CASE REPORT

Antithrombotic Therapy of a Young Adult with Giant Left Main Coronary Artery Aneurysm

A Case Report and Review of the Literature

Tingting Chen,[1*] MD, Jing Li,[1*] MD, Qing Xu,[1] MD, Xiaoyu Li,[1] MD, Qianzhou Lv,[1] MD and Hongyi Wu,[2] MD

Summary

Giant coronary artery aneurysm (CAA) is a rare disorder, defined as coronary artery dilatation, in which the diameter of the coronary artery exceeds more than 1.5 times of its normal size. The most common cause of CAA is coronary atherosclerosis for adults and Kawasaki disease (KD) for children and adolescents (especially for the giant CAA that occurred in adolescence). CAA complications include thrombus, acute myocardial infarction (AMI), vasospasm, rupture, ischemia, heart failure, and arrhythmia. So, antithrombotic therapy is crucial for patients with giant CAA.

Although giant CAA has been reported in some cases before, few of these cases described antithrombotic therapy particularly, let alone informed direct oral anticoagulant (DOAC) use in these patients. Here, we report a case of a young patient with acute coronary artery disease caused by huge CAA. Rivaroxaban combined with clopidogrel was used for his antithrombotic therapy. Moreover, we reviewed the existing reports to provide an overview of antithrombotic treatment in patients with giant CAA.

(Int Heart J 2020; 61: 601-605)

Key words: Embolization, Coronary angiography, Rivaroxaban, Direct oral anticoagulants

Coronary artery aneurysm (CAA) is defined as a local or diffuse dilatation of a coronary artery of more than 1.5 times of its original size.[1)] Giant CAA refers to the patient's coronary dilatation which exceeds at least four times the reference dimension or has a diameter exceeding 8 mm.[2)] It is a rare coronary pathology, with an incidence of 0.02% of all atherosclerotic patients.[2)] CAAs are mostly located in the right coronary artery (RCA), followed by the left anterior descending (LAD) artery and then left circumflex (LCX) artery consecutively. The occurrence of aneurysms of the left main coronary artery (LMCA) is extremely rare,[1)] making it difficult to standardize treatment or establish guidelines that support medical and surgical management.

Although giant CAAs were reported in some cases before, few of these cases described the drug therapy particularly, let alone informed direct oral anticoagulant (DOAC) use in these patients. In this report, we described the treatment of a young adult with giant CAA in the LMCA treated with rivaroxaban and clopidogrel. Furthermore, we reviewed previous reports to provide an overview of antithrombotic therapy in giant CAAs.

Case Report

A 22-year-old man was admitted for typical chest pain, nausea, vomiting, and sweating. He experienced exertional chest pain in the last 3 days. At the age of 6, he had prolonged hospitalization for fever, but the specific treatment experience had been forgotten. In addition, he smoked at a frequency of 20 cigarettes per day on average for 6 years, and he had poor medical compliance. He was treated at another hospital 1 day before the present admission for typical chest pain. Emergency coronary angiography revealed giant ectasia of the LMCA and the LCX artery. In addition, total thrombotic occlusion of the proximal LAD coronary artery and ectasia of RCA were observed. There were no significant lesions in the RCA. At that time, the patient was diagnosed with acute myocardial infarction (AMI) and coronary aneurysms, and KD was suspected. It was recommended that he be transferred to a higher-class hospital for further treatment.

Thus, he was transferred to our hospital 24 hour after his first admission to the previous hospital. His arterial blood pressure and heart rate were 100/74 mmHg and 120 per minute, respectively, upon admission. His electrocardiogram revealed sinus tachycardia, acute extensive ante-

From the [1]Department of Pharmacy, ZhongShan Hospital, FuDan University, Shanghai, China and [2]Department of Cardiology, ZhongShan Hospital, FuDan University, Shanghai, China.

*These authors contributed equally to this work.

Address for correspondence: Hongyi Wu, MD, Department of Cardiology, ZhongShan Hospital, FuDan University, No.180, Fenglin Road, Xuhui, Shanghai, China. E-mail: wu.hongyi@zs-hospital.sh.cn

Received for publication September 1, 2019. Revised and accepted December 24, 2019.

Released in advance online on J-STAGE April 29, 2020.

doi: 10.1536/ihj.19-451

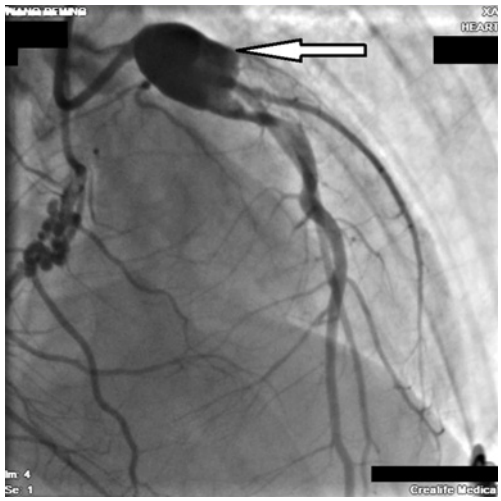

Figure 1. Coronary angiography revealed a giant coronary aneurysm in the distal LMCA and proximal LAD coronary artery (arrow). LMCA, left main coronary artery; LAD, left anterior descending.

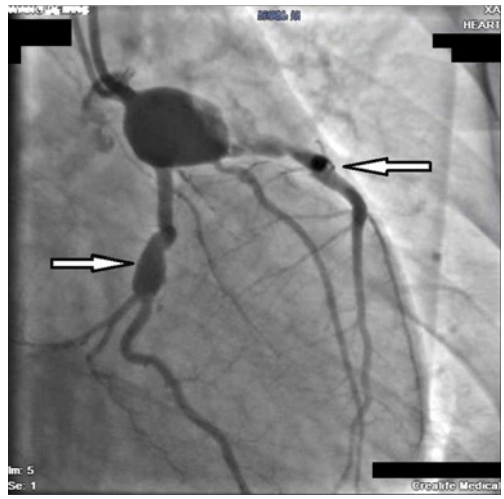

Figure 2. Coronary angiography revealed ectasia of the midportion of LCX and RCA (arrow). LCX, left circumflex artery; RCA, right coronary artery.

rior myocardial infarction and lateral myocardial infarction. His chest X-ray revealed infiltration on both lungs. Myocardial necrosis markers increased and reached a peak of 3204 U/L of CK; T 1.91 ng/mL, cardiac troponin; and 6331 pg/mL, NT-pro BNP. His echocardiography revealed a depressed left ventricular ejection fraction of 27% and hypokinesia in the ventricle, local ectasia of the coronary artery, and moderate mitral regurgitation and mild pulmonary hypertension.

The patient was admitted to the coronary care unit for ongoing monitoring and antithrombotic therapy optimization. He was treated with dual antiplatelet therapy (aspirin 100 mg/day and ticagrelor 90 mg/twice a day), combined with low-molecular-weight heparin (LMWH, 4100 IU/day), rosuvastatin (10 mg/day), metoprolol (23.75 mg/day), spironolactone (20 mg/day), torsemide (20 mg/day), and rabeprazole (10 mg/day).

The patient underwent second coronary angiography and percutaneous coronary intervention (PCI) 7 after admission. At PCI, giant ectasia with thrombosis was revealed in the distal LMCA and proximal LAD coronary artery (Figure 1). No significant lesions were observed in the midportion of the LAD coronary artery. Ectasia could be observed in the midportion of the LCX artery and RCA (Figure 2). The 0.014" SION wire was delivered to the distal part of the anterior descending branch, and the endovascular ultrasound catheter was sent to the middle part of the anterior descending branch for continuous and automatic retraction. The intravascular ultrasound (IVUS) examination revealed that the structure of the proximal central segment of the anterior descending branch was relatively normal, with the vascular diameter around 4 mm. Giant CAA was observed in the LMCA, with a diameter of 18-20 mm. The 5F TERUMO sub catheter was sent to the proximal-middle section of the anterior descending branch for repeated thrombus aspiration, and a large number of old mechanical thrombus was extracted.

The patient was transferred back to the cardiovascular department after PCI. He was administered rivaroxaban 10 mg/day, clopidogrel 75 mg/day, rosuvastatin 10 mg/day, metoprolol 11.875 mg/day, spironolactone 20 mg/day, and rabeprazole 10 mg/day. When his condition became manageable, he left the hospital 4 days later.

About 2 months later, the patient did not experience angina or thrombotic or bleeding complications. However, his echocardiography revealed enlarged heart with depressed left ventricular ejection fraction of 27%, severe mitral regurgitation, severe pulmonary hypertension, and pericardial effusion. He then underwent heart transplant for further treatment. The pathological findings of his heart revealed giant ectasia with thrombosis located at the beginning of the coronary artery and grayish brown plaques at the proximal segment of the anterior descending branch with a range of about 1.5 × 1.2 cm.

Discussion

The clinical manifestations of giant CAA have demonstrated that thrombosis, embolization, and rupture of the involved segments are the leading cause of AMI and sudden death, which are the consequences of hemodynamic instability within the aneurysmal pocket.[3] Heart surgery and PCI, involving thrombus aspiration and conservative treatment, are the feasible options for CAAs. Invasive approaches, such as surgery or PCI, should be considered for CAA in acute coronary syndromes.[4] Other etiologies include congenital, systemic lupus erythematosus, trauma, polyarteritis nodosa, syphilis, mycotic embolism, cocaine use, and Marfan syndrome.[4] Our patient experienced fever for a long time when he was 6 years old; thus, his giant CAA was probably a long-term complication of KD.

An ideal pharmacological management for CAAs has not been well defined due to lack of evidence. Anticoagulation therapy is currently recommended for giant CAAs due to the presence of pro-coagulant endothelial surface and stasis of flow within the aneurysm prone to thrombosis.[5-7]

The existing reports revealed new surgical procedures

Table. Review of Clinical Characteristics, Management, and Outcome of Giant Coronary Artery Aneurysm (CAA)

Author	Year	Age	Sex	Indication	Cause	Sites	Sizes	FU	Operation	Antithrombotic therapy	Adjuvant drug	Outcome
Pineda[8)]	2001	79	M	angina	AS	LMCA	1.1 × 1.1 cm	12 months	NO	ASA, warfarin	NA	stable
Chen[9)]	2002	50	M	angina	congenital	LMCA	≥2 cm	5 years	CABG	ASA warfarin	NA	stable
Gunduz[10)]	2004	63	M	NSTEMI	AS	LCA	NA	NA	NO	ASA	ACEI, β-blockers, lipid-lowering therapy	NA
Madsen[11)]	2006	70	M	NSTEMI	NA	LCX	12 × 19 mm	2 months	thrombus aspiration	ASA, clopidogrel	simvastatin, metoprolol	stable
Rognoni[12)]	2007	66	M	CF	NA	RCA	10 mm	2 years	elective open chest surgery	ASA	nitrate, atenolol, furosemide, enalapril	stable
Luz[13)]	2007	82	M	AMI	AS	RCA	NA	1 year	NO	DAPT	NA	stable
Chia[14)]	2007	41	M	angina	NA	LAD	NA	6 months	NO	warfarin	NA	stable
Sokhanvar[15)]	2008	36	M	epigastric pain	BD	LAD/ RCA	8 mm/9 mm	9 months	NO	ASA, warfarin	β-blocker, nitrate, enalapril, digoxin, spironolactone	AMI again
Pavlidis[16)]	2012	63	M	symptom-free	NA	LMCA	25 × 23 mm	NA	NO	DAPT	NA	NA
Tuncer[1)]	2013	80	F	angina	NA	LMCA	3.0 × 2.0 cm	8 months	NO	ASA	nitrate, β-blocker, ACEI, statin	stable
Çizgici[17)]	2013	49	M	AMI	BD	LAD	15 mm	NA	CABG	ASA, clopidogrel	NA	NA
Veenu[18)]	2014	63	M	NSTEMI	AS	RCA LCX LAD	8.1 × 1 cm 4.9 × 4.5 cm 4.3 × 1.2 cm	1 year	NO	DAPT	High-dose statins, β-blocker and ACEI	stable
Taniguchi[19)]	2015	28	F*	symptom-free	KD	LMCA	8 mm	13 months	NO	ASA, UFH	NA	stable
Motozawa[20)]	2015	24	M	AMI	KD	LAD	NA	10 days	thrombus aspiration	warfarin	NA	stable
Deaño[21)]	2015	41	M	epigastric pain	KD	RCA	9 cm	NA	proximal resection, distal ligation, CABG	DAPT†	NA	NA
Yanik[22)]	2016	70	M	AMI	AS	LAD	32 × 26 mm	3 months	CABG	ASA, clopidogrel	atorvastatin	stable
Potter[23)]	2016	36	F	STEMI	KD	RCA	7-8 mm	6 months	thrombus aspiration	ASA	bisoprolol, irbesartan, atorvastatin	stable
Y Li[4)]	2017	24	M	TE and AMI	NA	LMCA/ LCX	NA	15 months	thrombus aspiration	ASA, warfarin	NA	stable
Current case	2018	22	M	AMI	KD	LMCA	18 mm	4 months	thrombus aspiration	Rivaroxaban, clopidogrel	Rosuvastatin, metoprolol, spironolactone, and rabeprazole	receive heart transplantation

ACEI indicates angiotensin-converting enzyme inhibitors; AMI, acute myocardial infarction; AS, atherosclerosis; ASA, aspirin; BD, Behçet's disease; CABG, coronary artery bypass graft; CF, cardiac failure; DAPT, dual anti-platelet therapy; F, female; FU, follow-up period; KD, Kawasaki disease; LAD, left anterior descending artery; LCX, left circumflex artery; LMCA, left main coronary artery; M, male; NA, not available; NSTEMI, non-ST-segment elevation myocardial infarction; RCA, right coronary artery; STEMI, ST-segment elevation myocardial infarction; TE, thrombus embolization; and UFH, unfractionated heparin.*The patient was pregnant. †Anticoagulation with warfarin was recommended but refused by the patient.

or image performance, but few of them described the drug regimen in detail. We summarized the clinical characteristics, management, and outcome of 19 adult patients with giant CAA, including the patient in the present study, in which drug therapy was reported (Table).[1,3,8-23] Six of the patients (84.2%) were male, and only three (15.8%) were female. The ages ranged from 22 to 82 years old. Among the 19 patients, 5 developed giant CAA due to KD, and in another 5 patients, CAA occurred as a consequence of atherosclerosis and in 6, due to unknown etiologies. Of the 19 patients, 10 (52.6%) experienced acute myocardial infarction, and 2 were symptom-free. Moreover, 14 of the patients (73.7%) had left coronary aneurysms, and 10 (52.6%) underwent surgical procedures, including coronary artery bypass graft, thrombus aspiration, and elective open chest surgery. The main therapeutic drug of these patients was aspirin. Seven of the patients (36.8%) were treated with dual antiplatelet therapy, such as aspirin combined with clopidogrel, eight (42.1%) received anticoagulant therapy, six received warfarin, and one took heparin because of her pregnancy. Our patient was the only one who took novel anticoagulant. Nine of the patients (47.4%) were recorded to have taken adjuvant drugs, most of which were angiotensin-converting enzyme inhibitors (enalapril and irbesartan), β-blockers (metoprolol), and statins (simvastatin).

The previous reports indicated that there was no consensus with regard to the optimal treatment for giant CAA. In 11 of the cases (57.9%), treatment with aspirin combined with anticoagulants or another antiplatelet agent was reported, with warfarin being the main choice. DOACs use and triple therapy had not been reported.

Over the past few years, DOACs have emerged, including one direct thrombin inhibitor (dabigatran) and four factor Xa inhibitors (apixaban, edoxaban, rivaroxaban, and betrixaban).[24] The greater efficacy and safety of DOACs for the prevention of thromboembolic events in patients with atrial fibrillation or venous thromboembolism have been confirmed. Moreover, patients taking DOACs may have better medical compliance than those taking warfarin due to the lack of INR monitoring, which may be beneficial for young adults because they are more prone to non-compliance with medication. However, no studies have reported the use of DOACs for the prevention of embolism in giant CAA. Since our patient with poor medical compliance lives far from the hospital, periodical INR monitoring was difficult. He received anticoagulation therapy with rivaroxaban rather than warfarin because of his high risk of thrombosis, and clopidogrel was added. The 2017 AHA guidelines indicated that statins may be considered in patients with KD.[5] He continued taking rosuvastatin 10 mg per day. At 2 months follow-up, he did not experience angina, CAA, and thrombosis.

We wanted to conduct longer follow-up in order to evaluate the efficacy and safety of the treatment with rivaroxaban combined with clopidogrel. Unfortunately, the patient had to undergo heart transplant because the condition of his heart continuously deteriorated. It may not be enough to support the use of rivaroxaban in patients with giant CAA due to the insufficient follow-up time, but our case may at least provide new ideas for the treatment of giant CAAs.

Conclusion

We describe the use of rivaroxaban to prevent thrombosis in patient with giant CAA. To the best of our knowledge, this is the first case report on the use of rivaroxaban for CAA to prevent thrombotic events. Our report supports the value and reference to optimize the anticoagulation therapy in patients with giant CAA. In addition, more reports are needed to determine the proper use of anticoagulation therapy in patients with giant CAA.

Disclosure

Conflicts of interest: The authors declare no conflict of interests and no support from any organization for the submitted work. This research did not receive any specific grant from any funding agency.

References

1. Tuncer E, Onsel Turk U, Alioglu E. Giant saccular aneurysm of the left main coronary artery. J Geriatr Cardiol 2013; 10: 110-2.
2. Halapas A, Lausberg H, Gehrig T, Friedrich I, Hauptmann KE. Giant right coronary artery aneurysm in an adult male patient with non-st myocardial infarction. Hellenic J Cardiol HJC Hell Kardiol Epitheor 2013; 54: 69-76.
3. Li Y, Wu C, Liu W. Coronary artery ectasia presenting with thrombus embolization and acute myocardial infarction: A case report. Medicine 2017; 96: e5976.
4. Alioglu E, Turk UO, Engin C, Tengiz I, Tuzun N, Posacioglu H. Left main coronary artery aneurysm in young patient with acute myocardial infarction. J Cardiovasc Med (Hagerstown) 2009; 10: 494-6.
5. Denby KJ, Clark DE, Markham LW. Management of Kawasaki disease in adults. Heart 2017; 103: 1760-9.
6. Guidelines for diagnosis and management of cardiovascular sequelae in Kawasaki disease (jcs 2013). Digest version. Circ J Off J Jpn Circ Soc 2014; 78: 2521-62.
7. McCrindle BW, Rowley AH, Newburger JW, *et al*. Diagnosis, treatment, and long-term management of Kawasaki disease: A scientific statement for health professionals from the American Heart Association. Circulation 2017; 135: e927-99.
8. Pineda GE, Khanal S, Mandawat M, Wilkin J. Large atherosclerotic left main coronary aneurysm--A case report and review of the literature. Angiology 2001; 52: 501-4.
9. Chen SS, Skillington P, Calafiore P, Dick RJ. Giant left main coronary artery aneurysm: An unusual cause of acute myocardial infarction. Intern Med J 2002; 32: 614-5.
10. Gunduz H, Akdemir R, Binak E, Tamer A, Uyan C. Spontaneous rupture of a coronary artery aneurysm: A case report and review of the literature. Jpn Heart J 2004; 45: 331-6.
11. Madsen EH, Villadsen AB, Frøbert O. Acute coronary artery thrombosis and a giant coronary artery aneurysm: An atypical combination and an unconventional catheter-based intervention. Catheter Cardiovasc Interv 2006; 68: 399-402.
12. Rognoni A, Ferrero V, Teodori G, Ribichini F. Successful surgical treatment of a giant coronary aneurysm communicating with the right atrium. J Cardiovasc Med (Hagerstown) 2007; 8: 1061-4.
13. Luz A, Silveira J, Carvalho H, Gomes L. Right coronary artery aneurysm. Int J Cardiol 2007; 114: e122-3.
14. Chia PL, Lee CH, Lim JT. Progressive coronary artery aneu-

rysm presenting as acute myocardial infarction. Int J Cardiol 2009; 132: 280-2.
15. Sokhanvar S, Karimi M, Esmaeil-Zadeh A. Recurrent acute myocardial infarction with coronary artery aneurysm in a patient with Behcet's disease: A case report. J Med Case Rep 2009; 3: 8869.
16. Pavlidis AN, Malakos JS, Karavolias GK, *et al*. Left main coronary artery aneurysm. Herz 2012; 37: 565-6.
17. Çizgici AY, Öz F, Sezer M, Umman S. Giant left main coronary artery aneurysm complicated with anterior myocardial infarction in Behcet's syndrome. Anadolu Kardiyol Derg 2013; 13: E1-2.
18. Veenu J, Shetty GG, Adhyapak SM, Jayadev SM, Varghese K, Patil CB. Giant coronary artery aneurysms involving all three coronary arteries. Indian Heart J 2014; 66: 727-30.
19. Taniguchi K, Ono H, Sato A, *et al*. Strict management of a pregnant patient with giant coronary artery aneurysm due to Kawasaki disease. Pediatr Int 2015; 57: 990-2.
20. Motozawa Y, Uozumi H, Maemura S, *et al*. Acute myocardial infarction that resulted from poor adherence to medical treatment for giant coronary aneurysm. Int Heart J 2015; 56: 551-4.
21. Deaño RC, Shah AM, Khan ZS, *et al*. Giant coronary aneurysm diagnosed as incidental mediastinal mass. JACC Cardiovasc Interv 2015; 8: 114-5.
22. Yanık A, Arslan U, Akçay M, Menekşe S, Yazgan UG. Giant coronary artery aneurysm causing acute anterior myocardial infarction. Case Rep Med 2016; 2016: 5180472.
23. Potter EL, Meredith IT, Psaltis PJ. St-elevation myocardial infarction in a young adult secondary to giant coronary aneurysm thrombosis: An important sequela of Kawasaki disease and a management challenge. BMJ Case Rep 2016; 2016: bcr2015213622.
24. Franco Moreno AI, Martín Díaz RM, García Navarro MJ. Direct oral anticoagulants: An update. Med Clin 2018; 151: 198-206.