left coro-

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Figure 1. Chest X-ray shows a bulge in the third arch of the left heart border (B, arrow), although there was no observable mass on the chest X-ray taken 7 years before (A). Three-dimensional coronary artery computed tomography (C) and coronary angiogram (D) show the giant aneurysm (3 cm in diameter) (arrow) of the left anterior descending artery segment 6 in the left coronary artery to the main pulmonary artery fistula. Ao, aorta; PA, pulmonary artery; LV, left ventricle; RCA, right coronary artery; and LCA, left coronary artery.

nary artery.

Histological examination of the aneurysm showed that in the fistula conduit from the LAD, the wall consisted of almost normal arterial structure containing intima, internal elastic lamina, media, external elastic lamina, and adventitia with mild intimal thickening and mild atherosclerotic change (Figure 2A, B, C). However, the wall of the aneurysm had a gradual decrease of smooth muscle cells in the media (Figure 2D, E) with a lack of external elastic lamina from the entry of the fistula conduit from the LAD to the distal site of the aneurysmal wall (Figure 2E), and in aneurysmal wall at about 15 mm from the entry of the fistula conduit from the LAD (Figure 2D, E), the media and internal elastic lamina almost disappeared and changed to fibrosis without inflammatory cells (Figure 2D, E). Moreover, the remaining aneurysmal wall had been almost completely transformed by fibrosis in the media, in addition to disrupted external elastic lamina with intimal thickening (Figure 2G, H). Deposition of Alcian blue-positive materials was also strongly observed in the aneurysmal wall (Figure 2F, I), although there was mild deposition of Alcian blue-positive materials in the media of the fistula conduit (Figure 2C).

Discussion

The most common cause of coronary aneurysms is atherosclerosis, and non-atherosclerotic causes of giant coronary artery aneurysm include connective tissue disorders, vasculitis, infections, drug abuse, and trauma.⁷⁾ However, the precise mechanism of giant coronary aneurysm associated with coronary artery fistula (CAF) is not known.

We conducted a literature search for reports of giant coronary artery aneurysm associated with coronary fistula and investigated case backgrounds using the term “coronary aneurysm” and “coronary fistula” in PubMed until February 2017.

There have been 12 previous case reports of histological changes of giant coronary artery aneurysm (defined as diameter ≥ 2 cm) associated with coronary fistula (Table).^{4,8-18)} Among those reported cases and the present case (age range, 38 to 79 years; mean age, 64 ± 13 years; four men and nine women; maximum diameter of aneurysm, 33 to 100 mm, and mean diameter, 60 ± 19 mm), the aneurysms were located in the LAD of the left coronary artery in seven patients, in the circumflex of the left coronary artery in two patients, and in the right coronary

Figure 2. In the fistula conduit from the LAD, the wall consisted of almost normal arterial structure containing intima (I), internal elastic lamina (IEL), media (M), external elastic lamina (EEL), and adventitia (A) with mild intimal thickening (A, B) and mild degeneration and deposition of Alcian blue-positive materials in the media (C). However, the wall of the aneurysm had a gradual decrease of smooth muscle cells in the media (D, E; arrows) with a lack of EEL from the entry of the fistula conduit from the LAD to the distal site (E; arrow head of EEL), and about 15 mm from the entry of the fistula conduit from the LAD (D, E; *), the media and IEL disappeared and changed to fibrosis without inflammatory cells (D, E). Moreover, the remaining of the aneurysmal wall had been almost completely transformed by fibrosis, in addition to disrupted EEL with preserved internal elastic lamina (IEL) (G, H). Deposition of Alcian blue-positive materials was also seen in the aneurysmal wall (F, I). A, D, and G; Hematoxylin-eosin staining: B, E, and H; Elastica van Gieson staining: C, F, and I; Alcian blue staining: bar is 100 μ m.

Table. Histological Findings of Giant Coronary Artery with Coronary Fistula in Previous Reports and Our Report

Case	Age (years)	Sex	Aneurysm site	Drain site	Size (mm)	Histological findings	Rupture	Ref
1	69	F	LAD	PA	30 × 40	atherosclerosis	(+)	3
2	58	M	LCX	CS	70 × 60	atherosclerosis	(-)	8
3	76	F	LAD	PA	50 × 50	atherosclerosis	(+)	9
4	77	F	RCA	CS	80 × 70 × 80	atherosclerosis	(-)	11
5	76	F	RCA	LA	70 × 50	atherosclerosis	(-)	12
6	65	F	LAD	PA	52 × 62	atherosclerosis	(-)	14
7	52	M	RCA	RA	48	mucoid degeneration	(-)	10
8	79	F	LAD	PA	45 × 46	mucoid degeneration and inflammatory cells	(-)	13
9	51	F	LCX	RA	100 × 80	cystic medial change	(-)	16
10	75	F	RCA	LV	33	cystic medial degeneration and mild atherosclerosis	(-)	17
11	54	M	LAD	LV	80	dysplastic medial change	(-)	7
12	38	M	LAD	RCA	40 × 35	degenerative change, fatty infiltration, calcification	(-)	15
13	68	F	LAD	PA	30 × 30	disappearance and degeneration of media	(-)	this case

M indicates male; F, female; LCX, the circumflex of the left coronary artery; LAD, the left anterior descending of the left coronary artery; RCA, the right coronary artery; CS, coronary sinus; PA, pulmonary artery; LA, left atrium; RA, right atrium; and LV, left ventricle.

artery (RCA) in four patients. Further, there was LAD to pulmonary artery fistula in five patients, LAD to the left ventricle fistula in one patient, LAD to the RCA fistula in one patient, RCA to the right atrium fistula in one patient, RCA to the left atrium fistula in one patient, RCA to the left ventricle fistula in one patient, RCA to the coronary sinus fistula in one patient, RCA to the right atrium fistula in one patient, and LCX to the coronary sinus fistula in one patient.

The histological changes were as follows: atherosclerosis in six patients, mucoid degeneration in three patients (one case with infiltration of inflammatory cells), both atherosclerosis and mucoid degeneration in one patient, dysplastic medial change in one patient, and degenerative change with fatty infiltration and calcification in one patient. There was no difference in the incidence of histological changes among different coronary arteries or fistula-draining sites. Two of these reported 12 patients had aneurysm rupture, and both cases were related to atherosclerosis.

In the present patient, a lack of internal and (or) external elastic lamina and the presence of medial degeneration including decreased or disappeared smooth muscle cells, replacement fibrosis, and mucoid deposition were observed. These histological findings have not been reported in patients with giant coronary artery aneurysm associated with coronary fistula. However, Sakata, *et al.*¹⁹ suggested that a structural change of the CAF such as disrupted internal elastic lamina and phenotypic changes of the medial smooth muscle cells might contribute to aneurysmal formation (7-8 mm in diameter) in a patient with coronary-pulmonary arterial fistula. Thus, wall weakness related to medial degeneration in addition to a lack of internal and (or) external elastic lamina of the CAF conduit may have contributed to the development of the giant aneurysm in the present patient.

In conclusion, the structural abnormality of the wall of the fistula conduit that is unrelated to atherosclerosis and mucoid degeneration may be one of the mechanisms underlying giant aneurysmal formation in patients with CAF.

Disclosures

Conflicts of interest: The authors state that they have no conflict of interest.

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