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Case Report

# A case of de novo extra-stent ulceration induced by persistent plaque protrusion after carotid artery stenting with a CASPER stent for a large-volume unstable plaque ☆

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ABSTRACT

Plaque protrusion (PP) has been identified as a perioperative complication of carotid artery stenosis treated with carotid artery stenting (CAS). The CASPER stent (CS), a dual-layer micromesh stent, may be able to prevent PP. Despite using CS, de novo extra-stent ulceration induced by persistent PP is rare.

A 75-year-old male patient, whose superficial temporal artery-middle cerebral artery bypass tended to occlude, underwent CAS using a CS for symptomatic pseudo-occlusive internal carotid artery with a large-volume unstable plaque. This led to de novo extra-stent ulceration induced by persistent PP, resulting in ischemic stroke that necessitated the application of the stent-in-stent technique. There was no recurrence of cerebral infarction postoperatively at 12 months.

Here, we present, to the best of our knowledge, the first case of a patient with de novo extra-stent ulceration induced by persistent PP after CAS that led to de novo extra-stent ulceration. The inhibition of intimal formation on the stent surface caused by persistent PP was considered to be the underlying mechanism. The stent-in-stent technique is beneficial even in cases of PP accompanied by de novo extra-stent ulceration.



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## Introduction

Recently, carotid artery stenting (CAS) has been shown to be noninferior to carotid endarterectomy (CEA) for asymptomatic carotid artery stenosis, [1,2] leading to a gradual increase in the number of CAS procedures performed as an alternative to CEA. However, cerebral infarction due to perioperative plaque protrusion (PP) remains a significant concern [3,4].

The CASPER stent (CS) (TERUMO, Tustin, CA, USA), a dual-layer micromesh stent, was approved in Japan in 2020 for treating carotid artery stenosis. The CS is expected to exert a preventive effect against PP owing to its smaller cell area than that of conventional open-cell or closed-cell stents [3,5–7].

Following CAS, neointima forms on the stent surface via various immune responses, [8] subsequently stabilizing the extra-stent plaque. So far, there have been no documented reports of de novo extra-stent ulceration complications. In this report, we present a rare case of PP that persisted in a patient during and after CAS using a CS for a pseudo-occlusive internal carotid artery (ICA), leading to the development of a de novo extra-stent ulceration that necessitated stent-in-stent placement.

## Case report

The patient was a 75-year-old man who was diagnosed at 68 years of age with severe stenosis of the right carotid artery, observed using magnetic resonance imaging (MRI), which revealed an unstable plaque within the stenotic area. The intracranial ICA was poorly visualized, and single-photon emission computed tomography indicated a Stage II classification in the JET study [9]. Consequently, we assessed the risk of hyperperfusion syndrome following CAS as high. Therefore, the initial intervention was a superficial temporal artery-middle cerebral artery (STA-MCA) bypass to enhance cerebrovascular reserve, followed by a planned CAS. The patient underwent a right STA-MCA bypass (Fig. 1). Subsequently, CAS was scheduled; however, the patient declined the procedure and continued on antiplatelet therapy. He was admitted at the age of 74 years with scattered infarcts in the right cerebral hemisphere despite continuous dual antiplatelet therapy (DAPT) (clopidogrel, 75 mg; cilostazol, 200 mg). MRI indicated worsening of ICA visualization and further revealed a large-volume unstable plaque. Angiography revealed a delayed flow in the bypass and right pseudo-occlusive ICA (Fig. 2). One month following a stroke, a CS with a dual-layer micromesh stent was selected because of the unstable plaque. The CS (9 × 30 mm) was placed, and DAPT (prasugrel, 3.75 mg; cilostazol, 200 mg) was administered for a month. Intraoperative angiography and intravascular ultrasound (IVUS) revealed a convex plaque protrusion (PP) within the stent. Angiography revealed a contrast defect in the EZ filter wire (Boston Scientific, Marlborough, MA, USA), suggesting the presence of a large plaque or thrombus. Therefore, the patient received additional antiplatelet medications of aspirin (200 mg), ozagrel (80 mg), and argatroban (7.5 mg) intraoperatively only. Furthermore, percutaneous transluminal angioplasty (PTA) was performed within the stent using a Genity 4 × 30-mm balloon (Kaneka Medix, Osaka, Japan), followed by aspiration using a 6-Fr Thrombuster GR (Kaneka Medix). No additional stenting was performed because a final angiography showed improvement in the contrast-enhanced defect. The plaque adhered to the filter after retrieval (Fig. 3). Postoperative carotid echocardiography revealed no intra-stent plaques, and the patient was discharged on postoperative day 8.

The patient was prescribed triple antiplatelet therapy (TAPT) with aspirin (100 mg), prasugrel (3.75 mg), and cilostazol (200 mg) for 2 weeks postoperatively, after which the regimen was switched back to DAPT with aspirin (100 mg) and prasugrel (3.75 mg). However, 1 month postoperatively, the patient experienced a transient ischemic attack with left arm and facial paralysis for 10 minutes. Angiography revealed a mild intra-stent plaque, prompting a switch back to an intensified antithrombotic therapy with TAPT. Furthermore, the patient experienced another right cerebral infarction 4 months postoperatively. Angiography indicated an enlarged stent diameter compared to that immediately after the CAS and PP with de novo extra-stent ulceration. We thus diagnosed the patient with cerebral infarction caused by plaque dispersal from an ulcerated area. Therefore, we decided to perform CAS

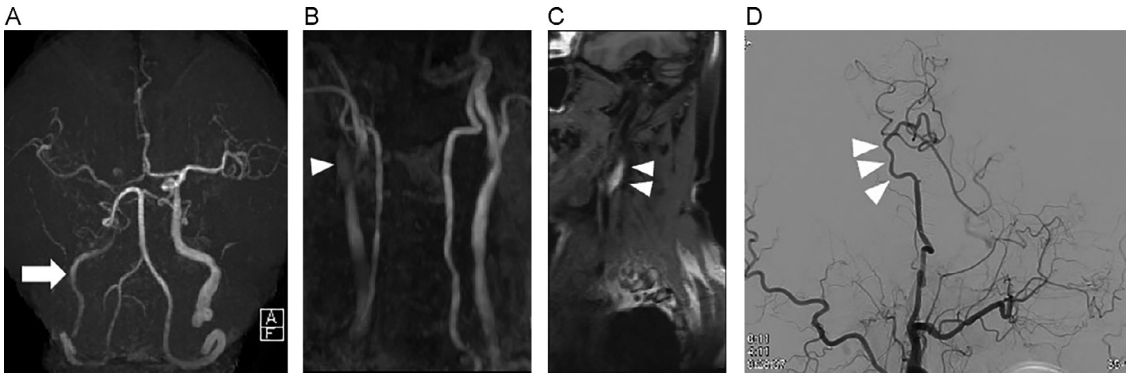


**Fig. 1 – (A, B) Magnetic resonance angiography reveals poor delineation of the internal carotid artery (arrows, arrowhead). (C) Black blood imaging demonstrates an unstable plaque (double arrowhead). (D) Angiography following bypass surgery reveals satisfactory delineation of the internal carotid artery (triple arrowhead).**

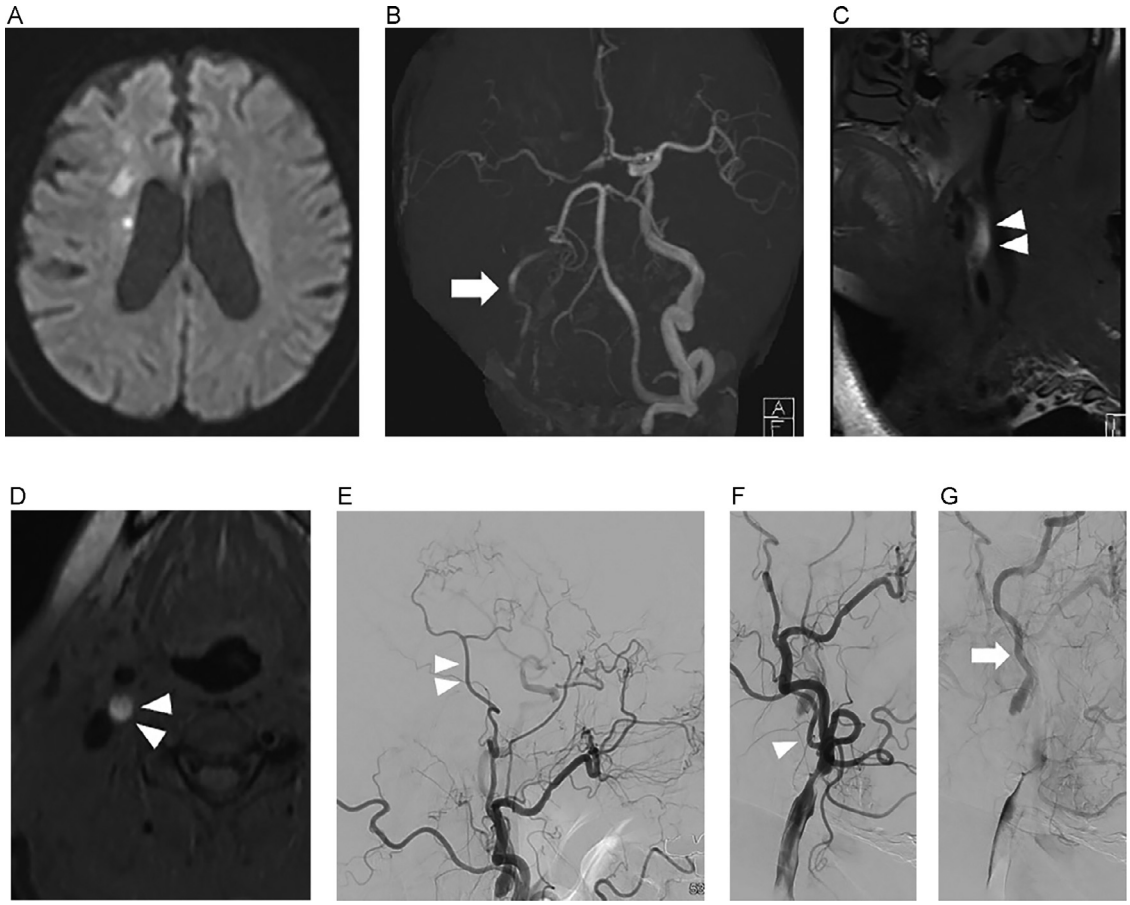


**Fig. 2 – Magnetic resonance imaging reveals (A) a new infarction in the right cerebral hemisphere and (B) further poor delineation of the intracranial carotid artery (arrow). (C, D) Black blood imaging reveals a large-volume unstable plaque (double arrowhead). Angiography illustrating (E) occlusion tendency of the bypass (double arrowhead), (F) pseudo-occlusion of the internal carotid artery (arrowhead), and (G) delayed blood flow in the intracranial internal carotid artery (arrowhead).**

using the stent-in-stent technique under TAPT. Preoperative IVUS confirmed the presence of extra-stent ulceration. The patient underwent predilation using a Genity 4.5 × 30-mm balloon (Kaneka Medix) at the site of CS implantation, followed by the placement of a PRECISE PRO RX 8 × 40-mm stent (Kaneka Medix) with crimping of the CS. Postoperative IVUS revealed no evidence of PP (Fig. 4). Upon discharge, the treatment was switched back to DAPT with aspirin (100 mg) and prasugrel (3.75 mg). No recurrence of cerebral infarction was found 12 months postoperatively.

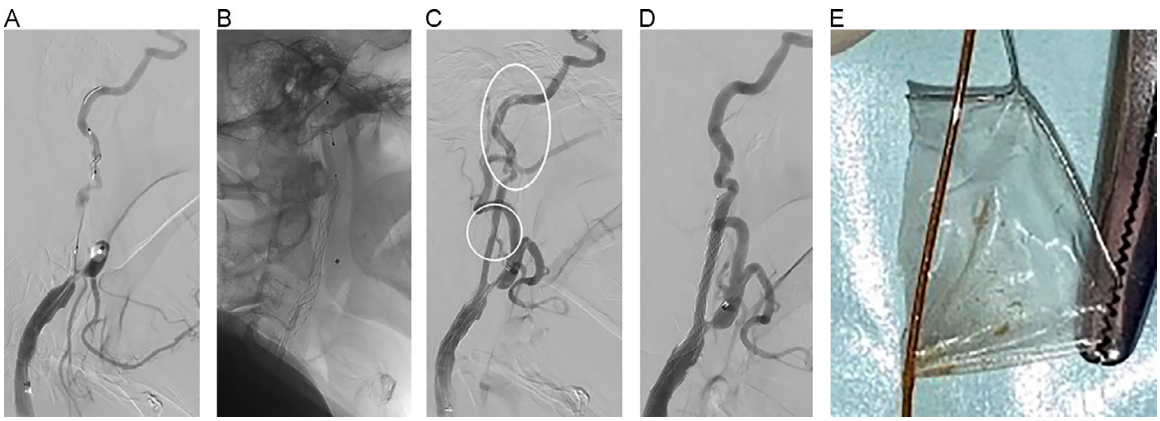


**Fig. 3 – (A) Deployment of the FilterWire EZ (B) post placement of the CASPER stent, (C) plaque protrusion on the stent surface and in contrast around the filter (circle), (D) disappearance of the plaque, and (E) plaque adherence to the filter postretrieval.**

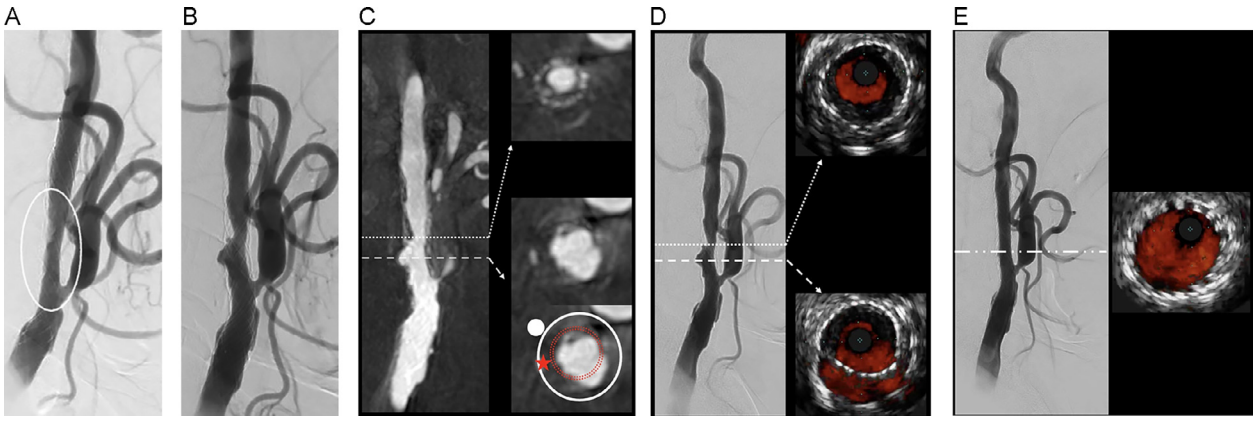


**Fig. 4 – (A) Angiography during the first postoperative month reveals plaque protrusion on the stent surface (circle). (B, C) Angiography 4 months postoperatively reveals plaque protrusion on the stent surface (top C) and extra-stent ulceration (bottom C). Vessel adventitia is indicated by a circle, and the stent is marked by a star. (D) Preoperative intravascular ultrasound reveals plaque protrusion on the stent surface (top) and an extra-stent ulceration (bottom). (E) Postoperative intravascular ultrasound reveals that blood flow no longer enters the extra-stent ulceration.**

## Discussion

### *Observations*

Here, we present a rare case of a patient with cerebral infarction caused by de novo extra-stent ulceration induced by persistent plaque protrusion following CS for pseudo-occlusive ICA characterized by a large-volume unstable plaque. The patient was treated successfully with CAS using the stent-in-stent technique.

Generally, ulceration serves a strong predictor of overall carotid plaque instability [10]. Ogata et al. [11] found that when the thin fibrous cap is breached, in can lead to the tear becoming large and the fibrous cap becoming mobile. Consequently, part of the plaque is carried away by the blood flow, resulting in ulcer formation. Ulcers can then enlarge due to shear stress. However, no reports exist on the mechanism of extra-stent ulceration following stent placement in the carotid artery. In this case, extra-stent ulceration was observed during repeated postoperative angiography. This finding revealed the disappearance of previous PP, resulting in recurrent symptomatic stroke in this patient.

PP was observed intraoperatively during the initial CAS and was initially resolved with intensified antithrombotic therapy, PTA, and aspiration. However, PP and stent expansion were noted at the 1-month postoperative angiography, with increased PP, extra-stent ulceration, and further stent expansion observed at 4-month postoperative angiography. Thus, we concluded that the patient developed a de novo extra-stent ulceration.

A previous study reported that PP in CAS occurred in 2.6% of 328 patients [3]. The risk factors for PP after CAS reportedly include unstable plaques, a large plaque volume, and long lesions. Given the etiology of PP, dual-layer micromesh stents, such as CS, are suitable for preventing PP [3,5–7]. A recent multicenter, prospective study on CS in Japan reported a perioperative ischemic stroke rate of 1.4% [12]. However, the development of PP was reported in 44% of patients treated with CS, [13] indicating that it is difficult to completely prevent PP, even when CS is used.

Neointima formation following CAS has been evaluated using angioscopy; Kondo et al. [14] reported the presence of neoendothelial tissue around the stent surface 1 month after CAS, and Fukutome et al. [15] reported that neointima was observed 2 months after CAS. Therefore, it is considered that neoendothelial tissue develops at least 1 month after CAS, followed by the formation of neointima. The stent surface is then stabilized in the second month.

In this case, stent expansion and PP could be observed from 1 month postoperatively, with further stent expansion and increased PP noted 4 months postoperatively. The mechanism is believed to be that persistent PP with stent expansion slowly occurred over 4 months, and although neoendothelial tissue development typically begins at 1 month, intimal formation on the stent surface was inhibited, and cerebral infarction resulted from the dispersion of fragile extra-stent plaque (Fig. 5). To the best of our knowledge, this is the first documented case in which de novo extra-stent ulceration induced by PP was observed over time using angiography, providing evidence of extra-stent plaque dispersal attributed to the inhibition of intimal formation on the stent surface.

Kotsugi et al. [3] recommended a stent-in-stent technique using closed cell stents until the disappearance of PP because a convex PP could cause ischemic stroke. It may be necessary to use a stent-in-stent technique to prevent PP during the initial CAS because persistent PP could occur before the formation of neo-endothelial tissue despite using a CS in the case of a large-volume unstable plaque and intraoperative PP of the convex type. In the present case, we did not use the stent-in-stent technique during initial CAS; thus, delayed PP with extra-stent ulceration was present. However, this technique could prevent ischemic complications for the second CAS, which is beneficial even in cases of PP accompanied by de novo extra-stent ulceration.

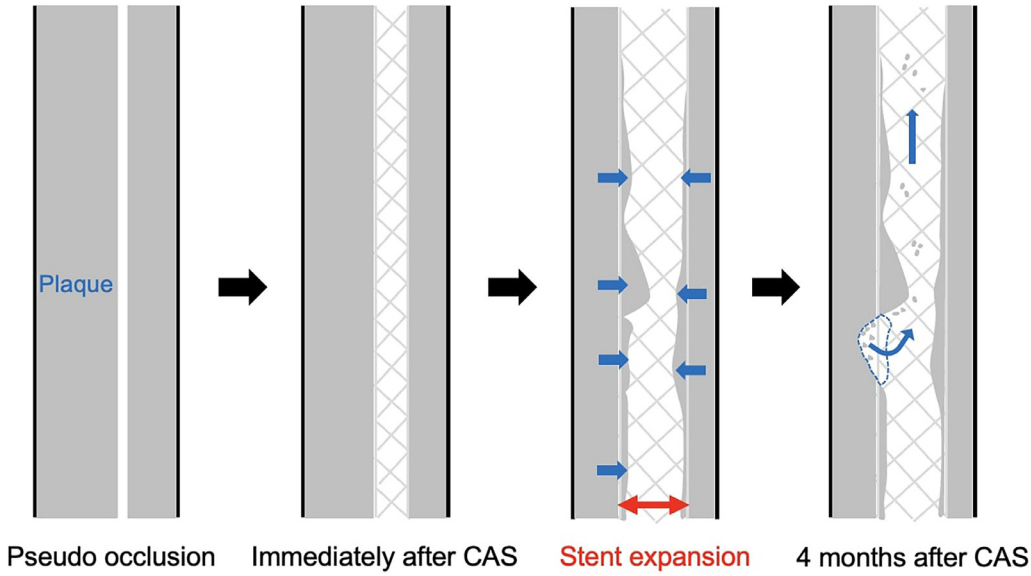


**Fig. 5 – Schematic demonstrating the formation process of de novo extra-stent ulceration.**

This was a single-case study; thus, evaluation of more cases and further research are needed to clarify the risk of PP with de novo extra-stent ulceration after CAS and the effectiveness of the stent-in-stent technique.

## Conclusion

Persistent PP can occur despite the use of a CS in cases where CAS is used for large-volume unstable plaques but rarely results in symptomatic de novo extra-stent ulcerations. The mechanism of de novo extra-stent ulceration is suggested to involve the inhibition of intimal formation on the stent surface caused by persistent PP. The stent-in-stent technique is beneficial even in cases of PP accompanied by de novo extra-stent ulceration.

## Patient consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

## Author contribution

Conception and design: Aiura, Matsuda. Acquisition of data: Aiura. Analysis and interpretation of data: Aiura, Matsuda. Drafting the article: Aiura, Matsuda. Critically revising the article: Aiura, Matsuda. Reviewed submitted version of manuscript: Aiura, Matsuda, Mizutani. Approved the final version of the manuscript on behalf of all authors: Matsuda. Statistical analysis: Aiura, Matsuda. Administrative/technical/material support: Matsuda, Matsumoto, Takano, Kubo, Irie, Hirose, Nakajyo, Sugiyama, Mizutani. Study supervision: Mizutani.

## Statement of ethics

Ethical approval was not necessary for the preparation of this article.

## Data availability statement

All data generated or analyzed during this study are included in this article and/or its online supplementary material files. Further enquiries can be directed to the corresponding author.

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