Title

Percutaneous Coil Embolization and Stent Implantation for Multiple Coronary-to-Pulmonary Artery Fistulas with Giant Coronary Aneurysms; a Case Report

Authors

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Author Contributions Statement

Y.N., T.M., and Y.N. performed the procedures. Y.N. and T.M. wrote the manuscript. All authors discussed the treatment strategy and commented on the manuscript. H.T. were responsible for the overall supervision of this case.

Conflict of interest

None declared.

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Learning Points

- Multiple coronary-to-pulmonary artery fistulas (CPAFs) with giant coronary aneurysms (CA) are extremely rare complex coronary anomalies for which the ideal management and approach are not well established.

- The appropriate timing of therapy initiation is evaluated with reference to the presence of symptoms and fistula and aneurysm sizes.

- The optimal therapeutic approach is determined with reference to the anatomy of the fistula with aneurysm and patient background characteristics.
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| Timeline          | Description                                                                                                                                 |
|------------------|--------------------------------------------------------------------------------------------------------------------------------------------|
| Presentation     | Referral to our hospital because of the gradual development of multi-nodular shadows within the anterior mediastinum                          |
| 1 month later    | Computed tomography angiography (CTA): Multiple coronary-to-pulmonary artery fistulas (CPAFs) with giant coronary aneurysms (CAs). The CA diameter had grown from 23 to 30 mm over 4 years. |
| 2 months         | Coronary angiography (CAG): CPAFs originating from the proximal right coronary artery (RCA). CPAFs with giant CAs originating from the proximal and mid left anterior descending artery (LAD). Intravascular ultrasound (IVUS) revealed the presence of an aneurysm-coronary septum at the orifice of the aneurysm. |
| 3 months         | Percutaneous coil embolization for CPAFs at RCA CAG: completely occlusion of CPAFs                                                                 |
| 4 months         | Percutaneous coil embolization for CPAFs at proximal LAD Percutaneous coil embolization and coronary stent implantation for CPAFs with giant CAs CAG: the mild residual flow into the aneurysm at mid LAD |
| 7 months (3 months after treatment) | CT: a partial thrombotic occlusion of the aneurysm at mid LAD                                                                                           |
| 16 months (12 months after treatment) | Clinically well and asymptomatic with no symptoms of coronary ischemia CAG: the mild residual flow into the aneurysm at mid LAD |
|                  | CT: completely occlusion of the aneurysm at mid LAD                                                                                               |
Introduction

Coronary artery fistula is a direct communication between a coronary artery and a great vessel or cardiac chamber and is noted in 0.1%-0.2% of patients who undergo coronary angiography (CAG) 1. Among them, multiple coronary-to-pulmonary artery fistulas (CPAFs) with giant coronary aneurysms (CA) are extremely rare. In cases with coronary artery fistula, surgical repair is associated with a high incidence of complications including perioperative myocardial infarction 2. Here we reported a case of successful percutaneous coil embolization and stent implantation for multiple CPAFs with giant CA.

Case presentation

Multi-nodular masses were detected within the anterior mediastinum of a previously healthy 74-year-old woman by plain chest computed tomography (CT) screening during comprehensive medical check-up despite a normal chest X-ray. Despite having no symptoms, she was referred to our hospital because of the gradual development of multiple nodules over a four-year period. She had no coronary risk factors and no history of Kawasaki’s disease and vasculitis. Her vital signs were normal. Blood tests showed slightly elevated brain natriuretic peptide (38.9 pg/mL [≤18.4 pg/mL]) and D-dimer (1.8 μg/mL [≤1.0 μg/mL]) levels. Twelve-lead electrocardiography (ECG) showed a normal sinus rhythm and incomplete right bundle
branch block. Transthoracic echocardiography showed a normal ventricular systolic function with no wall motion abnormalities or valvular heart disease. Contrast-enhanced cardiac CT showed multiple contrast-enhanced nodules adjacent to the ascending aorta (Figure 1A, Video 1). Three-dimensional reconstruction of the coronary arteries using CT angiography revealed multiple giant CA and abnormally enlarged and twisted arteries at the superior anterior part of the heart (Figure 1B). The largest aneurysm originating from the proximal left circumflex artery had become spontaneously occluded. Although the anterior mediastinal multi-nodular masses suggested mediastinal tumors, such as lymphoma, thymoma, thymic cyst, germ cell and mediastinal thyroid mass, contrast-enhanced cardiac CT excluded these diseases. Iatrogenic causes and coronary injury were also excluded, as the patient had never underwent surgery or coronary intervention. Genetic testing excluded an underlying connective tissue disorder. A whole-body CT scan detected no aneurysms in any other part of the body. On admission, CAG revealed two CPAFs originating from the proximal right coronary artery (RCA) (Figure 2A). Although the CPAFs originating from the left anterior descending artery (LAD) were accompanied by giant CA, the orifices of the fistulas from the LAD could not be identified by CAG (Figure 2B, Video 2). Selective contrast injection using a guide-extension catheter (GuidelinerV3; Japan Lifeline, Tokyo, Japan) and Intravascular
ultrasound (IVUS) revealed a CPAF originating from the proximal LAD and a saccular aneurysm in the middle LAD. The orifice of the CA was small due to the presence of an aneurysm-coronary septum (Video 3, Supplementary Figure 1A). Right heart catheterization (RHC) showed a significant increase in oxygen saturation between the right ventricle and pulmonary artery (71% and 78%, respectively), while the mean pulmonary artery pressure and pulmonary capillary wedge pressure were normal (19 and 9 mmHg, respectively). The ratio of pulmonary blood flow to systemic blood flow (Qp/Qs) was 1.3. There was no evidence of myocardial ischemia with adenosine Tallium-201 myocardial perfusion scintigraphy, which might detect myocardial ischemia caused by CPAF.

While there were no subjective symptoms and complications related to CPAF and CA, the CA diameter had grown from 23 to 30 mm over 4 years, indicating a risk of aneurysmal rupture (Figure 4A, B). Therefore, we decided to treat the CPAFs with CA after the heart team held discussions with cardiac surgeons and pediatric cardiologists. Other than discussions in the heart-team in our hospital, we discussed with adult congenital heart disease specialists and pediatric cardiologists in other hospitals before treatment, regarding the therapeutic indication and the therapeutic strategy for this patient. Surgical correction was not feasible, since it will be difficult to identify the orifice of the fistula originating from the LAD, which requires a
dissection of the cluster of CPAFs. Furthermore, the patient preferred minimally invasive treatment by a transcatheter approach. We therefore decided to perform transcatheter closure of these fistulas using detachable coils and a coronary stent.

Initial intervention was performed for the CPAFs of the RCA. A guidewire (SION blue; ASAHI intec, Aichi, Japan) and a steerable microcatheter (LEONIS Mova; Sumitomo Bakelite, Tokyo, Japan) were inserted into the fistula using a 7-Fr guiding catheter (JR-4, Heartrail II; Terumo Corp., Tokyo, Japan) from the right radial artery. The two fistulas of the RCA were embolized with 5 coils in total (Target XL360 soft; Stryker, Kalamazoo, Michigan) up to 6 mm in diameter and 20 cm in length. Post-embolization CAG confirmed the occlusion of all CPAFs from the RCA (Figure 3A). Embolization of the fistula at the proximal LAD was performed at a later date. The fistula was embolized with 6 coils up to 8 mm in diameter and 30 cm in length in a manner similar to the CPAFs of the RCA. The saccular aneurysm of the mid LAD was subsequently treated. Based on the previous IVUS findings, we planned to treat the aneurysm with stent-assisted coil embolization. Initially, a coil (3 mm in diameter and 90 mm in length) was deployed at the orifice of the aneurysm to disturb the blood flow into the aneurysm. A drug-eluting stent (DES) (CoCr-ZES 4.0/12 mm; Medtronic, Santa Rosa, CA, USA) was then delivered to cover the aneurysm orifice along
with the deployed coil. Unfortunately, the coil migrated distally due to interference between the coil and stent. Since the first stent could not fully cover the coil, we decided to implant a second stent (PtCr-EES 3.0/16 mm; Boston Scientific, Marlborough, MA, USA). Although final angiography showed a mild residual flow into the aneurysm, IVUS findings showed the aneurysm orifice was mostly covered by the stents (Video 4, Figure 3B, Supplementary Figure 1B). The periprocedural myocardial infarction (defined by elevation of cTn values > 5 × 99th percentile URL) was not documented with all procedures in this case.

Follow-up CAG showed that the blood inflow into the saccular aneurysm was minimal after six months (Supplementary Figure 2). This patient presented nasal bleeding one month after stent implantation, therefore she needed the de-escalation from DAPT with aspirin and clopidogrel to a single antiplatelet therapy (SAPT) with clopidogrel. Since then, her post-procedure course was uneventful. Three-month follow-up cardiac CT showed aneurysm shrinkage associated with partial thrombus formation (Figure 4C), and one-year follow-up cardiac CT revealed the aneurysm had become completely occluded, suggesting that aneurysm rupture had been successfully prevented by a transcatheter approach (Figure 4D).

Discussion
We reported a case with multiple CPAFs with giant CA, to our knowledge, this is the first report of successful percutaneous coil embolization and stent implantation for multiple CPAFs with giant CA.

The appropriate therapeutic indication for CPAFs has not been established. According to previous reports, the therapeutic indications depend on the size of the fistula, the presence of symptoms suggestive of myocardial ischemia and heart failure, the size of aneurysms, anatomy of the fistula, patient’s age, and the presence of associated cardiovascular abnormalities. According to a previous case series in Japan, among 23 cases of coronary artery aneurysm rupture, 96% (22/23) of the patients had an aneurysm diameter of 3 cm or larger. Hence it is considered that therapeutic intervention may be indicated for aneurysms larger than 30 mm to prevent rupture. Moreover, some cases have reported that an aneurysm had progressively enlarged during follow-up period. In our case, cardiac CT suggested that saccular aneurysm had significantly enlarged to only 4 years, indicating the risk of rupture. Although our patient had neither clinical symptoms including myocardial ischemia nor complications related to CPAF and CA, the size of the aneurysms and their expansion supported the indication for interventional treatment in this case.
The management strategies for CPAFs with CA include surgical repair or catheter embolization. In our case, the findings of IVUS revealed the anatomy of the aneurysmal orifice and aided us to determine a therapeutic strategy. We decided to perform transcatheter closure for these CPAFs and CA using detachable coils and coronary stents after the heart team discussions. We applied DESs rather than a covered stent because a high restenosis rate and prolonged requirement of dual antiplatelet therapy (DAPT) are remaining concerns in the implantation of covered stents. Indeed, although we planned 3-month DAPT in this case, we de-escalated from DAPT with aspirin and clopidogrel to a single antiplatelet therapy (SAPT) with clopidogrel, due to frequent nasal bleeding one month after stent implantation.

In conclusion, multiple CPAFs with giant CA were successfully treated using percutaneous coil embolization and stent implantation. A transcatheter approach for multiple CPAFs is a promising therapeutic option with advantages over other approaches in safety and invasiveness.

Consent

The authors confirm that written consent for submission and publication of this case report including images and associated text has been obtained from the patient in line with COPE guidance.
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**Figure titles and legends**

**Figure 1. Contrast-enhanced cardiac CT**

(A) Contrast-enhanced cardiac CT showed multiple contrast-enhanced nodules adjacent to the ascending aorta. (B) Three-dimensional reconstruction of coronary arteries using CT angiography.

**Figure 2. Coronary angiography**

(A) Right CAG showed two CPAFs originating from the proximal RCA. (B) Left CAG could not identify the orifices of the fistulas from the coronary artery.

**Figure 3. Coronary angiography**

(A) Post coil-embolization for CPAFs of the RCA. (B) Post coil-embolization for CPAFs of the proximal LAD, and post coil-embolization and stent implantation for giant CA of the mid LAD.

**Figure 4. Serial cardiac CT**

Serial cardiac CT findings (A) four years ago, (B) Pre-embolization, (C) three months later, and (D) one year later. White arrows showed saccular aneurysm originating from the mid LAD.

**Supplementary Figure 1. Image of the IVUS**

(A) IVUS findings of aneurysm anastomosis before stent implantation. (B) IVUS findings of
Supplementary Figure 2. Selective contrast injection via guide-extension catheter

(A) Pre-embolization. (B) Six months later.

Video 1. Contrast-enhanced cardiac CT image.

Video 2. Left coronary angiography.

Video 3. IVUS findings of aneurysm anastomosis before treatment.

Video 4. IVUS imaging of aneurysm anastomosis after stent implantation.
Figure 2

A. Coronary-PA fistula from mid LAD with aneurysm

B. Coronary-PA fistula from proximal LAD with aneurysm

RCA

Distal LAD
Figure 4

A  4-year ago

B  Pre-embolization

C  3-month later

D  1-year later
Figure 1

A

Distal LAD

B

Coronary-PA fistula from mid LAD with aneurysm