Intravascular ultrasound-guided sealing of left anterior descending aneurysm with microcavities causing distal embolization

In this article, we describe a patient with recurring episodes of unstable angina and evidence of an ectatic proximal left anterior descending artery at coronary angiography. Intravascular ultrasound (IVUS) analysis showed multiple microaneurysms within an ulcerated plaque. Percutaneous treatment with a large-diameter bare-metal stent was undertaken; a resolution of symptoms, and angiographic and IVUS images of immediate results and at 12-month follow-up are reported.

KEYWORDS: atherosclerosis ■ coronary angiogram ■ coronary microaneurysm ■ intravascular ultrasound

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Coronary ectasia and aneurysms are considered subsequent stages of an atypical form of positive vascular remodeling in atherosclerosis [1]. Being a 'luminogram', when aneurysm or ectatic coronary lesions are detected, coronary angiography is often severely limited. Unlike angiography, intravascular ultrasound (IVUS) provides detailed and high-quality transmural images of the coronary artery *in vivo*, which include both the lumen and arterial wall [2].

Case presentation

A 72-year-old man without a personal or family history of connective tissue disorder was referred to our hospital after a 1-month history of both effort and rest angina. At 1 year prior to referral, he had suffered an antero-apical ST-elevation myocardial infarction, and primary percutaneous coronary intervention (PCI), with direct stenting of a thrombotic lesion in the mid-tract of the left anterior descending coronary artery (LAD) had been performed. After 6 months, owing to recurring effort chest pain, he had undergone another cardiac catheterization, followed by PCI to a smooth, moderately severe stenosis of the proximal tract of the left circumflex artery. After another 3 months, owing to rest angina associated to minimal troponin increase in absence of chronic renal failure, he had had another coronary angiogram that reported the presence of an ulcerated plaque with microaneurysms in the proximal tract of LAD, without significant lumen narrowing. Upon reviewing the previous angiograms, it was found that this lesion had been present since the first PCI.

In our catheter laboratory, the right coronary artery was reported as ectatic, with a nonsignificant stenosis of the distal tract, and stents on the distal segment of LAD and on the proximal circumflex were patent (Figure 1A). IVUS analysis of the LAD, thus, was undertaken, using a commercially available system (Galaxy II, Boston Scientific, MA, USA) and a high-frequency ultrasound probe (Atlantis SR Pro, 40 MHz; Boston Scientific) with an automatic pullback speed of 0.5 mm/s. Nitrates were injected before the IVUS pullback. IVUS showed an extensively calcified plaque within the ectatic tract of the LAD, with multiple cavities connected with the lumen, and an intra-plaque ulceration appearance. 'Smoke effect', indicating sluggish blood flow, was also present (Figure 2).

In consideration of the repeated episodes of unstable angina, possibly relating to multiple embolic events, a cobalt–chromium 5.0 × 20 mm stent (Skylor™; Invatec, PA, USA) was successfully delivered to the proximal LAD to seal the aneurysmatic and ulcerated lesions, after clopidogrel preloading (Figure 1B). Postprocedural IVUS control showed excellent coverage of the ulcerated plaque, with closure of the multiple cavities and absence of the smoke effect (Figure 3). No recurring episodes of chest pain were recorded, and maximal exercise stress test was negative for ischemia. The 12-month follow-up coronary angiogram documented persisting optimal sealing of the aneurysmatic proximal tract of LAD without restenosis, as confirmed by IVUS (Figure 4).

Discussion

■ Coronary ectasia & aneurysms: definition, incidence & causes

Coronary artery ectasia (CAE) is arbitrarily defined as a diffuse dilatation of the coronary lumen exceeding the diameter of normal adjacent

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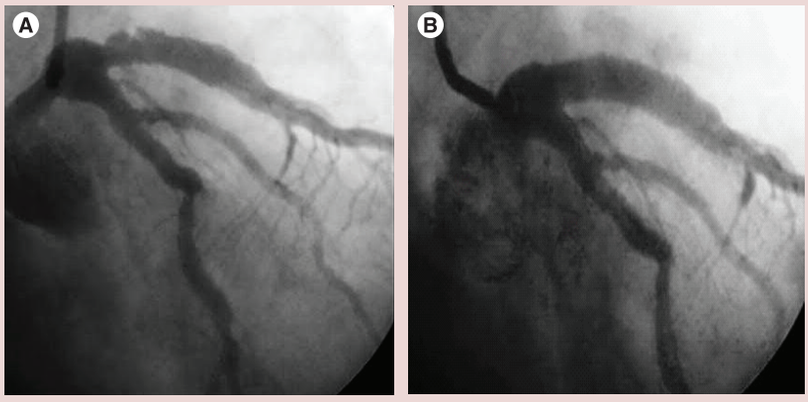

Figure 1. Coronary angiogram pre- and post-percutaneous coronary intervention. Composite image showing an angiographic right anterior oblique and caudal projection of the left coronary system before and after intervention.
(A) Diffuse left anterior descending coronary artery ectasia with microcavities.
(B) Complete sealing of ectasic tract of left anterior descending coronary artery after coronary intervention.

segments, or the diameter of the patient's largest coronary artery by 1.5-fold, and involving more than 50% of the coronary artery [1]. Coronary aneurysms are a more localized form of ectasia, involving a limited segment. A CAE classification, proposed by Markis, distinguishes a type I, corresponding to a diffuse ectasia of two or three vessels, a type II, characterized by diffuse disease in one vessel and localized disease in another vessel, a type III, when there is a diffuse ectasia of one vessel only, and a type IV, when ectasia is localized or segmental [3]. All three coronary vessels can be affected by CAE, but the right coronary artery is involved most frequently, followed by LAD and the circumflex arteries [4]. Coronary aneurysms are also frequent in saphenous vein grafts, probably resulting from late atherosclerotic degeneration of the graft [5].

Coronary artery ectasia or aneurysms are considered to be a variant of classical, occlusive coronary atherosclerosis in approximately 50–80% of cases [6] and, indeed, Ge *et al.* observed a significant atheromatos burden in the majority of CAE, with plaque areas evenly distributed between proximal and distal reference segments, as well as within the aneurysmal segment [7]. It is not clear which factors promote the development of aneurysms in the context of atheroma, but a role for chronic arterial inflammation is hypothesized [6]. Congenital coronary artery aneurysms are found in 20–30% of cases, while rarer causes of coronary aneurysms are vasculitis (10–20% of cases), such as the Kawasaki syndrome, connective tissue disorders, such as Ehlers–Danlos or Marfan syndrome (5–10% of cases), lue, mycosis and interventional coronary procedures [1]. The latter are usually associated with late development of pseudoaneurysms, which derive from intervention-associated deep-vessel dissections, and are characterized by loss of continuity of the external elastic lamina (EEL) [8].

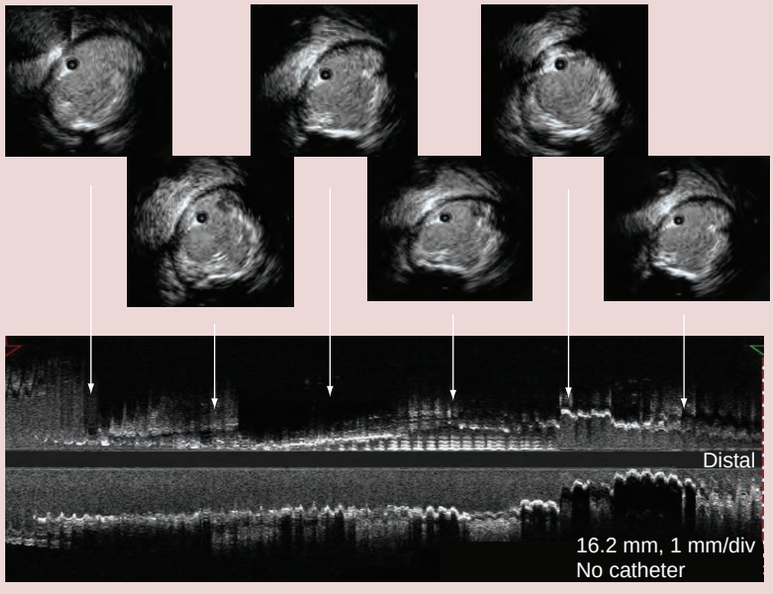

Figure 2. Baseline intravascular ultrasound analysis. Intravascular ultrasound analysis of ectasic left anterior descending coronary artery, showing multiple cavities connected with the lumen with an intraplaque ulceration (arrows: approximate correspondence of the intravascular ultrasound slices with longitudinal reconstruction).

■ Clinical presentation

The clinical presentation and the long-term cardiac complications are mostly associated with the severity of the coexisting coronary atherosclerosis, varying from asymptomatic to atypical chest pain, stable angina and even acute coronary syndromes. In a series of 3870 subjects undergoing coronary angiography, in the subgroup of patients presenting with acute coronary syndrome, coronary ectasia was associated with the culprit lesion in a third of cases [9]. In another study, including 54 patients with an angiographic diagnosis of ectasia, a major cardiac event at follow-up was documented in 37% of cases [10]. Experimental animal studies demonstrated that high-risk plaques with severe lipid infiltration and inflammation, and thin fibrous cap, can develop in ectatic coronary artery regions [11]. The aneurysmal segments might also produce a sluggish or turbulent blood flow, leading to an increased incidence of ischemic manifestations, regardless of the actual severity of the coexisting stenotic coronary lesions. Distal embolization from mural thrombus within the ectatic segment is a possible ischemic mechanism.

Rarely, pseudoaneurysms may increase in size, and rupture within the pericardium or within cardiac cavities, with catastrophic consequences [12].

■ Role of intravascular ultrasound in aneurysms diagnosis & management

The continuously expanding use of coronary angiography in the investigation of cardiovascular disease is likely to result in higher absolute numbers of patients diagnosed with CAE or aneurysms. While coronary angiography is generally the first step in the diagnosis of coronary aneurysms, providing information on their shape, size, topography and extent, and on the presence of coexistent coronary stenosis, it cannot provide any information on the artery wall. IVUS, on the other hand, is not only able to assess true lumen size at both minimal lumen area and reference points, but also provides a detailed visualization of the arterial wall, and can identify normal arterial segments adjacent to stenotic lesions, which are often falsely characterized as aneurysms by conventional angiography [2]. Crucially, IVUS can visualize the EEL, and distinguish true aneurysms from pseudoaneurysms, which is also important in terms of prognosis. Pseudoaneurysms, which are characterized by loss of vessel wall integrity (i.e., the appearance of damage to the adventitia or perivascular tissue), are thought to be at higher risk of rupture. Presumably, most postcoronary intervention aneurysms are true aneurysms when they are related to unhealed dissection, whereas most perforation-related enlargements are pseudoaneurysms. A systematic IVUS study of 77 patients with coronary dilatation (defined as a lesion lumen diameter 25% larger than reference) demonstrated that only a third of angiographically diagnosed aneurysms had the IVUS appearance of a true aneurysm (27%) or pseudoaneurysm (4%). Instead, most angiographically diagnosed aneurysms had the morphology of complex plaques (16%) or normal segments with adjacent stenosis (53%) [2]. Thus, IVUS should be considered essential in the evaluation of patient with coronary dilatation.

In addition, especially when large-sized or covered coronary stents are used (see later), IVUS can be considered extremely useful for sizing these bulky devices, and for optimizing the result, guiding aggressive postdilatation [12], as it was done in our case. This aspect is of special importance with covered stents, owing to the very high risk of restenosis and thrombosis (see later).

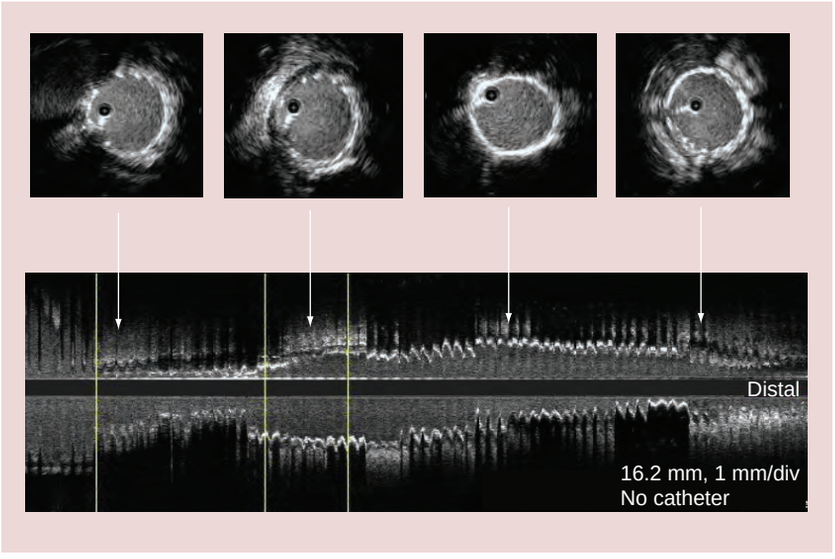

Figure 3. Intravascular ultrasound analysis postpercutaneous coronary intervention. Intravascular ultrasound analysis after stent apposition, showing an optimal covering of the ulcerated plaque with closure of the cavities (arrows: approximate correspondence of the intravascular ultrasound slices with longitudinal reconstruction).

■ Treatment

Treatment options consist of medical, surgical and percutaneous approaches, but the choice is quite controversial. Although an uneventful long-term follow-up has been reported for small coronary aneurysms – and ischemic event rates (cardiac death, myocardial infarction or unstable angina) among 121 patients with concomitant coronary aneurysms and obstructive coronary disease (defined as the presence of >70% stenosis) versus 115 coronary disease patients with no aneurysms were no different (12.4 vs 10.4%; p = not significant) [8] – larger ones (and especially pseudoaneurysms, which tends to be bigger) are at risk of rupturing [13]. However, there is a scarcity of data adequately addressing the medical management of patients. Older studies, based on the significant flow disturbances within the ectatic segments, suggested chronic anticoagulation as main therapy [14]. However, this treatment has not been tested prospectively, and could not be recommended unless supported by further studies. The coexistence of CAE with obstructive coronary lesions, and the observed incidence of acute coronary syndromes in those patients [14], have led to the generalized administration of aspirin in all patients with CAE. The role of single or double antiplatelet therapy, however, has not been yet evaluated in prospective randomized studies.

Percutaneous and/or surgical coronary revascularization can be considered in patients with coexisting obstructive lesions and/or symptoms

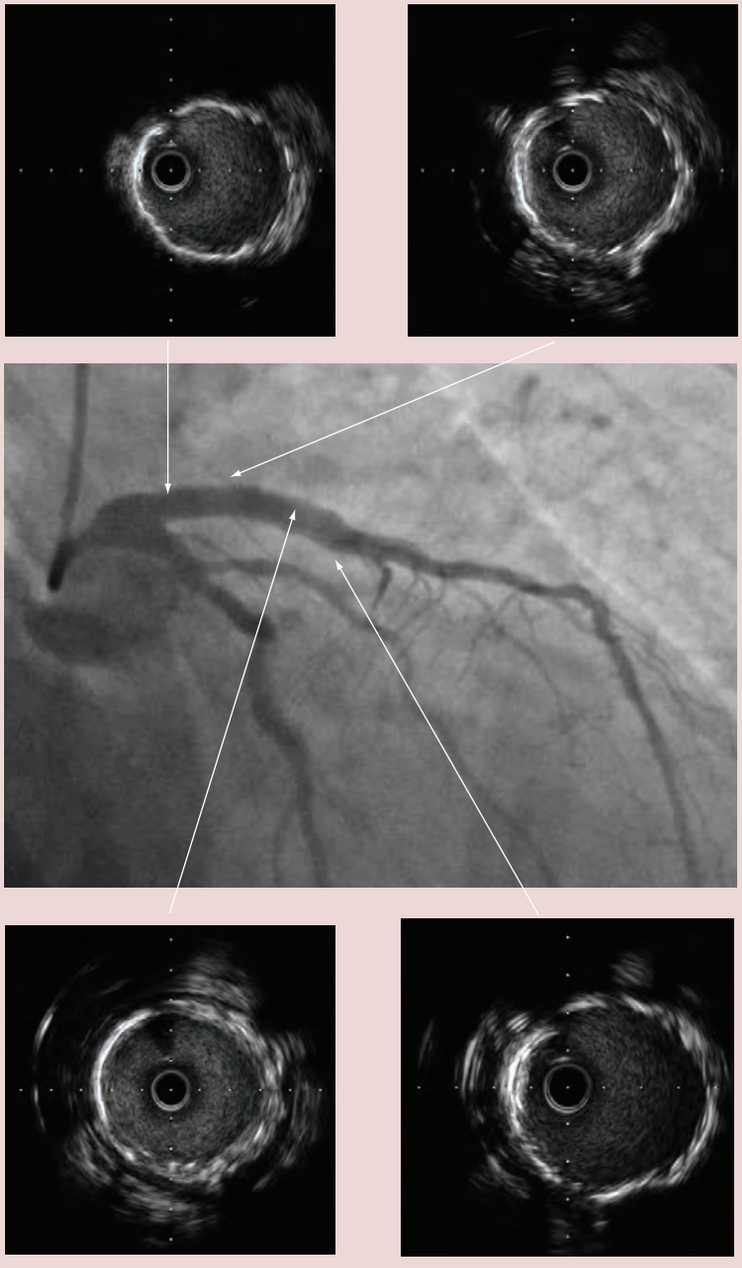

Figure 4. Follow-up coronary angiogram and intravascular ultrasound analysis. An angiographic right anterior oblique and caudal projection of the left coronary system at 12-month follow-up, showing the persistence of optimal sealing of aneuyrismatic proximal tract of left anterior descending coronary artery without restenosis. Intravascular ultrasound confirms good apposition of the stent and covering of microcavities (arrows: approximate location of the intravascular ultrasound slices).

or signs of significant ischemia despite medical therapy. The largest experience in adults has been with surgical management, which typically includes bypass grafting [14]. The main advantage of surgical approach is obviously the fact that the aneurysm can be excluded mechanically, while general anesthesia and prolonged recovery have to be taken into account.

Percutaneous treatment is a newer option, with a markedly smaller dataset, and includes stenting (using both noncovered or covered stents) and coiling. Noncovered stent implantation can often be attempted, generally in the presence of an intact arterial wall, and when a limited maximum diameter of the lesion is expected. Implantation of polytetrafluoroethylene (PTFE)-covered coronary stents, aimed at excluding and thrombosing the aneurysm, has been extensively studied [15], and seems burdened by high restenosis (31%) and thrombosis rates (5.7%) [16]. One of the largest studies retrospectively compared outcomes in a series of patients treated with either surgery (n = 18) or PTFE-covered stents (n = 24) [17]. Patients treated with stents tended to be older (60.5 vs 47.7 years old), and have smaller aneurysms (9.8 vs 35.1 mm). No deaths were reported in either group. Five of the 24 patients who received stents were found to have restenosis at follow-up angiography. Polytetrafluoroethylene-covered stents might also be able to entrap friable material, such as that present in coronary aneurysm and venous graft, thus, potentially reducing atheromatous tissue exposition to circulating inflammatory cells and limiting distal embolization. However, in the Randomized Evaluation of Polytetrafluoroethylene-Covered Stent in Saphenous Vein Grafts (RECOVERS) trial, the authors reported an increased incidence of nonfatal myocardial infarction in patients with saphenous vein graft stenosis treated with a PTFE-covered stent in comparison to a bare-metal stent, without a difference in restenosis rate [18].

Conclusion

We present the case of a patient with repeated acute coronary syndromes, which could not easily be matched with the coronary anatomy, as angiograms performed at two hospitals, including ours, did not indicate severe stenosis. He had no history of Kawasaki disease or other vasculitis, collagenosis or infective disorders; thus, an atherosclerotic cause of his aneurysm seemed very likely. Repetitive episodes of coronary microembolization, as a consequence of thrombosis superimposed to an ulcerated and aneurysmatic LAD, was the most probable cause of his recurring angina episodes, especially as at least one episode was associated with (albeit minimal) troponin T release. We elected to treat it with PCI, using a bare-metal stent, owing to the large coronary artery lumen (associated with very low risk of restenosis), and taking advantage of the neointimal proliferation associated with bare-metal stents in order to obtain better sealing

of the aneurysmatic coronary tract. This strategy proved successful in controlling symptoms, and no recurring episodes of chest pain were recorded in the next year. IVUS proved extremely useful in both diagnosis and treatment, and was also able to confirm the sealing of the microcavities at 12-month follow-up.

In our opinion, IVUS guidance should be considered mandatory when coronary aneurysms are detected and treated.

Future perspective

In consideration of the aging of the western population, and of the widespread application of coronary angiography, a diagnosis of coronary aneurysm will be very likely to increase in prevalence over the next 10 years. It is likely that the use of IVUS (and, perhaps, other intracoronary imaging techniques, such as optical coherence tomography) will increase as well, allowing a better understanding of the pathophysiology of the disturbances associated with coronary aneurysms, and may offer advice on treatment and guide a patient's percutaneous treatment. Clinicians need to be aware of the possibility of IVUS imaging in such patients, in order to refer them to centers with significant experience in this field.

Financial & competing interests disclosure

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Executive summary

- The most common cause of coronary artery aneurysms in the western world is atherosclerosis. Kawasaki disease, however, should not be underestimated, and is something to be aware of.
- Coronary angiography is generally the first step in the diagnosis of coronary aneurysms, but it is severely limited, being a 'luminogram'.
- Evaluation of coronary aneurysm by coronary angiography, generally, should be completed by intravascular ultrasound (IVUS) analysis, which is crucial to assess true lumen size and associated stenosis, and provides a detailed visualization of the arterial wall.
- Clinical presentation and the long-term cardiac complications of coronary aneurysms are related mainly to the severity of the coexisting coronary atheroma, and vary from asymptomatic to acute coronary syndromes. In some cases, however, the flow disturbances created by the aneurysm(s) can be solely responsible for the patient's symptoms.
- Treatment options consist of medical, surgical and percutaneous approaches. Percutaneous and/or surgical coronary revascularization can be considered in patients with coexisting obstructive lesions, and symptoms or signs of significant ischemia, despite medical therapy.
- In special cases, including our case study, the treatment of the coronary aneurysm alone (with no associated stenosis) may facilitate the disappearance of angina symptoms. In these cases, a microembolic origin of those symptoms is strongly suspected. However, this strategy should be considered a last resort when all other causes have been excluded.
- Optimal IVUS imaging and interpretation is a key factor in aneurysms diagnosis and treatment.

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