Multisystemic Cholesterol Embolization after Carotid Stenting

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ABSTRACT Cholesterol embolization (CE) is well known as a multi-systemic disorder that frequently occurs after cardiac catheterization or cardiovascular surgery. CE after carotid stenting has been rarely reported. We describe a case in which carotid stenting triggered rapid progression to CE. Carotid stenting was performed in a 73-year-old man with severe stenosis of the left carotid artery. Peri-procedural magnetic resonance images revealed multi-focal acute brain infarctions. Ten days after the procedure, the patient developed hypertension, bilateral livedo reticularis of the toes, and renal dysfunction with eosinophilia. A skin biopsy showed evidence of cholesterol emboli in the arterioles. CE after carotid stenting was diagnosed. The patient received corticosteroid therapy including pulse therapy which was effective in diminishing further deterioration of renal function. CE should be suspected in patients who present with signs of ischemia following carotid stenting. Corticosteroids may prove beneficial in cases of CE-induced renal dysfunction.

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Introduction

Cholesterol embolization (CE) is a well described phenomenon caused by peripheral embolization of small cholesterol crystals that dislodge from ruptured atherosclerotic plaques that are present in the proximal regions of vasculature. These micro-emboli are commonly associated with irreversible, multiple organ dysfunction such as renal failure, distal gangrene, with livedo reticularis and severe pain, pancreatitis, gastrointestinal bleeding, multi-focal myocardial necrosis, and/or cerebral atrophy with encephalopathy. The development of multi-focal ischemic lesions is ominous, leading to serious morbidity and mortality ranging from 37% to 90% . CE is a serious complication associated with cardiac catheterization and cardiovascular surgery, especially in patients with multiple ath-

erosclerotic risk factors. The incidence of CE detected clinically after cardiac catheterization ranges from less than 0.1% to 2%. However, CE after carotid stenting has been rarely reported. We report a case of CE after carotid stenting.

Case Report

A 73-year-old man was admitted to our hospital complaining of transient left homonymous hemianopia and right upper extremity numbness. He was an obese man (body weight = 70.7 kg and body mass index = 28.5 kg/m^2). He had a history of hypertension, diabetes mellitus, and hyperlipidemia. Diffusion-weighted magnetic resonance imaging revealed a small acute infarction in the right occipital lobe (Fig. 1a). Angiography was performed via the brachial artery, and severe stenosis of the left cervical internal carotid artery was detected (Fig. 2a). The patient's pre-procedural laboratory investigations showed the following: white blood cell count, 5,590/mm³; serum creatinine, 0.84 mg/dl; blood urea nitrogen, 12.1 mg/dl; and total cholesterol, 238 mg/dl.

Carotid stenting was performed via the femoral artery
cholesterol embolization after carotid stenting

Fig. 1. Diffusion weighted magnetic resonance images.
a: On admission, showing a minimal acute infarction in the right occipital lobe.
b: Post-treatment, showing large acute infarctions in the bilateral occipital lobe.

Fig. 2. Lateral view of left common carotid angiograms.
a: Pretreatment, showing severe stenosis of left carotid bifurcation.
b: Post-treatment, showing favorable dilatation by stent placement.

Fig. 3. Photograph of the left foot showing livedo reticularis.

on the second hospital day. Post-procedural angiography showed favorable dilatation of the stenosis (Fig. 2b), and there was no distal occlusion due to embolism. However, the patient complained of serious narrowing of his visual field postoperatively, and post-procedural diffusion-weighted magnetic resonance image revealed new ischemic changes in the occipital lobes bilaterally (Fig. 1b).

Ten days after the procedure, the patient developed hypertension and bilateral livedo reticularis in his toes (Fig. 3). Laboratory investigations revealed the following: serum creatinine level, 1.29 mg/dl; blood urea nitrogen, 15.9 mg/dl; C-reactive protein, 4.61 mg/dl; aspartate transaminase, 60 U/l; alanine transaminase, 118 U/l; and creatinine phosphokinase, 32 U/l. Eosinophilia (10% of a white blood cell count of 7,860/mm$^3$) was also observed. Twenty days after the initial procedure, serum creatinine and blood urea nitrogen levels gradually increased to 4.29 mg/dl and 65.4 mg/dl, respectively. Postoperative trans-esophageal
Fig. 4. Postoperative transesophageal echocardiography (TEE) demonstrated an irregular shaped atheromatous plaque at the descending aorta (arrow heads).

Fig. 5. Skin biopsy of the left foot reveals cholesterol clefts and thickened intima in the small arteries (Hematoxylin and eosin stain; original magnification, ×400).

Echocardiography (TEE) on twenty one days after procedure showed an irregular shaped atheromatous plaque (Fig. 4) at the descending aorta, with evidence that this plaque may have fractured. On sixteen days after the initial procedure, a skin biopsy specimen of the left toe demonstrated cholesterol emboli in the arterioles (Fig. 5). Laboratory data along with findings of the skin biopsy indicated CE as the etiology for the renal dysfunction. Eighteen days after the initial procedure, steroid pulse therapy (methylprednisolone 1000 mg/day for three days) was initiated, which led to recovery of renal function, as evidenced by a decrease in the serum creatinine levels to 2.9 mg/dl. During the steroid pulse therapy, a continuous intravenous injection of insulin was administered to control the blood glucose levels. To date, further diabetic complications including retinopathy, hypertension, and hyperlipidemia have not occurred. Although the dose of steroid was rapidly tapered off, the patient’s renal function was not normalized but sustained without further deterioration to renal failure (Fig. 6).

Discussion

CE is a multi-systemic disorder that is often observed in patients with severe atherosclerosis after anti-coagulation therapy and various types of arterial operations. Cholesterol crystals are dislodged from atherosclerotic lesions of the aorta or large arteries and shower emboli, predominantly into smaller vessels. Embolized crystals induce an inflammatory response and lead to permanent organizing occlusion of the artery. As a result, CE causes many complications including renal insufficiency, hypertension, ischemia of the intestinal tract, and peripheral vascular insufficiency, with claudication, digital pain, livedo reticularis, or gangrene. Although CE can occur spontaneously, there are usually several triggering factors including vascular injury, angiographic procedure (particularly those using a trans-femoral approach) anti-coagulation therapy and thrombolysis. The interval from the inciting event to the onset of CE can be anywhere from a few days to several months. Risk factors for CE
include old age (defined as 60 years or over), male sex, hypertension, diabetes mellitus, and smoking. Characteristic laboratory findings include eosinophilia, high amylase levels, abnormal liver functions, high CPK, an increased level of C-reactive protein, and a high erythrocyte sedimentation rate. The criteria for the diagnosis of CE have not yet been established; however, the clinical diagnosis of CE is made by assessing whether there are substantive risk factors, suggestive physical findings, and supporting laboratory results. When present, positive histopathological findings are used for unequivocal confirmation of established CE.

In the present case, our patient had multiple risk factors including old age, male sex, hypertension, diabetes mellitus, and hyperlipidemia. Clinical symptoms such as renal dysfunction and livedo reticularis along with supporting laboratory findings including eosinophilia and increased levels of C-reactive protein developed following carotid stenting. Skin biopsy revealed cholesterol emboli in the small-sized arteries and TEE revealed an irregularly shaped atheromatous plaque in the descending aorta. These findings were completely compatible with the criteria for diagnosis of CE. The cerebral infarction observed on admission may have been a possible symptom of CE in this patient. There is the possibility that CE developed spontaneously; however, because cholesterol crystals were dislodged from the plaque, it is hypothesized that the carotid stenting triggered the rapid progression of CE in our patient. Additionally, the rapid progression of CE might have been caused by the carotid stenting rather than the angiography of the previous day, because CE has been reportedly induced by catheterization via femoral artery.

The incidence of CE detected clinically after cardiac catheterization is relatively low, ranging from less than 0.1% to 2%. Drost and Kealy reported the incidence of CE as low as 0.15% and 0.79%, respectively, following diagnostic procedures. The incidence of CE after carotid stenting has been rarely reported. Given the increased use of carotid stenting, however, the sequelae of CE may become more frequent and further investigations into the relationship between carotid stenting and CE are warranted.

To date, the optimum treatment of CE has not been established. In addition to dialysis in cases of renal failure, plasma exchange, corticosteroids, statins, and prostaglandins have been reported to be effective in the management of CE. However, the efficacy of steroid therapy is controversial. Several reports showed that some patients with CE benefited from low-dose corticosteroid therapy. In recent case reports, the daily dose of prednisolone var-

![Diagram](image-url)
ied, typically between 0.5 and 1.0 mg/kg\textsuperscript{2,10-13}. Generally, steroid pulse therapy has not been recommended due to its serious side effects, especially in diabetics. However, some case reports describe favorable effects of high-dose corticosteroids and steroid pulse therapy in limiting CE-induced renal deterioration\textsuperscript{3,10-12,14-16}.

The rational of using corticosteroids is to modulate the induction of immunologic reactions after cholesterol crystals of plaques lodge in distal arterioles and capillaries. The crystals induce infiltration of mononuclear cells and formation of giant cells, followed by engulfment of crystals, and infiltration of neutrophils and eosinophils. Subsequently, endothelial proliferation, intravascular fibrosis, and intravascular thrombi formation occur. The involvement of immunologic mechanisms is also supported by clinical observation such as frequent appearance of eosinophilia and reports that showed the release of interleukin-5 by activated T cells in a patient with CE. Involvement of the complement activation has also been suggested\textsuperscript{21}.

**Conclusion**

CE after carotid stenting has been rarely reported. CE should be suspected in patients who present with signs of ischemia after carotid stenting. Further investigation into the incidence and prognosis of CE after carotid stenting is necessary. Corticosteroids may be beneficial to control CE-induced renal dysfunction.

**References**

症例報告

頭動脈ステント留置術後に急速増悪した全身性コレステリン塞栓症の1例

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要旨 コレステリン塞栓症は冠動脈撮影や血管手術後に生じる重篤な全身合併症の一つであるが頭動脈ステント留置術後のコレステリン塞栓症に関してはほとんど報告がない。今回、頭動脈ステント留置後に急速な進展を呈したコレステリン塞栓症の1例を報告する。症例は73歳の男性、左頸部内頭動脈高度狭窄に対し、ステント留置術を施行した。術後10日目ころより、高血圧の増悪・下肢網状皮斑・好酸球上昇を伴う急速な腎機能低下が出現。皮膚生検にて皮膚の小動脈にコレステリン結晶の塞栓を認め、頭動脈ステント留置術により急速に進展したコレステリン塞栓症と診断した。パルス療法を含めたステロイド投与を行うことにより、腎機能障害はその後増悪することなく経過した。ステント留置後などの脳血管内手術後にもコレステリン塞栓症が起こりうるため、術後に全身の虚血症状についても十分注意すること、及びステント留置後のコレステリン塞栓症に関してはその予後や発現頻度に関し更なる研究が必要である。さらに、コレステリン塞栓症における腎機能障害の改善にステロイド加療は有効であると考えられた。
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キーワード：コレステロール塞栓、血管内治療、副腎皮質ステロイド、腎機能障害、多臓器機能不全

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