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CASE REPORT
Cardiovascular imaging

Giant aneurysmal degeneration after subintimal fluoropolymer-coated paclitaxel-eluting stent implantation for the superficial femoral artery occlusion: a case report

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Background Drug-eluting therapies remarkably reduce the incidence of restenosis and have revolutionized endovascular strategies for femoropopliteal lesions in patients with peripheral artery disease, nevertheless, concerns have arisen over the risk of aneurysmal degeneration after using an Eluvia polymer-based drug-eluting stent (DES).

Case summary We present a case of an 80-year-old male who developed a giant aneurysm long-term after Eluvia implantation. He noticed a pulsatile mass in his thigh without any decrease in the ankle-brachial index 27 months after subintimal DES placement for superficial femoral artery (SFA) chronic total occlusion. Duplex ultrasonography (DUS) showed a giant cavity outside the vessel and a to-and-fro flow between the cavity and the SFA at the Elvia stents overlapped in the subintimal space. Endovascular-covered stents successfully sealed the cavity and reduced the size of the aneurysm at follow-up DUS.

Discussion The aneurysmal degeneration, the so-called 'low echoic area' around the stent by ultrasound, is a relatively common finding after Eluvia DES implantation. It is thought to have little association with clinical events up to 2 years, however, the nature of this phenomenon remains unclear, and some cases present with clinical worsening. In this case, the development of a giant aneurysm could be induced by the overlapping stent not only by the local drug and polymer overdose but also by the increased mechanical force exerted against the fragile outer wall of the subintimal structure.

Keywords Case report • Aneurysm • Endovascular treatment • Subintimal angioplasty • Drug-eluting stent • Superficial femoral artery • Duplex ultrasonography

ESC curriculum 2.1 Imaging modalities • 9.3 Peripheral artery disease

Learning points

- Consider the potential risk of progressive aneurysmal degeneration that may occur after subintimal drug-eluting stent implantation.
- To understand the importance of long-term ultrasonography follow-up after subintimal stenting and the role of endovascular-covered stenting in treating the giant aneurysm.

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Introduction

Drug-eluting therapies remarkably reduce the incidence of restenosis and have revolutionized endovascular strategies for femoropopliteal lesions in patients with peripheral artery disease. The Eluvia polymer-based drug-eluting stent (DES) has shown promising clinical outcomes.[1] However, concerns have been raised regarding the risk of aneurysmal degeneration, as reported in several studies.[1–3] In this case, we present a patient who developed a giant aneurysmal degeneration over two years after the implantation of the Eluvia stent for the superficial femoral artery (SFA) chronic total occlusion (CTO). The patient was successfully treated with an endovascular-covered stent sealing.

Summary figure

Presentation	Patient presented with left-rest foot pain. Angiography showed long-segment occlusion from the left external iliac artery (EIA) to the superficial femoral artery (SFA).
Day 0	First, a bare-nitinol stent was implanted to treat the left EIA occlusion.
Day 22	Endovascular treatment (EVT) for SFA occlusion was performed due to persistent intermittent claudication. Two Elvia stents were implanted with spot stenting.
12 months	Intermittent claudication worsened, and angiography revealed the left SFA re-occluded. Re-EVT with subintimal overlapping Elvia stents.
39 months	Patient noticed a pulsatile mass in his thigh. Duplex ultrasonography (DUS) showed a giant aneurysm outside the overlapped Elvia stents. Endovascular-covered stents successfully sealed the giant aneurysm.
42 months	Follow-up DUS showed a complete disappearance of blood flow into the cavity and a reduction in aneurysm size.

Case presentation

An 80-year-old man was referred to our hospital due to left-rest foot pain. On initial examination, the vital signs and physical examination were unremarkable except for decreased left popliteal and left dorsalis pedis artery pulsations. The electrocardiogram showed a sinus rhythm with no abnormal findings, and the left ankle-brachial index (ABI) had decreased to 0.51. Three years earlier, he had undergone TURBT for bladder cancer, and two years later, he received ESD for oesophageal cancer. Regarding the risk of arteriosclerosis, he had a history of smoking for over 50 years and had been prescribed an angiotensin receptor blocker for hypertension.

Pre-procedural angiography showed total occlusion from the left external iliac artery (EIA) to the distal part of the SFA. Phased endovascular treatment (EVT) was performed for EIA occlusion and SFA occlusion. Initially, the left femoral artery was punctured, and intraplaque angioplasty was performed retrogradely using the knuckle wire technique. Subsequently, an 8 mm wide bare-nitinol stent was implanted for the left EIA occlusion, resulting in and good antegrade flow to the left deep femoral artery. Despite the treatment, his intermittent claudication persisted. As a result, EVT was performed to address the SFA occlusion (*Figure 1*). A stiff 0.014 inch guidewire was used to penetrate the proximal fibrous cap under the guidance of intravascular ultrasound (IVUS). After that, the guidewire was stepped down to a hydrophilic one but inserted into the subintimal space from the proximal to the distal part of the SFA. In an attempt to re-enter the intraluminal lumen with stiffer guidewires but failed. The OUTBACK®Elite re-entry device was then used to achieve distal intraluminal lumen re-entry. Intravascular ultrasound imaging revealed that the guidewire had passed through the subintimal space from the proximal to the distal SFA along the occluded segment. The IVUS-derived lumen diameter at the proximal and distal reference sites were 6.0 and 5.5 mm, respectively. A 5.0 mm balloon was used for pre-dilatation, followed by the deployment of two self-expanding paclitaxel-eluting stents (Eluvia) with spot stenting. One 6.0 mm × 80 mm Eluvia was deployed for the proximal lumen to the sublumen, and another 6.0 mm × 120 mm Eluvia was deployed for the sublumen to the distal lumen.

After post-dilatation with a 5.0 mm balloon, a completion angiogram showed excellent antegrade flow without any contrast staining through the lesion. The patient's symptoms improved rapidly and the claudication in his left leg significantly reduced after the SFA intervention. Dual antiplatelet therapy with aspirin and clopidogrel and lipid-lowering therapy with high-intensity statin were continued during the follow-up period. However, after 12 months of EVT, his left intermittent claudication worsened again. Angiography revealed that the left SFA was re-occluded (*Figure 2*) and re-EVT was performed using a 0.014 inch hydrophilic guidewire and a 5.5 Fr catheter to navigate the occlusive lesion. The guidewire was inserted by stepping up to a stiff guidewire and then into the distal intraluminal lumen. Pre-dilatation was performed with a 5.0 mm balloon, followed by deploying two additional 6 mm wide Eluvia stents; one was intentionally placed in the subintimal space continuously with the previously placed stents. The second stent was placed over the first stent due to persistent haziness, partially overlapping in the subintimal space. Twenty-seven months after the last Eluvia implantation, he noticed a progressive pulsatile mass in his thigh. During the follow-up periods, he remained asymptomatic without any decrease in the ABI. Duplex ultrasonography (DUS) (*Figure 3*, Supplementary material online, *Video S1*) and computed tomography angiogram (see Supplementary material online, *Video S2*) showed a huge cavity outside the vessel and a to-and-fro flow between the cavity and the SFA at the location where two stents overlapped at the subintimal space. The aneurysm size was a maximum of 41 × 32 mm in short and 73 mm in long axes. The Eluvia stents had a continuous hypoechoic halo along their entire length, which indicated aneurysmal degeneration. Covered stents were used to close the entry point, and arteriography conducted after the covered stent implantation confirmed the disappearance of the aneurysm with no endoleak (*Figure 4*, Supplementary material online, *Video S3A* and *B*). Follow-up DUS revealed that the blood flow into the cavity disappeared and the size of the aneurysm decreased 3 months after covered stent implantation (*Figure 5*, Supplementary material online, *Video S4*).

Discussion

Recently, Eluvia polymer-based DES for treating complex femoropopliteal disease showed promising 2-year results, nevertheless, concerns have arisen over the risk of aneurysmal degeneration.[1–3] This aneurysmal degeneration, the so-called 'low echoic area' around the stent by ultrasound, has also been reported as a 'halo' sign, although this finding is relatively common ranging from 16.8% to 20%, no association with clinical events has been observed up to 2 years after Eluvia DES implantation.[2,3] Despite this finding could resolve spontaneously, however, the nature of this phenomenon remains unclear. One case presented with clinical worsening caused by the occlusion of the stent,[1] and another has been a case in which aneurysms worsened more than 2 years after

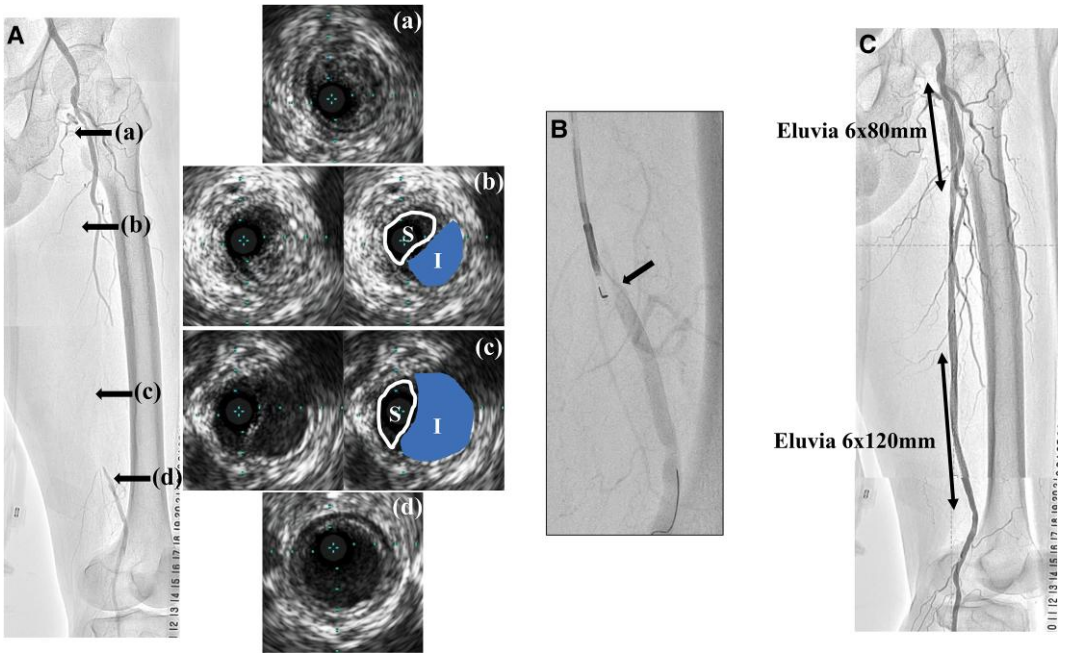

Figure 1 Angioplasty for the left SFA with spot Eluvia drug-eluting stent placement. Initial angiography showed total occlusion in the left SFA. IVUS after wire-crossing revealed that the guidewire was passed through subintimal space (*A*). Fluoroscopic image of re-entry site using OUTBACK®Elite (arrow) at the distal portion of SFA (*B*). Completion angiogram demonstrates good antegrade flow without any contrast staining through the SFA lesion (*C*). S, subintimal; I, intraluminal.

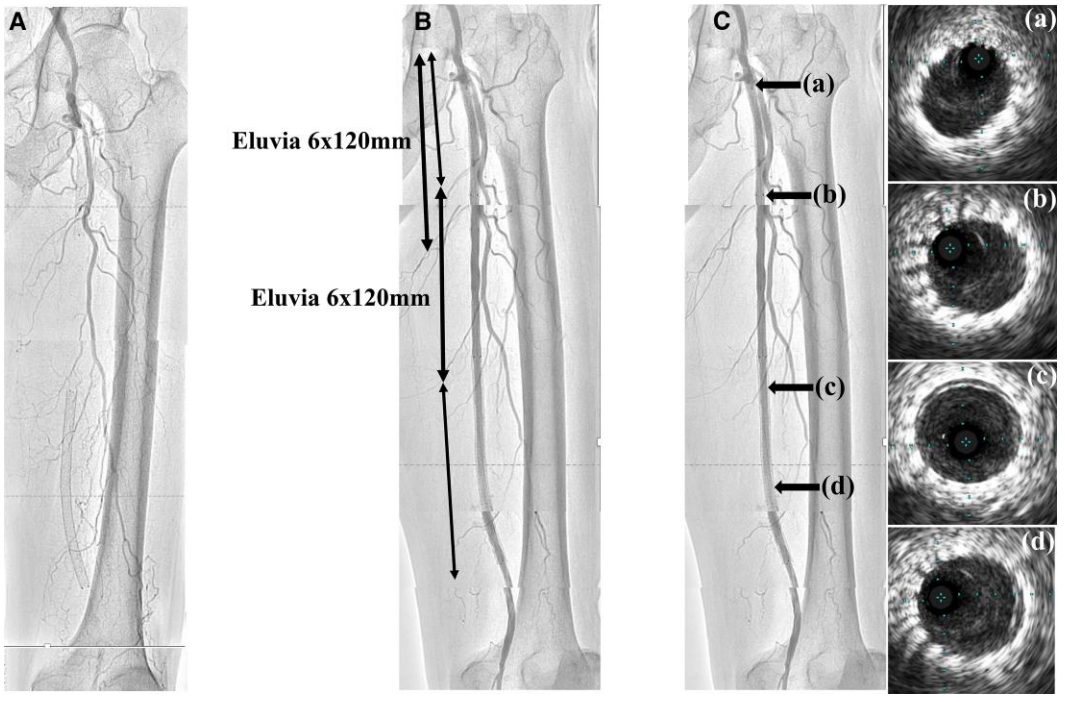

Figure 2 Re-angioplasty for the left SFA with overlapping Eluvia drug-eluting stent placement. Initial angiography showed re-occlusion in the left SFA (*A*). Two additional Eluvia stents were placed with overlapping (*B*). Completion angiogram demonstrates good antegrade flow without any contrast staining outside the stents. IVUS showed excellent stent expansion from proximal to distal SFA, with no aneurysmal changes (*C*).

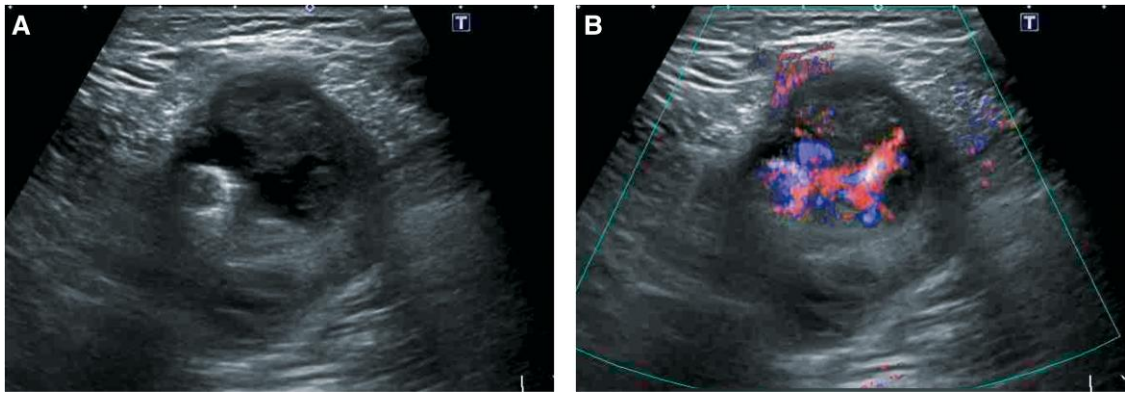

Figure 3 Duplex ultrasonography images of giant aneurysmal degeneration. Short-axis duplex images show a huge cavity outside the vessel (*A*) and a to-and-fro flow between the cavity and the SFA (*B*) at the location where two stents overlapped in the subintimal space. There was a continuous hypoechoic halo around the entire length of the Eluvia stents. See Supplementary material online, *Video S1*.

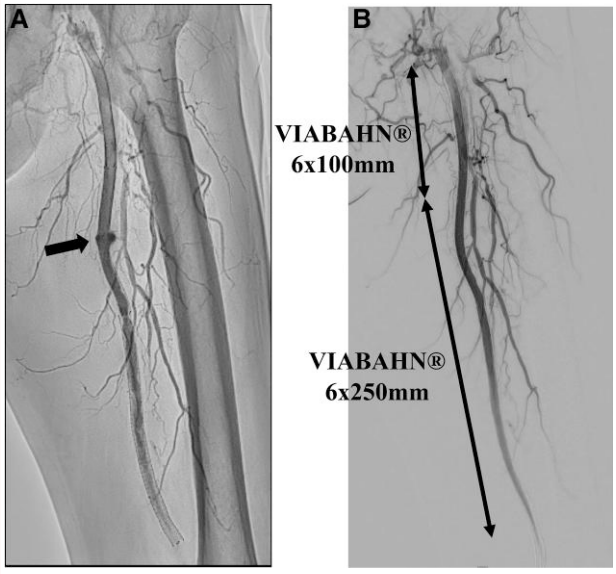

Figure 4 Deployment of covered stents across the aneurysmal segment. Arteriography showed continuous blood flow into the aneurysm (arrow) in the proximal SFA (*A*). See Supplementary material online, *Video S3A*. Final arteriography revealed that the aneurysm disappeared with no detected endoleak (*B*). See Supplementary material online, *Video S3B*.

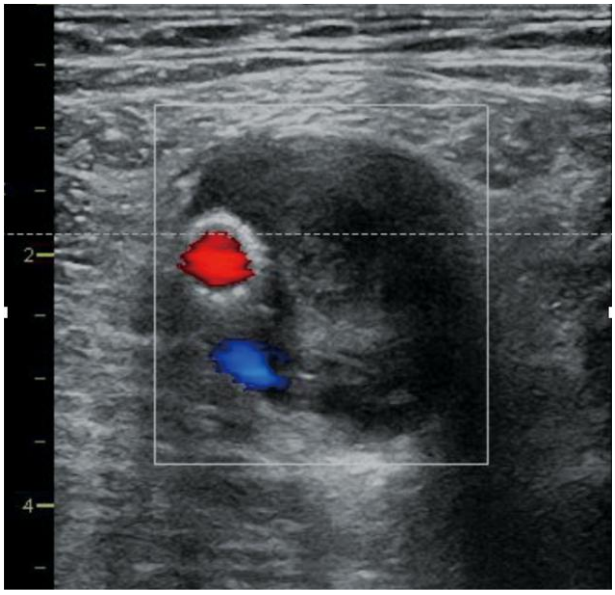

Figure 5 Follow-up duplex ultrasonography images after covered stent sealing. Short-axis duplex image revealed a complete disappearance of blood flow into the cavity and a reduction in aneurysm size. See Supplementary material online, *Video S4*.

implantation.[4] To our knowledge, this is the first report of an aneurysm developing to such a huge extent after Eluvia implantation and for a CTO lesion.

This case was indeed a long-segment CTO and surgical treatment might be an option according to the 2017 ESC Guidelines on the Diagnosis and Treatment of Peripheral Arterial Diseases.[5] However, our hospital has extensive experience in EVT, and based on the consensus with the vascular surgeon and the patient's wishes, we decided on EVT. As the mechanism of first stent occlusion was thought to be thrombus occlusion due to recoil in the subintimal space where the stent was not implanted, additional DESs (which had to be partially overlapped) were selected with the expectation of scaffolding. Several mechanisms, learned from the coronary arteries, are proposed to cause vessel wall degeneration. Delayed re-endothelialization, inflammatory changes in the medial wall, and hypersensitivity reaction to paclitaxel and polymer may result in medial disruption and aneurysm formation.[6,7] Prolonged paclitaxel exposure or the polymer coating might also contribute to the development of aneurysmal degeneration.[8]

Conversely, giant aneurysms have been reported after self-expandable nitinol stent implantation other than DES.[9,10] One of these cases demonstrates the pseudoaneurysm rupture after subintimal stent implantation

probably due to stent fracture and its mechanical stress.[9] The CAPSICUM study[3] revealed that subintimal wire passages were significantly associated with an increased risk of aneurysmal degeneration in terms of subintimal angioplasty creating and enlarging subintimal fragile space between the intimal and medial layers of the arterial wall. In our case, a localized giant aneurysm with sustained blood flow developed at the site of the overlapped Eluvia DES without apparent stent fracture. Thus, the mechanisms of a large aneurysm in our case may have been caused by the overlapping stent exerting increased mechanical force on the fragile outer wall of the subintimal structure and by a local drug and polymer overdose.

As for the treatment of aneurysms, an invasive surgical repair should be considered, although implantation of endovascular-covered stents is also an option.[11] In this case, less invasive covered stent implantation successfully sealed the giant aneurysm. Overall, the pathophysiology and nature of aneurysmal degeneration following Eluvia implantation appear to be multifactorial, and it's advisable to avoid overlapping stents for subintimal angioplasty, especially in the long-segment CTO lesions. And further in such cases, long-term follow-up ultrasonography is mandatory regardless of limb ischaemia.

Lead author biography

The author graduated MD in the Faculty of Medicine, Kochi University, Kochi, Japan in 1998 and completed a PhD at Kanazawa University's Graduate School of Medical Sciences in Japan in 2005. He is affiliated with the Department of Cardiology, Ishikawa Prefectural Central Hospital in Japan, specializing in cardiovascular interventions and intravascular imaging.

Supplementary material

Supplementary material is available at *European Heart Journal – Case Reports* online.

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Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

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