CASE REPORT

Three-vessel coronary artery aneurysmal disease complicated by multivessel thrombosis and cardiogenic shock: the saving role of intracoronary thrombolysis

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SUMMARY

The benefit of intracoronary thrombolytics in ST-elevation myocardial infarction (STEMI) is not well established. Mainstays of STEMI management include intravenous thrombolytics, percutaneous coronary interventions and surgical revascularisation. However, in cases of STEMI secondary to coronary artery aneurysmal disease (CAAD), standard treatment options may not be suitable due to high thrombus burden, perioperative risk and factors unique to each patient. Thus, STEMI management in CAAD can represent a therapeutically challenging clinical scenario. Here, we describe a patient with severe three-vessel CAAD complicated by multivessel thrombosis and cardiogenic shock for whom traditional management options including placement of haemodynamic support devices were not feasible. As an alternative measure, the patient was treated with intracoronary thrombolysis with remarkable clinical stabilisation and angiographic resolution of thrombosis. He remains clinically stable several years later without recurrent events. This case serves to demonstrate the potential lifesaving benefit of intracoronary thrombolysis in complicated multivessel CAAD.

BACKGROUND

Coronary artery aneurysmal disease (CAAD) is defined as one or more focal saccular or fusiform coronary dilatations that exceed 1.5 times the diameter of normal adjacent segments.¹ The estimated prevalence of CAAD ranges from 0.3% to 5.3% with most lesions found incidentally on coronary angiography or other thoracic imaging modalities.^{2–4} The mechanism of CAAD involves progressive disruption and weakening of the vascular wall with subsequent dilation.^{2–5} A majority of cases of CAAD are secondary to atherosclerosis.^{2,6} As such, patients with CAAD often have traditional atherogenic risk factors. Rare causes of CAAD include auto-immune inflammatory diseases (Kawasaki disease, Takayasu arteritis, giant cell arteritis, Behçet's disease, systemic lupus erythematosus, rheumatoid arthritis or polyarteritis nodosa), hereditary connective tissue diseases (Marfan's syndrome and Ehlers-Danlos), infection, drugs (cocaine and amphetamines), congenital and iatrogenic following percutaneous coronary intervention (PCI).^{2,5,7–9}

The most commonly affected artery in CAAD is the right coronary artery (RCA) (40%–70%) followed by the left anterior descending (LAD) artery (32.3%) and the circumflex (CFX) artery (23.4%). Three-vessel involvement is a rare occurrence (3.5%).^{2,5,6,10}

The most common clinical manifestation of CAAD is acute coronary syndrome (ACS).^{2,5,11,12} In these cases, thrombosis within areas of aneurysm is a frequent finding. ACS may further be explained by sluggish blood flow through the aneurysm itself or distal thromboembolism with absent or reduced antegrade coronary flow. In addition, patients with CAAD are more likely to have concurrent coronary stenosis. These features of CAAD may explain why patients with ACS may have higher rates of cardiovascular morbidity and mortality than those without aneurysms.^{2,5,6,13–15} Interestingly, cardiogenic shock as an early manifestation of atherosclerotic CAAD has not been well described.

Treatment for CAAD is unclear, and management strategies for CAAD presenting with ACS have not been systematically studied. As such, patients with CAAD can represent a therapeutically challenging clinical scenario. In the absence of randomised trials, the treatment for CAAD is individualised and based on patient's specific clinical manifestations, extent of CAAD and thrombus burden. Provider and institutional expertise in the management of these cases plays an equally important role.

In the acute phase of CAAD and ACS, current management options include antiplatelet therapy in combination with intravenous unfractionated heparin. These therapies are used to prevent further extension of thrombi rather than to resolve existing thrombi.^{1,2,13,16} PCI with or without aspiration thrombectomy or surgical correction of CAAD is other available options. However, these interventions have been associated with high failure rates and increased morbidity and mortality.^{2,13–15,17} In addition, lack of randomised controlled data comparing medical therapy, PCI or surgery in CAAD precludes the routine recommendation of one therapeutic strategy over another. Therefore, non-standard therapeutic options for CAAD such as intracoronary thrombolysis may have a beneficial effect in this patient population.

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Figure 1 (A) This RAO angiographic view demonstrates multiple aneurysms (orange arrowheads) in the first and principal D1 branch, proximal CFX artery and LAD artery. Also, an occlusive thrombus in the mid CFX artery (red arrow) and partially occlusive thrombus (yellow arrows) in the ostial to proximal D1 branch and LAD artery are noted. (B) This RAO cranial angiographic view further illustrates the aneurysmal disease (orange arrowheads) and tortuosity of the LAD artery and D1 branch, distal occlusion (likely thrombotic) of the LAD artery (red arrow) and reduced antegrade flow of the distal D1 branch. (C) This LAO view of the RCA demonstrates a proximal, severe and eccentric stenosis (red arrow) and multiple aneurysms (orange arrowheads) of its proximal and mid portions as well as diffuse distal disease. CFX, circumflex; LAD, left anterior descending; LAO, left anterior oblique; RAO, right anterior oblique; RCA, right coronary artery.

Here, we describe a patient with severe three-vessel CAAD complicated by multivessel thrombosis and ischaemic cardiogenic shock who was successfully treated with intracoronary thrombolysis.

CASE PRESENTATION

A 79-year-old man with hypertension, type II diabetes mellitus, dyslipidaemia and known coronary artery disease presented with acute chest pain of 3-hour duration. Initial ECG revealed evidence of inferior–posterior ST-segment elevation myocardial infarction (STEMI). Initial troponin level was 4.8 ng/mL. After initial therapy with antiplatelet therapy and intravenous heparin, emergent coronary angiography revealed severe three-vessel CAAD with extensive occlusive and non-occlusive multivessel thrombosis. Following angiography, the patient developed sustained and progressive hypotension unresponsive to intravenous fluids which required dopamine infusion up to 7.5 µg/kg/min. Right heart catheterisation and abdominal aortography in anticipation of intra-aortic balloon pump placement were performed.

INVESTIGATIONS

1. Coronary angiography demonstrated severe three-vessel CAAD with occlusive thrombus of the CFX artery, partially occlusive thrombus of the ostial to proximal LAD artery and principal proximal diagonal (D1) branch, distal thrombotic occlusion of the LAD and reduced antegrade flow in the distal D1 branch (figure 1A,B). The RCA demonstrated severe proximal stenosis with multiple interposed aneurysms (figure 1C).
2. Right heart catheterisation performed while on dopamine infusion demonstrated: (1) prominent V waves indicative of ischaemic left ventricular stiffness and/or ischaemic mitral regurgitation, which interfered with accurate assessment of pulmonary capillary wedge pressure; (2) moderate to severe pulmonary hypertension with systolic, diastolic and mean pressures of 58 mm Hg, 30 mm Hg and 43 mm Hg, respectively; (3) elevated right ventricular systolic and diastolic pressures; (4) right atrial pressure of 17 mm Hg and (5) Fick cardiac output and index normalised by dopamine therapy of 5.45 L/min and 2.87 L/min/m², respectively.
3. Aortography demonstrated significant tortuosity of the abdominal aorta and severe tortuosity and aneurysmal

disease of the iliofemoral arteries (figure 2A,B), which made placement of an intra-aortic balloon pump or impella not feasible.

DIFFERENTIAL DIAGNOSIS

In this patient, the differential diagnosis to atherosclerotic CAAD includes inflammatory connective tissue diseases or arteritis. However, given the patient's age, male gender, multiple atherogenic risk factors, known CAD and associated peripheral arterial disease, the presentation was most consistent with atherosclerotic CAAD.

TREATMENT

After a multidisciplinary discussion involving the cardiothoracic surgeon, the interventionalist and the referring cardiologist, PCI, aspiration thrombectomy and surgical revascularisation were not considered viable treatment options due to the diffuse aneurysmal involvement of all three coronaries, multivessel thrombus burden and the patient's unstable and rapidly deteriorating clinical status. Similarly, the patient was not considered a candidate for PCI due to unsuitable anatomy.

Figure 2 Abdominal aortogram (A) and pelvic arteriography (B) demonstrate significant abdominal aortic tortuosity (red arrowhead in A) and bilateral tortuosity and aneurysmal disease of the iliofemoral arteries (orange arrowheads in B), which made placement of an intra-aortic balloon pump or impella relatively contraindicated.

Figure 3 (A) This RAO caudal angiographic view after three doses of 10 mg of intracoronary tPA demonstrates resolution of the partially occlusive thrombus in the LAD artery and D1 branch (filling defects no longer present; yellow arrows). However, occlusive thrombosis persisted in the CFX artery (red arrow). (B) This RAO cranial view demonstrates restoration of flow of the distal LAD artery and improved flow of the distal D1 branch (green arrows). CFX, circumflex; LAD, left anterior descending; RAO, right anterior oblique; tPA, tissue-type plasminogen activator.

Intracoronary thrombolysis was therefore used as a measure to restore myocardial perfusion to all three involved vessels. The patient received three doses of 10 mg of intracoronary tissue-type plasminogen activator (tPA) at 10–15 min intervals delivered via the diagnostic catheter. Between injections, the catheter was left in place. Left coronary angiography was taken immediately before the second dose and repeated before and after the third dose of tPA. Progressive resolution of thrombus and improved antegrade flow in the LAD artery and D1 branch was noted after each dose of tPA (figure 3A,B). No recanalisation of the CFX artery was observed during the procedure.

OUTCOME AND FOLLOW-UP

Following intracoronary thrombolysis, the patient's haemodynamics stabilised and his chest pain resolved. He was then transferred to the intensive care unit on low-dose dopamine. Bedside echocardiogram after intracoronary thrombolysis demonstrated (1) mildly reduced left ventricular ejection fraction of 45%–50%, (2) minor segmental wall motion abnormalities, (3) preserved right ventricular systolic function and (4) no significant valvular disease.

He was weaned off of dopamine during his short course in the intensive care unit. Although no recanalisation of the CFX artery was observed during the procedure, the patient's improved clinical status, normalised ECG and peaked troponin level of only 22.6 ng/mL were consistent with a small myocardial infarction and possible restoration of CFX blood flow.

On discharge, the patient was sent home on standard medical therapy including dual antiplatelet therapy with aspirin and clopidogrel. After nearly 4 years of follow-up, he remains clinically stable with no recurrent cardiovascular events.

Given the patient's uneventful clinical course and unsuitable coronary anatomy, PCI and surgical revascularisation procedures have not been performed. For the same reasons, additional tests to detect myocardial ischaemia have not been clinically warranted.

DISCUSSION

To our knowledge, this is the first case that describes three-vessel CAAD complicated by multivessel thrombosis and cardiogenic shock treated with intracoronary thrombolytics.

ACS is a common manifestation of CAAD. However, CAAD accounts for only a small fraction of total cases of ischaemic heart disease.^{2 5 6 11 12} Because CAAD is a rare presentation of ACS, no therapeutic randomised trials have been conducted. Observed management strategies in CAAD include medical therapy, use of PCI and surgical revascularisation with varying degrees of success.^{2 11 13 18}

Patients with CAAD have an increased risk for intracoronary thrombosis. Thrombosis in these patients occurs due to disruption of the intima and media layers, endothelial dysfunction, non-laminar blood flow and increased activation of clotting factors.^{2 5 6 10 11 16} Subsequent complications, including ACS, most likely occur due to these combined effects. In these cases, ACS is also explained by sluggish blood flow through the aneurysm itself, distal thromboembolism, reduced antegrade coronary flow and commonly associated stenosis of coronary arteries. Taken together, these factors likely contributed to the severe clinical picture seen in the present case.

In the acute setting, reducing the risk of thrombosis in CAAD may be achieved by antiplatelet therapy in combination with intravenous anticoagulants, or intravenous or intracoronary platelet glycoprotein IIb/IIIa receptor inhibitors.^{2 5 11 13 16} These measures may prove essential in reducing complications in patients, the acute management of patients with CAAD and ACS. Given that these therapies are mainly aimed at prevention of thrombogenesis and thrombus propagation, they may have limited effect in resolving existing thrombi. Further, the benefit of aspiration thrombectomy in ACS is still in question,^{16 19} and the effect of this intervention in CAAD has not been studied.

CAAD may serve as a relative contraindication to PCI. PCI poses several risks in patients with CAAD owing to difficulties in placing a wire in distal parts of the lesion, risk of vessel perforation due to thinned arterial walls, high thrombus burden, distal embolisation, no-reflow phenomenon, stent overlapping, stent malposition and stent thrombosis.^{2 9 11 14 20 21} Although PCI with covered stents has been successfully performed in patients with CAAD and ACS, this experience is based on selected isolated case reports and retrospective case series.^{14 20–22} In a recent retrospective analysis of a single centre STEMI registry, Iannopolo *et al*,¹⁴ compared the 30 day and 1 year event rates of primary PCI for STEMI in 32 patients with CAAD versus 2280 patients without CAAD. The 30 day and 1 year rates of new myocardial infarction and stent thrombosis ranged from 12.7% to 19.9% in those with CAAD as compared with 1.6%–5.7% in those without CAAD (all $P < 0.001$). Also, the 1 year rates of death or myocardial infarction after PCI was higher in those with than those without CAAD (26.2% vs 12.7%, respectively, $P = 0.026$). Of interest, the higher rate of stent thrombosis in patients with CAAD occurred irrespective of the use of bare-metal or drug-eluting stents, the concomitant use of aspiration thrombectomy or the type of antiplatelet therapy (glycoprotein IIb/IIIa inhibitors, clopidogrel or ticagrelor). This data suggest that primary PCI for STEMI due to CAAD, even when performed in centres with high level of expertise may be associated with unacceptable rates of morbidity and mortality.

Surgical revascularisation is another treatment option for CAAD and ACS.^{2 5 17 18} However, as is the case for PCI, data are limited and there are currently no standardised clinical or

angiographic selection criteria for patients to undergo such a procedure. Also, no randomised controlled trials comparing medical therapy alone, PCI and surgery have been conducted. Proposed indications for surgical correction of CAAD include patients with giant (≥ 20 mm) aneurysms at high risk for rupture, patients with associated severe obstructive coronary artery disease, patients with recurrent ACS despite adequate medical therapy or failed PCI. Surgical interventions for CAAD include resection of the aneurysm, proximal and/or distal ligation, aneurysmal thrombectomy and aneurysmectomy with or without bypass grafting.^{17 18}

Intravenous recombinant tPA, given at a dose of 100 mg over 1 hour, is the fibrinolytic agent of choice in the treatment of STEMI when PCI is unavailable.¹⁶ Major complications associated with intravenous tPA include severe bleeding (1.8%, most commonly from the gastrointestinal tract) and 1.4% for stroke (0.7% for intracerebral haemorrhage). Although data for complications of intracoronary tPA are limited, the rate of complications may be lower than those reported with intravenous doses given the lower dosing required.

The reported benefit of intracoronary thrombolysis in infants and children with Kawasaki disease and coronary aneurysms is limited.^{23 24} Similarly, the benefit of intracoronary thrombolysis in atherosclerotic CAAD and ACS has not been well described.²⁵ The remarkable favourable response to intracoronary thrombolysis in the present case suggests that this therapy may be a reasonable adjuvant or primary therapeutic alternative in adult patients with atherosclerotic CAAD, ACS and high thrombus burden.

To date, there are no randomised trials comparing single or dual antiplatelet therapy, anticoagulation therapy or combined therapy for secondary prevention of ACS in patients with CAAD who do not undergo PCI. Currently, data in this regard are derived from isolated case reports or case series that use one of the three therapies.^{5 11 12} Consequently, there is no specific recommendation regarding the type or duration of anti-thrombotic therapy in these patients. However, lifelong dual antiplatelet therapy appears to be one of the most common treatment strategies. Our patient has been treated with low-dose aspirin and clopidogrel with no recurrent ACS over a 4-year follow-up period.

Learning points

- ▶ Three-vessel coronary artery aneurysmal disease (CAAD) accounts for a small percentage of cases of CAAD (3.5%).
- ▶ Multivessel CAAD can be complicated by multivessel thrombosis and ischaemic cardiogenic shock.
- ▶ Standard treatment options for acute coronary syndrome (ACS) in patients with CAAD may not be feasible due to highly distorted coronary anatomy, high thrombus burden and high rates of complications related to percutaneous coronary intervention and surgical revascularisation.
- ▶ Intracoronary thrombolysis may be a reasonable therapeutic alternative in patients with CAAD complicated by ACS, particularly in those with high thrombus burden in whom other preferred management strategies are ineffective or are not feasible.
- ▶ Tissue-type plasminogen activator 10 mg at intervals of 10–15 min three times, as used in the present case, may be a reasonable regimen of intracoronary thrombolysis in CAAD and ACS.

Contributors LPR wrote and formatted the manuscript and conducted the literature review. The other authors listed, CR, MS and CAR, participated in the management of the patient, edited and reviewed the manuscript, and approved the case before submission.

Competing interests None declared.

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