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CASE REPORT
Other

Symptomatic atherosclerotic plaque progression in a first-generation carotid stent: management and 5-year clinical and imaging outcome—a case report

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Background Restenosis in first-generation (single-layer) carotid stents (FGS) is believed to represent an exaggerated healing response of (neo)intimal hyperplasia (NIH) formation. Rather than NIH, we describe symptomatic in-FGS unstable plaque (neo)atherosclerosis mandating re-revascularization. To halt continued plaque evolution, we propose a novel treatment strategy involving a microNet-covered stent (MCS, second-generation carotid stent) to sequestrate the plaque from the vessel lumen. A durable long-term result is documented using multi-modal imaging.

Case summary With a seemingly optimal result of FGS (Precise) symptomatic carotid lesion revascularization followed by optimal medical therapy, a late (≥3 years) progressive in-stent restenosis (ISR) arose. At Year 11, crescendo ipsilateral transient ischaemic attacks occurred. Angiography showed an ulcerated tight lesion throughout stent length. Intravascular ultrasound (IVUS) virtual histology imaging revealed thin-cap fibroatheroma. Reintervention was performed under distal protection. Undersized balloon predilatation to insert a stent caused symptomatic no-flow, and aspiration catheter was used to reduce the filter load. A MCS (CGuard) was implanted and post-dilated to ensure full lumen gain; IVUS confirmed complete plaque sequestration. The optimal anatomic result remained unchanged throughout 5 years (ultrasound and computed tomography verification); this was accompanied by clinical cure.

Discussion This is the first demonstration of in-FGS (neo)atherosclerosis resolution using an MCS to sequestrate and insulate the atherosclerotic plaque. We show that ISR may be underlined by atherosclerotic plaque progression via the FGS single-layer stent struts that may show vulnerable plaque phenotype and may be associated with cerebral ischaemia. The anatomically and clinically effective exclusion of the atherosclerotic plaque by an MCS enabled lasting, optimal endovascular reconstruction and clinical cure.

Keywords Neoatherosclerosis • In-stent atherosclerosis • Single-layer stent • In-stent restenosis • Case report • MicroNet-covered stent • Plaque insulation • Carotid artery disease

ESC Curriculum 2.1 Imaging modalities • 9.3 Peripheral artery disease

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Learning points

- Incomplete atherosclerotic plaque coverage with first-generation (FGS, single-layer) stent use in carotid artery stenting may be associated with in-stent atherosclerosis progression (thus addressing carotid stenosis with FGS is a "treatment", not cure).
- Endovascular management of 'in-stent restenosis' ('ISR') resulting from (neo) atherosclerosis progression may be associated with cerebral embolism.
- Cerebral protection device use is mandatory in case of in-stent lesion.
- Predilation of in-stent material should be performed only if necessary for stent delivery.
- The in-FGS plaque growth may be non-linear and sudden-onset cerebral ischaemia may occur.
- MicroNet-covered stent (MCS) enables plaque insulation with optimal long-term outcome (MCS cure).
- The management of 'ISR' should prevent symptoms occurrence rather than being performed in reaction to cerebral damage.

Introduction

Neointimal hyperplasia is considered the fundamental mechanism of in-stent restenosis (ISR) after carotid artery stenting (CAS).[1] The process of an 'exaggerated' healing response, involving smooth muscle cell altered phenotype (neo-fibroblasts) proliferation and proteoglycan-rich extracellular matrix production, is usually benign clinically.[1] It is not entirely clear why some patients implanted with first-generation, single-layer carotid stents (FGS) develop symptoms of cerebral ischeamia with ISR despite absence of stent haemodynamic stenosis or occlusion[1–3]; cerebral embolism might play a role. Fundamental determinants of ISR are residual stenosis and stent type.[1,2] Restenosis is an important endpoint in studies comparing stenting and surgery.[3]

Employing multi-modality imaging, we describe (i) a clinically hostile atherosclerotic plaque progression in FGS, and (ii) a new management strategy involving use of a novel microNet-covered stent (MCS), to effectively sequestrate the atherosclerotic plaque with a durable anatomic and clinical result. We demonstrate that MCS may represent treatment-of-choice for FGS failure and it may protect against in-stent (neo)atherosclerosis, offering a new health delivery method.

Timeline

May 2005	Right (dominant) hemispheric ischaemic stroke in relations to severe, irregular right internal carotid artery (RICA) stenosis extending from ≈5 to ≈20 mm distal to the vessel origin
June 2005	Neuroprotected RICA stenting with a workhorse stent (*NB*. only single-layer stents available until 2014/2015)
2006–2009	Normal in-stent duplex ultrasound (DUS) velocities; eccentric, focal in-stent tissue present without progression
2010–2014	Non-linear progression of DUS velocities indicating mild-to-moderate 'in-stent restenosis' assumed to represent neointimal hyperplasia
May 2015	Significant (3.1/0.9 m/s; peak-systolic/end-diastolic velocity) 'in-stent restenosis' detected; the patient declines interventional work-up due to asymptomatic course
January 2016	Crescendo ipsilateral transient ischaemic attacks Urgent admission for interventional work-up; DUS velocities 4.7/1.8 m/s (critical lesion) Interventional procedure: Angiographic confirmation of tight in-stent irregular lesion Intravascular ultrasound (IVUS) verification; major lesion irregularities, small residual lumen Virtual histology modality demonstration of a large necrotic core in direct luminal contact MicroNet-covered stent implantation for plaque insulation and endovascular reconstruction of normal anatomy; complete exclusion of the neoatherosclerotic plaque confirmed by IVUS
2017–2021	Normal, stable DUS stent-in-stent (MCS in FGS) velocities (≈0.8/0.4 m/s)
April 2021	Evidence of normal-healed stent-in-stent (microNet-covered, second-generation in single-layer nitinol); endovascular optimal reconstruction maintained by ultrasound and computed tomography angiography: anatomic and clinical cure

Case presentation

In January 2016, a 58-year-old man with multi-level atherosclerosis on optimized medical therapy since 2005 (including aspirin, high-dose statin and angiotensin-converting enzyme inhibitor) was admitted for interventional work-up due to episodes of right hemisphere transient ischaemic attacks (crescendo TIAs; aphasia, left-arm numbness and parestesia of increasing intensity; left-handed patient, dominant hemisphere). A similar clinical picture had preceded his right (dominant) hemispheric ischaemic stroke nearly 11 years earlier. Following stroke, the patient had undergone neuroprotected right internal carotid artery (RICA) stenting using a single-layer nitinol stent (Precise, Cordis) with an optimal angiographic result. Yearly clinical and duplex ultrasound (DUS) follow-up indicated, from the post-procedural Year 3 onwards, progressive in-stent velocities that were considered mild-to-moderate until Year 10 when they reached 3.1/0.9 m/s (peak-systolic/end-diastolic). With the neurological consultation (then) of 'no contraindications to re-angioplasty' the patient, in absence of clinical symptoms recurrence, declined reintervention. However, crescendo TIAs that followed several months later led to urgent admission for vascular work-up. Admission DUS showed turbulent flow throughout

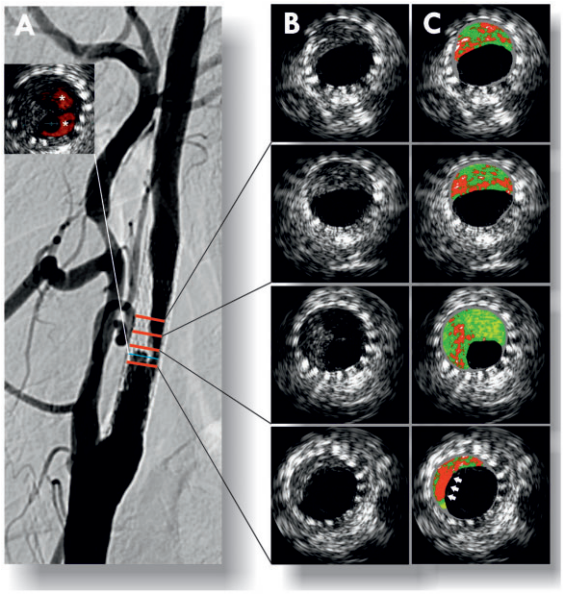
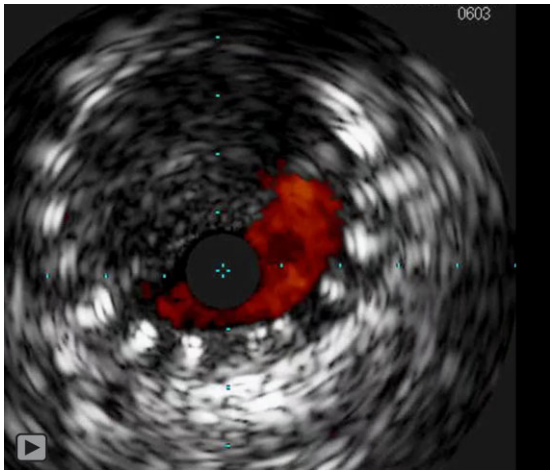


Figure 1 In-stent recurrent stenosis that developed progressively after right internal carotid artery stenting with a single-layer stent. Catheter angiography (*A*) demonstrated an ulcerated tight lesion throughout the whole stent (Precise, Cordis, 6.0 × 30 mm) length. *Top/upper-left corner*: Intravascular ultrasound (Philips/Volcano 20 MHz) showed a small residual lumen and definite ulceration and mixed-echogenicity plaque (*B*). Virtual histology intravascular ultrasound modality (*C*) revealed a thin-cap fibroatheroma rather than 'neointimal hyperplasia' typically expected with 'restenosis'. There was a large peak confluent necrotic core area (3.21 mm^2) in a direct contact with the vessel lumen,[5] indicating the minimal fibrous cap thickness below the virtual histology intravascular ultrasound resolution of ≈120 µm and consistent with a high-stroke-risk lesion morphology.[4] The segment of maximal stenosis severity was distal to the thin-cap fibroatheroma (arrows) site, consistent with a 'fire[thin-cap fibroatheroma]-and-smoke[organizing thrombotic tail]' mechanism.[16]



Video 1 Baseline intravascular ultrasound (IVUS) imaging of the in-stent lesion (Precise, implanted 11 years before). Manual pull-back was performed from the distal reference segment (right internal carotid artery, RICA) throughout the stent length to the common carotid artery. Cross-sectional frames were recorded using 'ChromaFlo' enhancement of lumen detection. Note the segment with small residual lumen and definite ulceration (representative frame in *Figure 1*). A separate run was performed to determine the in-stent mass composition (virtual histology), *cf*. *Figure 1*.

the stent with velocities of 4.7/1.8 m/s. NeuroVascular Team recommended RICA re-angioplasty (Ethics Committee-approved clinical registry with patient informed consent).

Routine femoral access was gained. Catheter angiography demonstrated an ulcerated, tight lesion throughout the stent length (*Figure 1A*). Unfractionated heparin was titrated to activated clotting time >250 s. Following distal neuroprotection (filter) placement, intravascular ultrasound (IVUS, *Figure 1B* and *Video 1*) evaluation was performed with virtual histology (VH) modality[4] to determine the in-stent lesion type (*Figure 1C*).

IVUS demonstrated minimal lumen of only 1.5 × 2.8 mm (3.5 mm^2) and in-stent plaque burden of 84.1% (cf. *Video 1*). The lesion was highly ulcerated (*cf*. *Figure 1*) suggestive of spontaneous cerebral embolism, as per the clinical presentation. Virtual histology revealed large irregular areas of necrotic core in contact with the lumen (example in *Figure 1C*; thin-cap fibroatheroma—TCFA phenotype).[4,5] Upon 3.0 × 20 mm (undersized) balloon predilation, a nearly complete flow cessation occurred due to the filter basket obstruction with plaque debris (*cf*., *Figure 2B and F*; *Videos 2* and *Video S1*). The angiographic 'no-flow' elicited ipsilateral cerebral ischaemia (clouded consciousness and aphasia, dominant hemisphere). A large (7F) aspiration catheter was used to reduce the filter load. The filter was then removed in a deliberate 'half-open' position (Supplementary material online, *Video S2*), leading to immediate flow restoration and symptom resolution. A new filter was inserted. To sequestrate the plaque, MCS[6] (CGuard 8 × 40 mm, Inspire MD, *Figure 2G and I*) was implanted (Supplementary material online, *Video S3*) with a ≈5 mm margin on each end of the Precise stent (*Figure 2G*). Consistent with our routine 'coronary-like' MCS post-dilatation strategy,[7] the stent-in-stent was optimized to the point of lack of residual stenosis (*Figure 2H* and *Video 3*). The (2nd) filter basket was empty (*Figure 2J*), indicating an effective microNet prevention of plaque embolism. The angiographic result was optimal, with the absence of any residual stenosis and full reconstruction of normal anatomy (*Figure 2K*). Post-procedural IVUS demonstrated an optimal vessel lumen and a complete exclusion of the plaque from the lumen (*Figure 2L* and Supplementary material online, *Video 3*). AngioSeal device was used for vascular access closure. The patient was discharged on continued optimal medical therapy (including aspirin, high-dose statin and angiotensin-converting enzyme inhibitor).

After re-revascularization, yearly DUS showed normal, stable stent-in-stent velocities. Five years later, DUS remains normal and there is absence of any in-stent re-restenosis on computed tomography angiography (*Figure 3*), consistent with lasting

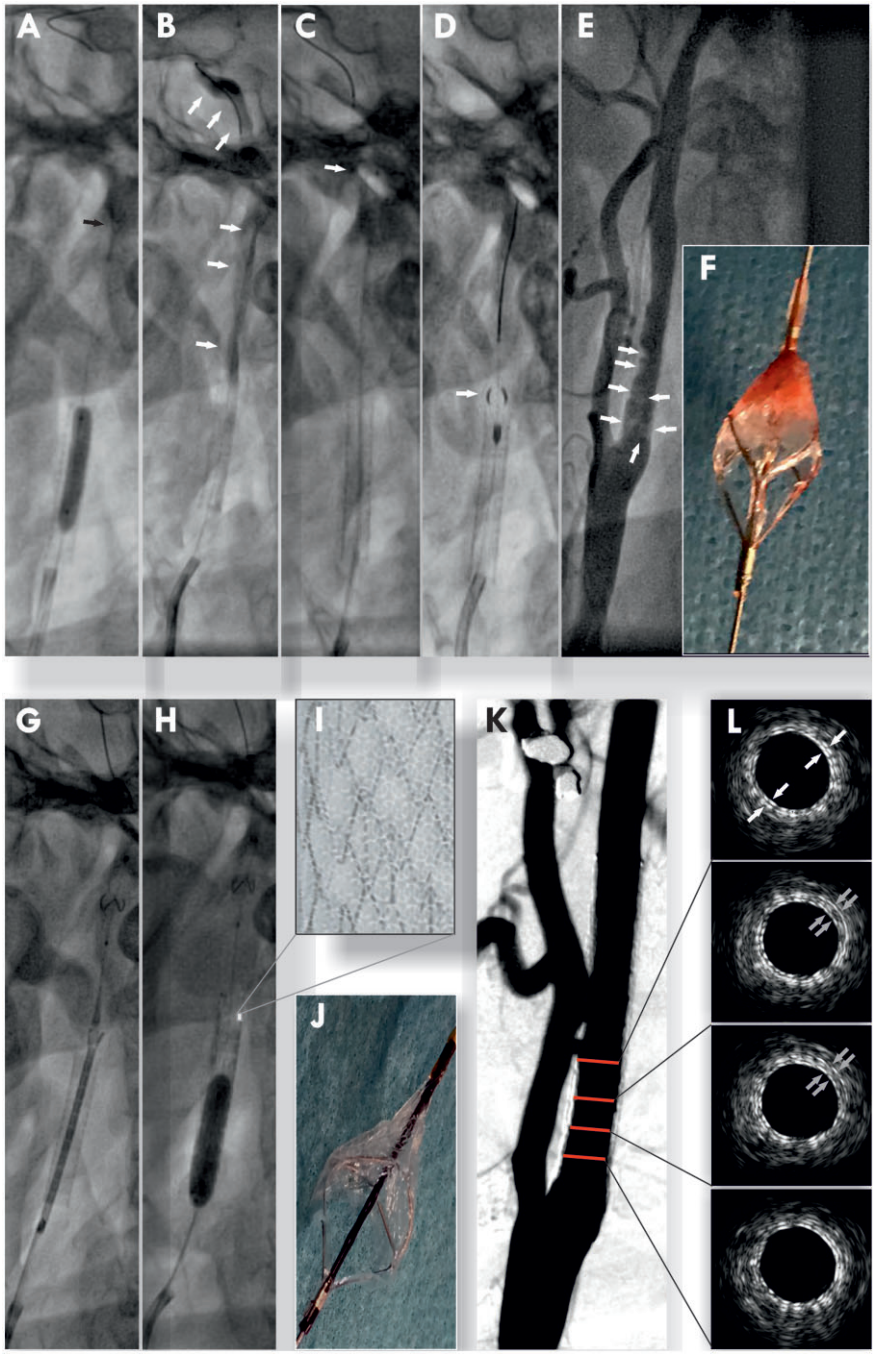
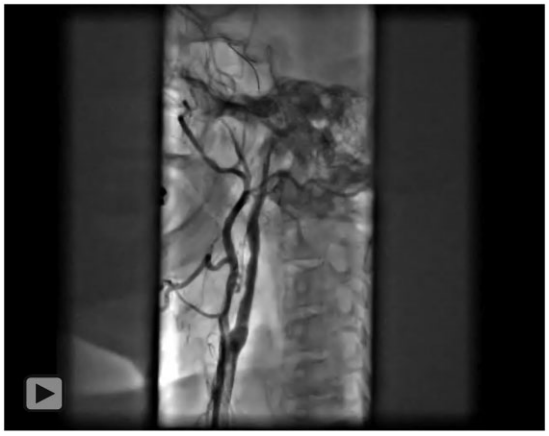
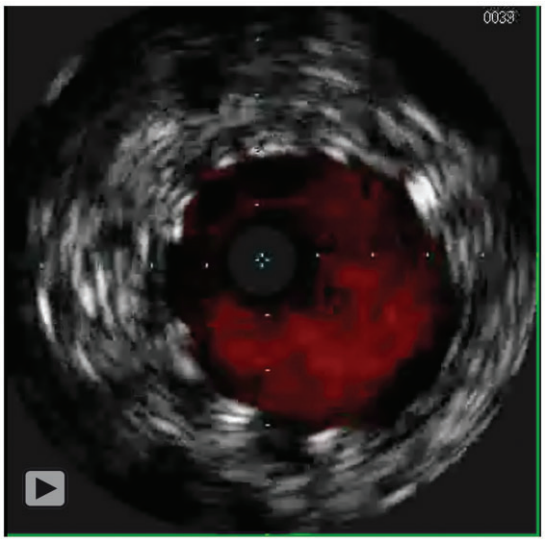


Figure 2 Neuroprotected re-angioplasty and stenting: plaque exclusion and sealing using a second-generation, microNet-covered stent. (*A*) A neuroprotected (filter basket, Emboshield, Abbott, indicated with a black arrow) predilation with an undersized (4.0 × 20 mm) semi-compliant balloon up to 12 atm is shown. This led to nearly complete contrast stagnation (*B*, arrows) due to the filter basket obstruction with atherosclerotic plaque fragments; the angiographic 'no-flow' and sudden onset of cerebral ischaemia symptoms (clouded consciousness and aphasia). A 7-F aspiration catheter (Export AP, Medtronic) was employed (*C*) to reduce the filter debris load prior to the filter removal in a deliberate half-open configuration (arrow, *D*). Flow restoration (*E*) showed protruding-to-the-lumen plaque remains (arrows); the removed filter, packed with debris, is shown in (*F*). Following another Emboshield filer deployment a self-tapering microNet-covered stent (CGuard, 8.0 × 40 mm, Inspire MD) was implanted within the atherosclerotic plaque-containing first-generation stent with ≈5 mm margins (*G*) and was sequentially post-dilated (*H*) with 5.5 × 20 mm semi-compliant balloon up to 20 atm for a routine 'coronary-like' optimal angiographic result.[7] (*I*) is a magnified image of the of the microNet-covered stent, whereas (*J*) shows an empty filter, consistent with an effective trapping of the remaining plaque (compare *E*, arrows) by the microNet-covered stent, preventing passage of the embolic material into the lumen. (*K*) A post-procedural final angiographic image consistent with absence of residual stenosis; post-procedural intravascular ultrasound imaging (*L*) confirmed a full endovascular reconstruction of the lumen and absence of any plaque prolapse double-arrows indicate the atherosclerotic plaque effectively sealed between the two stents, and excluded from the lumen.



Video 2 Intraprocedural angiography demonstrating contrast stagnation in the operated vessel due to the magnitude of filter basket load with plaque debris. Diminished blood supply to the dominant, 'isolated', hemisphere resulted in immediate neurologic symptoms of cerebral ischaemia. This imaging was performed during preparation of a thrombectomy (7F) device to reduce the filter basket load prior to filter removal (aimed to minimize the risk of embolic material loss from the basket during filter removal); for removal of the filter in "half-open" position see Video S2 in the supplementary material.



Video 3 Post-procedural IVUS imaging of the MCS-in-FGS used to reconstruct the lumen and, at the same time, eliminate the (neo)-atherosclerotic plaque. Manual pull-back was performed similar to that in Video 1. Cross-sectional frames show MCS optimal lumen reconstruction throughout the FGS length in absence of any plaque prolapse (*cf.* ref. 15). For representative still-frames images see *Figure 2*.

angiographic reconstruction of normal anatomy and an effective clinical cure.

Discussion

We report resolving in-FGS atherosclerosis progression by using a second-generation MCS employed to fully insulate the atherosclerotic plaque, enabling optimal endovascular reconstruction of normal anatomy.

To determine the tissue type developed within the FGS, we used IVUS with the VH modality due to its ability (in contrast to optical coherence tomography)[10] to penetrate throughout the plaque depth.[5] The 20 MHz IVUS resolution (≈120 μm) is sufficient to determine the carotid plaque 'thin' fibrous cap of ≤200–250 μm (that is ≈ 4-fold greater than in coronary TCFAs[4,5]). The unstable plaque phenotype (TCFA)[4,5] was consistent with episodes of cerebral ischaemia presenting as crescendo TIAs. The site of peak lumen stenosis was located distally to the TCFA segment (i.e. the site of plaque rupture with likely thrombus formation episodes, *Figure 1*; *cf.*, the 'fire-and-smoke' mechanism[5]).

It is not surprising that the FGS single-layer nitinol structure may fail to inhibit plaque growth into the lumen.[8,9] The native atherosclerotic plaque may migrate into stent horizontally through the large uncovered areas between the FGS struts.[10] Recent work shows that the presence of in-stent hypodense area following FGS CAS is a predictor of ISR.[11] Plaque prolapse with FGS may provide a mechanism for in-stent plaque progression rather than (neo)intimal hyperplasia as the restenosis mechanism. Thus the atherosclerosis progression ISR type may develop irrespective of apparently favourable FGS-CAS results and it may not be amenable to endovascular resolution other than plaque sealing.[10] In our recent cohort of 53 cases of angiographically significant (>70%) ISR, more than one in every five restenotic lesions occurred beyond 2 years after the initial procedure.[2]

Our identification of carotid FGS in-stent (neo)atherosclerosis rather than pathological neointimal hyperplasia as an ISR mechanism is consistent with emerging data on the different mechanisms of what has been so far termed 'ISR'.[9,12] 'Early' (1–3 years) restenosis may primarily represent neointimal hyperplasia typically associated with ISR, whereas 'late' FGS restenosis may be more often due to continued (or neo)atherosclerotic plaque evolution.[9] To resolve the problem of symptomatic plaque progression within FGS, we have used MCS that had not been available earlier.[12] FGS implantation for in-FGS (neo)atherosclerosis may result in (continued) plaque prolapse-related distal embolism[12] that, in contrast, is inhibited by MCS.[6,13,14]

An important consideration is whether this patient should have been treated with CAS rather than carotid endarterectomy (CEA) in the first place. On initial presentation, the patient was offered a choice of two guideline-based treatment modalities (CEA and CAS) and opted for the less invasive one (Neurovascular Team-accepted management). Long-term results of carotid revascularization with FGS CAS and CEA are equivalent while the patient quality of life may be better using the less invasive method, with the cognitive function and the risk of cranial nerve palsy as important considerations. One fundamental difference between surgical management of carotid disease (endartherectomy) and endovascular treatment (stenting) is

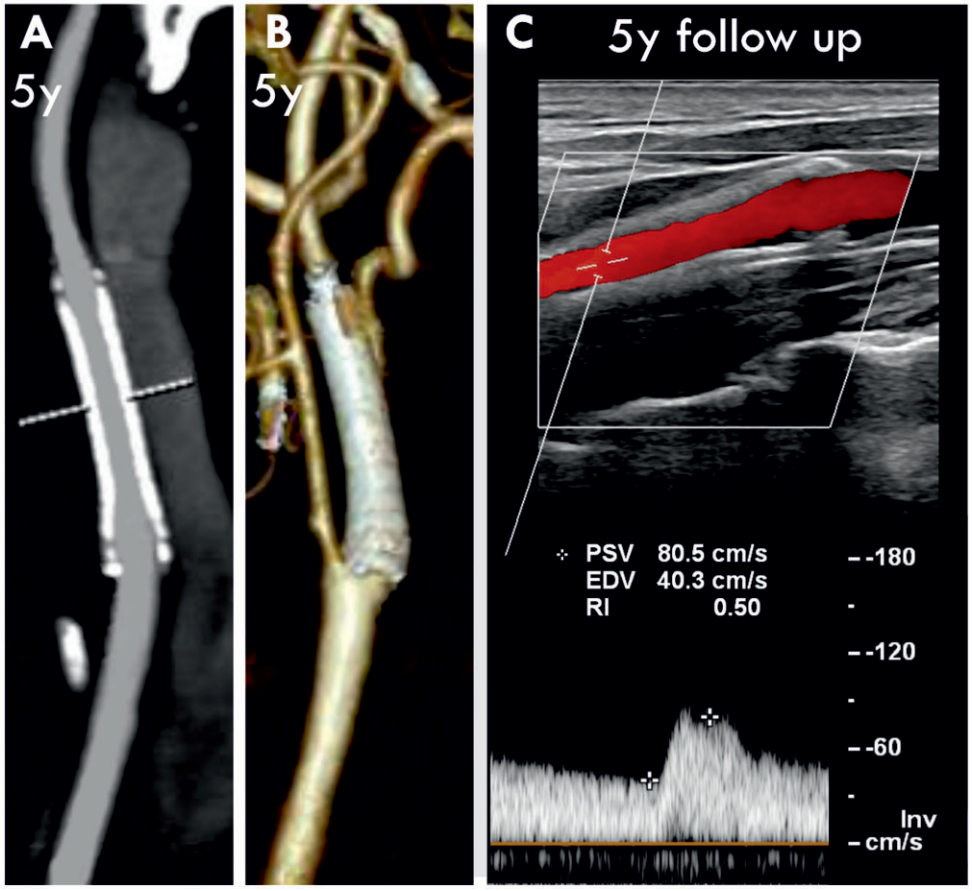


Figure 3 Long-term outcome, by computed tomography angiography and duplex ultrasound, of microNet-covered stent use for sealing of atherosclerosis symptomatic progression in a first-generation carotid stent. (*A*) (curved planar reformation) and (*B*) (3D reconstruction) are computed tomography angiography images 5 years after the microNet-covered stent use for symptomatic plaque progression in a first-generation carotid stent, demonstrating a re(re)-stenosis-free normal lumen and an effective long-term reconstruction of normal 3D anatomy with a fully patent external carotid artery. (*C*) Transcervical duplex Doppler demonstrating normal stent lumen with a laminar flow (top) and normal-artery in-stent velocities (bottom) at 5 years after reintervention for symptomatic (neo)atherosclerosis progression in FGS. The images are consistent with a durable reconstruction of normal anatomy that has been accompanied by an optimal clinical result.

that the surgeon, by removing the plaque, removes the periprocedural and post-procedural problems of the plaque. In contrast, with the first generation of carotid stents at least, the problem of the plaque may remain due to the plaque incomplete sequestration from the lumen (lack of insulation)-as determined in this report. Evidence is accumulating that the MCS may eliminate—by insulation the plaque—the periprocedural and long-term plaque-related problems.[6,13,14]

Classic (neointimal hyperplasia-based) ISR is typically treated with balloon angioplasty and it may involve drug-eluting balloon use.[2] In contrast, balloon dilatation of (neo)atherosclerotic plaque constrained intraluminal to the metallic frame of the stent may result in mobilizing plaque elements and causing distal embolism as shown in our report. A 'caged' (i.e. within stent) plaque predilation may have different consequences than predilating an unconstrained native atherosclerotic plaque (the latter may result in an overall reduction of the embolic load). The clinical scenario of our case suggests that avoiding predilation should be considered #1 strategy in case of in-stent neoatherosclerosis. We did consider primary stenting; however, IVUS showed a minimal diameter of the residual channel of only 1.5 mm (*Figure 2*), which is significantly less than the stent crossing profile of 2.03 mm. Thus, there appeared to be a significant likelihood of plaque mobilization and distal embolism with pushing the stent through a non-predilated lesion. This necessitated predilation.

With large-balloon (5.0–5.5 mm) high-pressure (up to 20 atm) MCS optimalization (that is our routine technique), we achieved a full reconstruction of the vessel lumen that would have been unlikely using FGS.[12] Thus, MCS availability may play an important part in shifting the decision-making balance in management of in-stent (neo)-atherosclerosis by using the endovascular route vs. surgical removal of the stent and vessel reconstruction. The latter is known to be a higher risk than conventional endarterectomy.

Another significant aspect of the present report is our long-term (5-year) clinical and imaging follow-up, demonstrating a lasting resolution of an important clinical and procedural challenge (*Figure 3*).

Patient perspective

Patient-expressed reflections on the disease course and management are the following: (i) 'I hoped the brain symptoms [with ISR] would not occur; I am happy that re-intervention was managed before another stroke', (ii) 'the suggestion for an earlier [prior to symptoms] re-intervention [for significant "ISR"] was right', (iii) 'avoiding, if possible, neck surgery remains important', and (iv) 'I wish the feasibility to pacify that plaque from inside [the lumen] had been there initially to get this done right the first time'.

All in all, consistent with an evolution towards patient-centred and lesion-centred management in vascular medicine,[15] this work demonstrates feasibility to achieve complete insulation of the in-stent atherosclerotic plaque with MCS, leading to an optimal long-term result of clinical cure and with angiographic (computed tomography angiography) and functional (transcervical ultrasound) lasting reconstruction of normal anatomy (*Figure 3*).

Conclusions

Incomplete atherosclerotic plaque coverage with FGS use in CAS may be associated with in-stent atherosclerosis progression. The in-FGS plaque growth may be non-linear and sudden-onset cerebral ischaemia may occur in relation to unstable plaque phenotype. Symptom-preventive rather than reactive treatment should be considered to avoid cerebral damage. Endovascular management of 'ISR' resulting from (neo)atherosclerosis progression may be associated with cerebral embolism; thus cerebral protection device use is mandatory and lesion predilation should be avoided whenever feasible.

Further larger-scale work is needed to determine the prevalence of in-stent (neo)atherosclerosis phenotype in FGS-'ISR', and the role of MCS plaque insulation in in-stent (neo)atherosclerosis prevention and management.

Lead author biography

Lukasz Tekieli graduated in Medicine from Jagiellonian University in 2002. He was granted PhD in the field of endovascular interventional medicine in 2010 for his insights into carotid artery stenting complication mechanisms. He holds specialty in cardiology and vascular medicine. He is a senior operator in cardiovascular interventions and a multidisciplinary interventional team member in John Paul II Hospital in Krakow. Presently, his main areas of interest involve cardiovascular risk stratification, intravascular imaging, and cerebrovascular interventions including stroke treatment.

Supplementary material

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

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

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.

Conflict of interest: None declared.

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References

1. Dai Z, Xu G. Restenosis after carotid artery stenting. *Vascular* 2017;**25**:576–586.
2. Tekieli L, Musialek P, Kablak-Ziembicka A, Trystula M, Przewlocki T, Legutko J et al. Severe, recurrent in-stent carotid restenosis: endovascular approach, risk factors. Results from a prospective academic registry of 2637 consecutive carotid artery stenting procedures (TARGET-CAS). *Adv Interv Cardiol* 2019;**15**:465–471.
3. Bonati LH, Gregson J, Dobson J, McCabe DJH, Nederkoorn PJ, van der Worp HB et al. Restenosis and risk of stroke after stenting or endarterectomy for symptomatic carotid stenosis in the International Carotid Stenting Study (ICSS): secondary analysis of a randomised trial. *Lancet Neurol* 2018;**17**:587–596.
4. Diethrich EB, Margolis MP, Reid DB, Burke A, Ramaiah V, Rodriguez-Lopez JA et al. Virtual histology intravascular ultrasound assessment of carotid artery disease: the carotid artery plaque virtual histology evaluation (CAPITAL) study. *J Endovasc Ther* 2007;**14**:676–686.
5. Musialek P, Dabrowski W, Mazurek A, Tekieli L, Banys RP, Rigla J et al. Quantitative virtual histology for *in vivo* evaluation of human atherosclerosis—a plaque biomechanics-based novel image analysis algorithm: validation and applications to atherosclerosis research. In: *Intravascular Ultrasound: From Acquisition to Advanced Quantitative Analysis*. Editor: Balocco S. 1st ed. Amsterdam/Oxford/Cambridge (Netherlands/UK/USA): Elsevier, 2020; p71–96.
6. Schofer J, Musiałek P, Bijuklic K, Kolvenbach R, Trystula M, Siudak Z et al. A prospective, multicenter study of a novel mesh-covered carotid stent the CGuard CARENET trial (Carotid Embolic Protection Using MicroNet). *JACC Cardiovasc Interv* 2015;**8**:1229–1234.
7. Mazurek A, Borratynska A, Malinowski KP, Brozda M, Gancarczyk U, Dluzniewska N et al. MicroNET-covered stents for embolic prevention in patients undergoing carotid revascularisation: twelve-month outcomes from the PARADIGM study. *EuroIntervention* 2020;**16**:E950–E952.
8. Musiałek P, Roubin GS. Commentary: Double-layer carotid stents: from the clinical need, through a stent-in-stent strategy, to effective plaque isolation. . . the journey toward safe carotid revascularization using the endovascular route. *J Endovasc Ther* 2019;**26**:572–577.
9. Otsuka F, Byrne RA, Yahagi K, Mori H, Ladich E, Fowler DR et al. Neoatherosclerosis: overview of histopathologic findings and implications for intravascular imaging assessment. *Eur Heart J* 2015;**36**:2147–2159.
10. Tekieli L, Pieniazek P, Musialek P, Kablak-Ziembicka A, Przewlocki T, Trystula M et al. Zotarolimus-eluting stent for the treatment of recurrent, severe carotid artery in-stent stenosis in the TARGET-CAS population. *J Endovasc Ther* 2012;**19**:316–324.
11. Yamashita K, Kokuzawa J, Kuroda T, Murase S, Kumagai M, Kaku Y. In-stent hypodense area at two weeks following carotid artery stenting predicts neointimal hyperplasia after two years. *Neuroradiol J* 2018;**31**:280–287.
12. Matsumoto H, Yako R, Masuo O, Hirayama K, Uematsu Y, Nakao N. A case of in-stent neoatherosclerosis 10 years after carotid artery stent implantation: observation with optical coherence tomography and plaque histological findings. *Neurol Med Chir (Tokyo)* 2014;**54**:139–144.
13. Karpenko A, Bugurov S, Ignatenko P, Starodubtsev V, Popova I, Malinowski K et al. Randomized controlled trial of conventional versus MicroNet-covered stent in carotid artery revascularization. *JACC Cardiovasc Interv* 2021;**14**:2377–2387.
14. Stabile E, de Donato G, Musialek P, Deloose K, Nerla R, Sirignano P et al. Use of dual-layered stents for carotid artery angioplasty: 1-year results of a patient-based meta-analysis. *JACC Cardiovasc Interv* 2020;**13**:1709–1715.
15. Podlasek A, Grunwald IQ, Musiałek P. The evolution from an "average" study patient to patient-specific characteristics to guide interventions in vascular medicine. *Pol Arch Intern Med* 2021;**131**:5–8.
16. König A, Margolis MP, Virmani R, Holmes D, Klauss V.Technology insight: in vivo coronary plaque classification by intravascular ultrasonography radiofrequency analysis. Nat Clin Pract Cardiovasc Med 2008;**5**:219–229.