A THESIS FOR THE DEGREE OF MASTER OF SCIENCE

Cerebral vasoconstriction after carotid artery stenting associated with isolated cerebral circulation

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뇌혈류 고립과 경동맥 스텐트 삽입술 후 발생한 뇌혈관 수축과의 연관성

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NOMENCLATURE

CAS : Carotid Artery Stenting

NTO : Near Total Occlusion

ICA : Internal Carotid Artery

MRA : Magnetic Resonance Angiography

MCA : Middle Cerebral Artery

NIHSS : National Institutes of Health Stroke Scale

mRS : modified Rankin Scale

CT : Computed Tomography

CBF : Cerebral Blood Flow

CPP : Cerebral Perfusion Pressure

MAP : Mean Arterial Pressure (MAP)

TCD : TransCranial Doppler

HPS : HyperPerfusion Syndrome

CTA : Computed Tomography Angiography

초록

배경 및 목적

경동맥 스텐트 삽입술은 경동맥 협착증의 치료로 널리 행해지고 있다. 경동맥 스텐트 삽입술 후 많은 변화가 일어날 수 있는데, 이 중 하나가 뇌혈관 수축이다. 이러한 뇌혈관 수축은 뇌졸중과 같은 시술 후 합병증과 연관이 있기 때문에 유의 깊게 관찰하여야 한다. 이 연구에서는 내경동맥이 거의 막힌 환자에서 경동맥 스텐트 삽입술 직후의 뇌혈관 조영술을 통해 뇌혈관 수축을 관찰하고자 하였다.

대상과 방법

2008년 12월부터 2019년 5월까지 스텐트 삽입술을 시행한 314명 환자들의 임상자료와 영상자료를 후향적으로 분석하였다. 이 중 30명에서 내경동맥이 거의 막혀 있었다. 두 명의 영상의학과 전문의가 시술 전 자기공명 혈관영상을 통해 뇌혈류의 고립이 있는지와 내경동맥 스텐트 삽입술 직후의 뇌혈관 조영술을 통해 뇌혈관 수축이 있는지를 판단하였다. 뇌혈류의 고립은 자기공명 혈관영상에서 내경동맥과 중간대뇌동맥의 신호 강도가 감소되어 있으면서, 동측 앞대뇌동맥의 교통이전부분과 뒤교통동맥이 보이지 않는 경우로 정의하였고, 뇌혈관 수축은 시술 전, 후의 뇌혈관 조영술 결과를 비교하여

시술 전보다 시술 후에 뇌혈관이 좁아진 경우로 정의하였다.

결과

내경동맥의 근접 폐색이 있는 30명의 임상자료와 영상자료를 분석하였고, 남성이 27명(90.0%)이었으며, 환자들의 평균 연령은 69.0세였다. 이 중, 11명(36.7%)에서 두개내 뇌혈관 수축을 보였고, 나머지 19명은 뇌혈관 수축을 보이지 않았다. 두 군 사이에 동반질환, 경동맥 협착으로 인한 증상 유무, 복용하던 항혈소판제의 종류, 평균 시술 시간, 초기 NIHSS (National Institutes of Health Stroke Scale) 점수와 mRS (modified Rankin Scale) 점수에 있어 통계적으로 유의한 차이는 보이지 않았다. 그러나 뇌혈관 수축은 뇌혈류 고립이 있는 환자에서 통계적으로 유의하게 높은 빈도로 발생하였다. (뇌혈류 고립이 있는 군 64.2%, 뇌혈관 고립이 없는 군 12.5%; $p<0.05$) 뇌혈관 수축이 발생한 11명의 환자에서 두통이나 다른 신경학적 증상은 없었다.

결론

내경동맥이 거의 막힌 환자에서 경동맥 스텐트 삽입술 이후 뇌혈관 수축은 약 1/3의 환자에서 발생하며, 뇌혈류의 고립이 있는 환자에서 유의하게 높은 빈도로 발생한다. 이러한 뇌혈관 수축의 임상적 영향을 평가하기 위해 향후 대규모 연구가 필요하다.

Abstract

Background and Purpose

Carotid artery stenting (CAS) is widely performed for treatment of carotid stenosis. Many changes can occur after carotid artery stenting, and one of which is cerebral vasoconstriction. Cerebral vasoconstriction should be observed carefully, because it is associated with post-procedural complication such as stroke. The purpose of this study is to present our observation on cerebral vasoconstriction in the ipsilateral anterior circulation during immediate post-stenting angiography in patients with near total occlusion (NTO) of proximal internal carotid artery. (ICA)

Materials and Methods

We retrospectively reviewed 314 patients' data from December 2008 to May 2019. There were 30 patients with carotid NTO. Two neuroradiologists reviewed time-of-flight (TOF) magnetic resonance angiography (MRA) to evaluate the presence of isolated circulation, and reviewed the final cerebral angiographic finding of CAS to evaluate the presence of cerebral vasoconstriction. Isolated circulation was defined as 1) signal intensity drop of the ipsilateral middle cerebral artery/ICA territory and 2) absence of ipsilateral A1 segment and posterior communicating artery when evaluated on TOF MRA. Cerebral vasoconstriction was defined as the narrowing of cerebral vessels on post-stenting angiography compared to pre-stenting angiography.

Results

A total of 30 patients with NTO were analyzed. 11 patients showed vasoconstriction in the treated territory, and 19 patients did not show significant vasoconstriction after CAS. There were no statistically significant differences in comorbidity, frequency of symptomatic lesions, antiplatelet medication, mean procedure time, and initial National Institutes of Health Stroke Scale and baseline

modified Rankin Scale scores between the two groups. However, cerebral vasoconstriction is more likely to happen in patients with isolated territory from the contralateral anterior and posterior circulation (64.2% in the isolated territory group and 12.5% in the not-isolated territory group; $p<0.05$). No headache or neurologic deficit was noted in all 11 patients with cerebral vasoconstriction.

Conclusions

Cerebral vasoconstriction after CAS occurs in about one third of patients with NTO of proximal ICA, and it occurs more frequently in patients with isolation of the cerebral circulation. A large-scale study is necessary to assess the clinical implication of cerebral vasoconstriction after CAS.

CHAPTER 1

INTRODUCTION

Carotid artery stenting (CAS) and carotid endarterectomy are widely performed for the treatment of carotid stenosis to improve cerebral perfusion and lower stroke risk. Not only morphology of the stenotic vessel but also hemodynamics of cerebral perfusion alters after carotid revascularization. Some changes are immediately notable based on post-procedural angiographic finding, among which is cerebral vasoconstriction. Cerebral vasoconstriction should be observed carefully, because it is associated with post-procedural complication such as stroke.

Cerebral vasoconstriction cases after carotid endarterectomy have been often reported.[1-6] In contrast, cerebral vasoconstriction cases after CAS have been rarely reported.[7-12]

The purpose of this retrospective study is to present our observation on cerebral vasoconstriction in the ipsilateral anterior circulation during immediate post-stenting angiography in patients with near total occlusion (NTO) of the proximal internal carotid artery (ICA).

CHAPTER 2

MATERIALS AND METHODS

2.1 Design and patient selection

We retrospectively reviewed patients' data from December 2008 to May 2019. A total of 389 stenting procedures (in 314 patients) were performed in our hospital. Of those, there were 319 carotid stenting procedures (in 244 patients) for carotid atherosclerotic stenosis and 30 patients with carotid NTO. (Fig. 1) NTO was defined as ipsilateral distal ICA less than the contralateral distal ICA or ipsilateral distal ICA equal to or less than the ipsilateral external carotid artery.[13]

Two interventional neuroradiologists reviewed the final cerebral angiographic finding of CAS to evaluate the presence of cerebral vasoconstriction. Cerebral vasoconstriction was defined as the narrowing of cerebral vessels on post-stenting angiography compared to pre-stenting angiography.

Moreover, pre-procedural digital subtraction angiography or magnetic resonance angiography (MRA) images were reviewed to determine if the vascular territory was isolated from the contralateral anterior or posterior circulation. Isolated circulation was defined as 1) signal intensity drop of the ipsilateral middle cerebral artery (MCA)/ICA territory and 2) absence of ipsilateral A1 segment and posterior communicating artery when evaluated on time-of-flight MRA. (Fig. 2)

In 26 of the 30 cases (86.6%), the results of independent review from the two radiologists showed complete agreement and the discrepancies in four patients were resolved after consensus meeting of the two neuroradiologists.

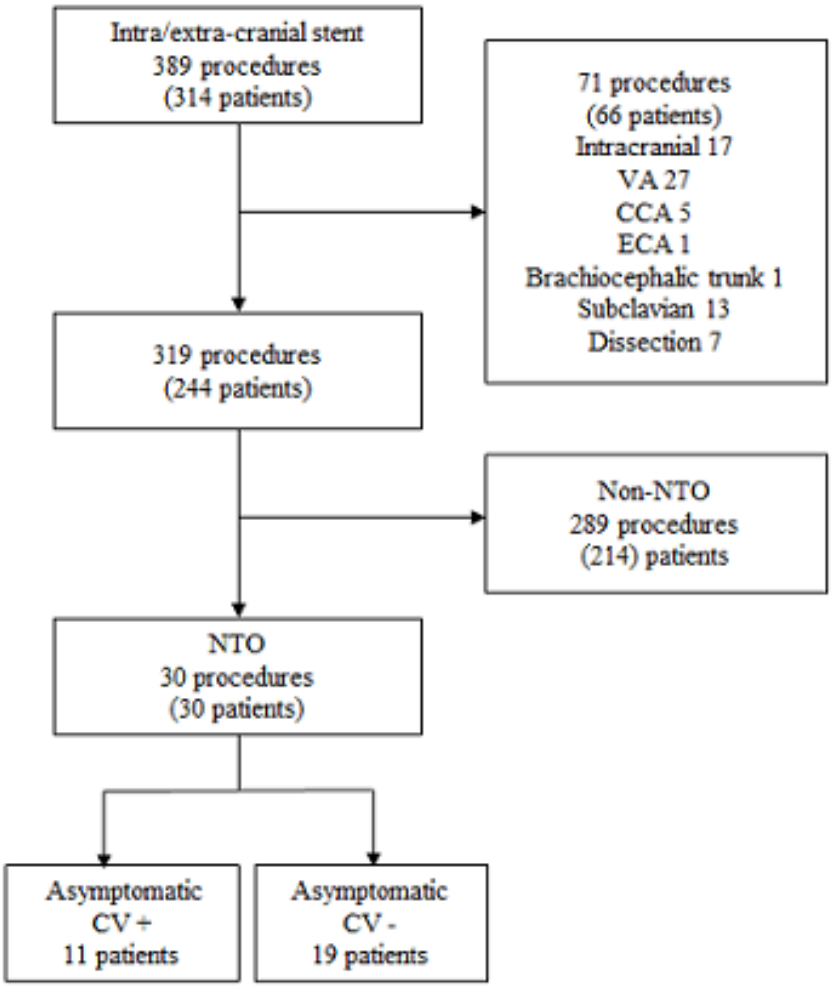

Fig. 1. Patient flow diagram

VA: vertebral artery, CCA: common carotid artery, ECA: external carotid artery, NTO: near total occlusion, CV: cerebral vasoconstriction

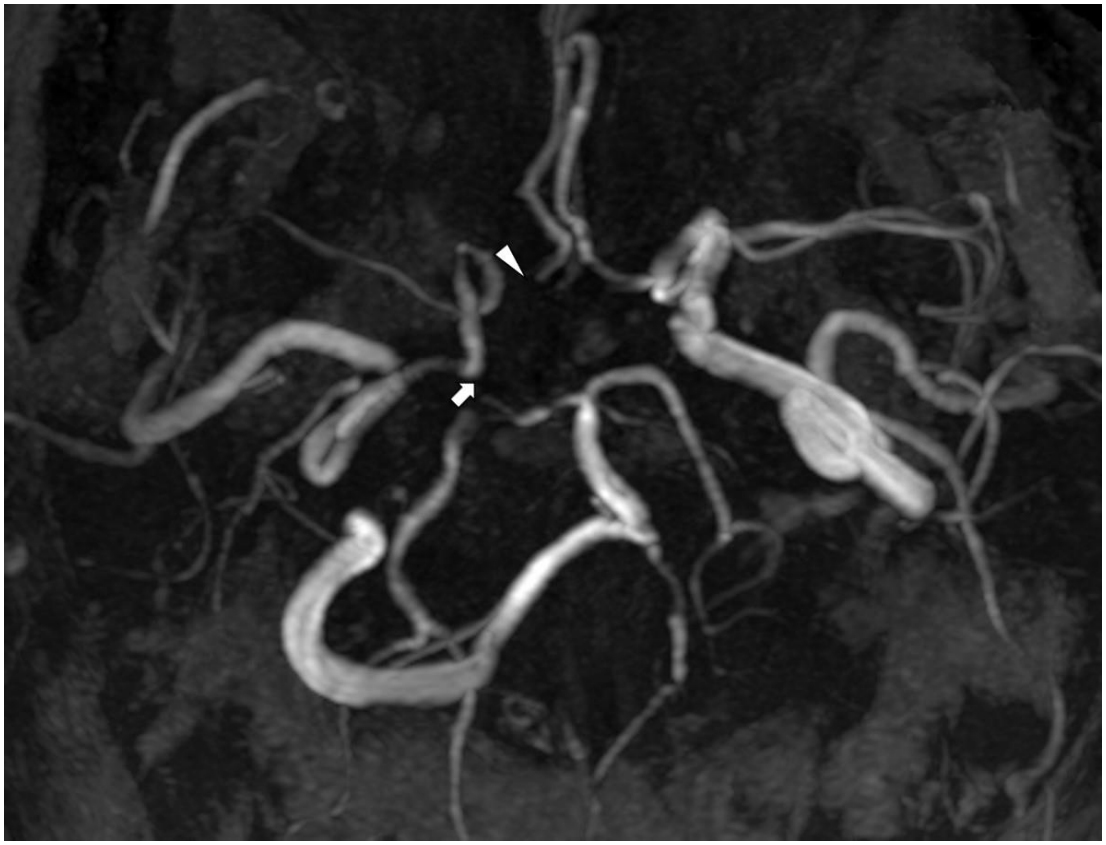

Fig. 2. A representative case of isolated circulation. (case no. 4)

Signal intensity drop of the right MCA/ICA territory and absence of right A1 segment (white arrow head) and posterior communicating artery (white arrow) on TOF MRA in the patient with right proximal ICA stenosis

MCA: middle cerebral artery, ICA: internal carotid artery, TOF: time of flight, MRA: magnetic resonance angiography

2.2 Data collection

Demographic data and medical history (including age, sex, hypertension, diabetes mellitus, cigarette smoking, alcohol drinking, hyperlipidemia, atrial fibrillation, coronary artery disease, active cancer, and previous stroke) were collected. Procedural data collected were

laterality, procedure time, deployed stents, balloon catheters, and embolic protection devices (EPDs). Additionally, data on the presence of symptoms caused by carotid stenosis, antiplatelet medication, plaque echogenicity on carotid Doppler ultrasonography, and initial National Institutes of Health Stroke Scale (NIHSS) and baseline modified Rankin Scale (mRS) scores were collected.

Moreover, data on the incidence of post-procedural parenchymal hemorrhage and discharge NIHSS and 3-month mRS scores were collected.

2.3 Procedural technique

All CAS procedures were performed using a biplane angiography unit (Axiom Artis Zee Biplane, Siemens). All patients received aspirin (100 mg/day) and clopidogrel (75 mg/day) treatment at least 7 days before the procedure. All procedures were performed under local anesthesia.

A bolus of intravenous heparin (50 IU/kg of body weight, 3000–5000 IU) was injected after the placement of the guide catheter. Subsequently, 1000 IU/h infusion was administered among all patients.

The Guider Softip XF Catheter (Boston Scientific Corp, Plymouth, MN, USA) was used as a guide catheter in all patients, except in two in whom the ENVOY Catheter (Cordis Corporation, Hialeah, FL, USA) was used. Distal EPD was deployed in all patients except for one. The types of EPD were Spider FX (Medtronic, Minneapolis, MN, USA), Filterwire EZ (Boston Scientific Corp, Natick, MA, USA), and Emboshield Nav6 (Abbott Vascular, Santa Clara, CA, USA).

We applied pre- and post-stenting dilatation in all patients except for two. Only pre-stenting

balloon dilatation was performed in one patient, and only post-stenting balloon dilatation was done in another patient. The Ryujin balloon catheter (Terumo, Tokyo, Japan) and Ultrasoft SV (Boston Scientific Corp, MN, USA) were applied until 2011. Afterwards, the Sterling balloon catheter (Boston Scientific Corp, Natick, MA, USA) was used.

We applied open cell type stents in all patients and a combination of open and closed cell type stents in one patient. In most cases, Precise (Cordis, Warren, NJ, USA) was applied. However, in some cases, Protégé (ev3 Inc, Plymouth, MN, USA), Acculink (Abbott Vascular, Abbott Park, IL, USA), and Carotid WALLSTENT (Boston Scientific Ireland Ltd, Ireland) were applied.

Following CAS, angiography of the proximal ICA and intracranial area and immediate post-procedural computed tomography (CT) were performed in all patients.

2.4 Statistical analysis

Statistical analysis was performed using the Statistical Package for Social Sciences version 18.0 software for windows (IBM Corporation). Patients were classified into two groups based on the presence of cerebral vasoconstriction. Univariate analysis was carried out using the Mann–Whitney *U* test for continuous variables and the Fisher's exact test for categorical variables. A p-value<0.05 was considered as statistically significant.

CHAPTER 3

RESULTS

The patients' baseline characteristics are shown in Table 1.

A total of 30 patients with NTO were analyzed. Of those, 27 patients (90.0%) were men, and the mean age was 69.0 years (range, 51-81 years). The left ICA was treated in 16 patients (53.3%), and 19 patients (63.3%) had symptomatic stenosis.

11 patients showed multifocal vascular narrowing considered as vasoconstriction in the treated territory, whereas 19 patients did not show significant vasoconstriction after CAS. There were no statistically significant differences in comorbidity, frequency of symptomatic lesions, antiplatelet medication, mean procedure time, and initial NIHSS and baseline mRS scores between the two groups. None of the 30 patients were taking vasoactive drugs.

However, vasoconstriction is more likely to happen in patients with isolated territory from the contralateral anterior and posterior circulation (64.2% in the isolated territory group and 12.5% in the not-isolated territory group; $p<0.05$). Vasoconstriction was observed in a larger number of patients than expected (11/30, 36.6%). Small- and medium-sized vessels of the ipsilateral M2-3 and A2-3 were noted, and these changes were mostly multifocal. All patients with vasoconstriction were asymptomatic.

Table 2 shows the characteristics of 11 patients with asymptomatic cerebral vasoconstriction after CAS. No headache or neurologic deficit was noted in all 11 patients with cerebral vasoconstriction. There was no post-procedural hemorrhage in all 30 patients with NTO who underwent CAS, and no patient had worsened NIHSS score by more than 2 points or worsened mRS score at discharge. In addition, no patient had decreased mRS score for 90 days, except for four patients who were lost to follow-up.

Fig. 3 shows cerebral vasoconstriction after CAS in two patients (case no. 24 and case no. 30)

Table 1. Baseline characteristics of patients with/without asymptomatic cerebral vasoconstriction after carotid stenting

	All (N = 30)	Without CV (N = 19)	With CV (N = 11)	*P* Value
Age, years	69.0 [64.0–75.0]	70.0 [66.0–75.5]	65.0 [62.5–73.0]	0.425
Sex, female	27 (90.0%)	18 (94.7%)	9 (81.8%)	0.613
Laterality, right	14 (46.7%)	9 (47.4%)	5 (45.5%)	1
Comorbidities				
Hypertension	19 (63.3%)	12 (63.2%)	7 (63.6%)	1
Diabetes mellitus	15 (50.0%)	7 (36.8%)	8 (72.7%)	0.13
Smoking	18 (60.0%)	12 (63.2%)	6 (54.5%)	0.938
Alcohol	10 (34.5%)	6 (33.3%)	4 (36.4%)	1
Hypercholesterolemia	10 (33.3%)	8 (42.1%)	2 (18.2%)	0.348
Coronary artery disease	4 (13.3%)	4 (21.1%)	0 (0.0%)	0.281
Atrial fibrillation	3 (10.0%)	3 (15.8%)	0 (0.0%)	0.449
History of Stroke	8 (26.7%)	4 (21.1%)	4 (36.4%)	0.627
Cancer	1 (3.3%)	0 (0.0%)	1 (9.1%)	0.778
Symptomatic lesion	19 (63.3%)	12 (63.2%)	7 (63.6%)	1
Isolation of ipsilateral MCA				0.011
Isolation (-)	16 (53.3%)	14 (73.7%)	2 (18.2%)	
Isolation (+)	14 (46.7%)	5 (26.3%)	9 (81.8%)	
Antiplatelet medication				0.795
No medication	6 (20.0%)	4 (21.1%)	2 (18.2%)	

Aspirin	3 (10.0%)	2 (10.5%)	1 (9.1%)	
Clopidogrel	5 (16.7%)	3 (15.8%)	2 (18.2%)	
Aspirin+Clopidogrel	14 (46.7%)	9 (47.4%)	5 (45.5%)	
Aspirin+Clopidogrel+Cilostazol	1 (3.3%)	1 (5.3%)	0 (0.0%)	
Clopidogrel+Warfarin	1 (3.3%)	0 (0.0%)	1 (9.1%)	
Plaque echogenicity (on DUS)				0.322
Not performed	13 (43.3%)	8 (42.1%)	5 (45.5%)	
Hypoechoic	9 (30.0%)	5 (26.3%)	4 (36.4%)	
Isoechoic	1 (3.3%)	0 (0.0%)	1 (9.1%)	
Hyperechoic	7 (23.3%)	6 (31.6%)	1 (9.1%)	
Mean duration of procedure (min)	38.0 [31.0–48.0]	41.0 [30.5–52.0]	35.0 [31.5–47.0]	0.747
Initial NIHSS	1.0 [0.0– 2.0]	1.0 [0.0–2.0]	1.0 [0.0–3.5]	0.837
Baseline mRS				0.145
0	23 (76.7%)	16 (84.2%)	7 (63.6%)	
1	5 (16.7%)	3 (15.8%)	2 (18.2%)	
2	2 (6.7%)	0 (0.0%)	2 (18.2%)	

CV = Cerebral vasoconstriction, MCA = middle cerebral artery, DUS = Duplex ultrasonography, NIHSS = National Institutes of Health Stroke Scale, mRS = modified Rankin Scale

Table 2. Patients with asymptomatic cerebral vasoconstriction after carotid stenting

Patient	Age	Sex	Laterality	Isolation of cerebral circulation	Pattern & territory	Location	Symptom	Symptom to stenting (days)	Procedure time (min)	Stents	Initial NIHSS	Discharge NIHSS	90 days mRS
1	69	M	L	+	multifocal	PP, TO	Hemiparesis	5	23	Protege 9x40	1	0	0
3	62	M	R	-	multifocal	CM	None	-	34	Precise 7x40	5	5	F/U loss
4	81	F	R	+	multifocal	PC, CG	None	-	40	Precise 8x40	0	0	0
10	79	M	R	+	multifocal	CM, PP, TO	Hemiparesis	92	46	Precise 9x40	0	0	0
12	71	M	L	+	solitary	Superior division	None	-	55	Precise 9x40	0	0	0

						M3							
13	54	M	L	+	multifocal	FP, CM	Amaurosis fugax	122	51	Precise 6x40	2	1	1
20	65	M	R	+	multifocal	PF, TO, PC, AP, PP	Hemiparesis	12	35	Precise 9x40	5	4	1
24	63	M	L	+	multifocal	PC, A2	Hemiparesis	119	31	Precise 9x40	5	5	F/U loss
26	65	M	R	-	multifocal	Superior division M2, PC	None	-	30	Precise 9x40	0	0	0
27	58	M	L	+	multifocal	AFM, LFB, PC	Hemiparesis	77	48	Precise 8x40	1	0	0
30	75	F	L	+	multifocal	AP, AG	Transient	25	32	Precise	0	0	1

							arm weakness			8x40			

NIHSS: National Institutes of Health Stroke Scale, mRS: modified Rankin Scale, R: right, L: left, PP: posterior parietal artery, TO: temporo-occipital artery, PC: artery to precentral gyrus, CG: artery to central gyrus, FP: frontopolar artery, CM: callosomarginal artery, AP: anterior parietal artery, PF: prefrontal artery, LFB: lateral frontobasal artery, AMF: anterior medial frontal branch of callosomarginal artery, AG: angular artery, F/U: follow up

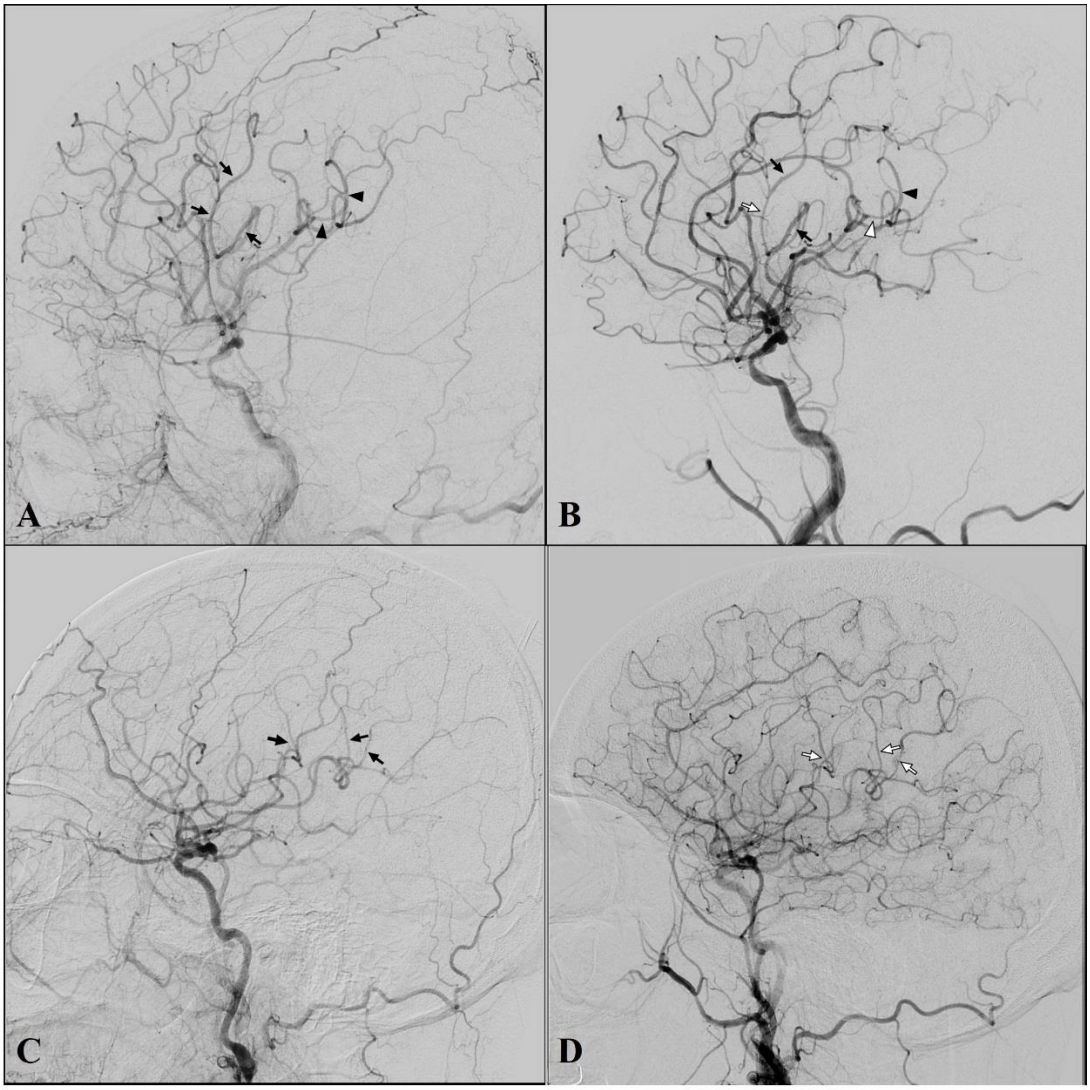

Fig. 3. Two representative cases of vasoconstriction after carotid artery stenting (A & B: case no. 24, C & D: case no. 30).

A: A superior division branch of left MCA is marked with black arrows, and an inferior division branch is pointed with black arrowheads on angiography image before stenting.

B: On post-stenting angiography, those branches are showing narrowing-and-dilatation appearance, and the narrowed (believed to be constricted) segments are marked with white arrow and white arrowhead, respectively.

C: On pre-stenting angiography, distal branches of left MCA is marked with black arrow.

D: On post-stenting angiography, these segments appear to be constricted (white arrow).

MCA: middle cerebral artery

CHAPTER 4

DISCUSSION

There have been many reports of changes in hemodynamic status or cognitive function after CAS. However, few have reported the morphological changes in intracranial vasculature after CAS. Morphological changes of the intracranial artery were noted immediately after CAS in patients with NTO, and smooth vascular narrowing was observed. In our study, all patients with vasoconstriction were asymptomatic, indicating that these morphological changes in the intracranial vasculature are physiological responses to increased cerebral perfusion, which is a type of autoregulation.

Cerebral autoregulation is a homeostatic process that regulates and maintains constant cerebral blood flow (CBF) in a range of blood pressures. The conceptualization of cerebral autoregulation was first proposed by Lassen as a triphasic curve consisting of the upper limit, the plateau and the lower limit.[14] In healthy adults, CBF is constantly maintained between 50 and 150 mmHg cerebral perfusion pressure (CPP) or 60 and 160 mm Hg mean arterial pressure (MAP), where CPP = MAP – intracranial pressure. (Fig. 4)[15] The vascular adjustments underlying autoregulation consist of constriction of cerebral resistance vessels when CPP increases and vasodilation of these vessels when CPP decreases.[16] However, during cerebral ischemia, these mechanisms become dysfunctional and fail to compensate for CBF reduction.[17]

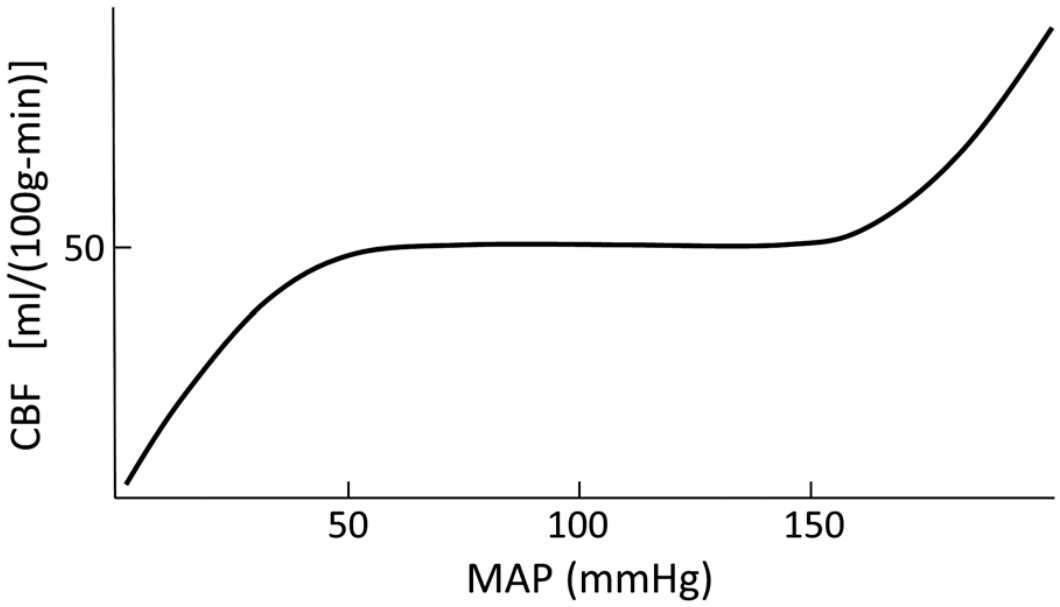

Fig. 4. Cerebral autoregulation.

The original cerebral autoregulation curve consist of the lower limit, the plateau and the upper limit. CBF is constantly maintained between 60 and 160 mm Hg MAP. (adapted from "Cerebral blood flow and autoregulation: current measurement techniques and prospects for noninvasive optical methods. by Fantini S. et al. Neurophoton. 2016;3(3):031411)[15]

CBF: cerebral blood flow, MAP: mean arterial pressure

Moreover, autoregulation is impaired by stenosis or occlusion of ICA. Two investigations using transcranial Doppler (TCD) sonography found that cerebral autoregulation is impaired in patients with severe ICA stenosis or occlusion.[18,19] They estimated the cerebral hemodynamic reserve by measuring cerebrovascular reactivity induced by breathing CO_2, and a correlation between the degree of stenosis and loss of autoregulation was noted in both groups.[18,19] Of these, Reinhard et al. found that cerebral autoregulation is most severely impaired in patients without Willisian collaterals, because cerebral hemodynamic status is poor.[19] Furthermore, Haubrich et al. demonstrated that impaired cerebral autoregulation may recover after CAS.[20]

Compensatory mechanisms maintain cerebral perfusion in the initial stages of CBF reduction. Powers categorized these cerebrovascular adjustments into three stages: stage 0, when CPP is normal; stage 1, when CPP is reduced and autoregulation dilates the cerebral vessels to maintain CBF; and stage 2, when the compensatory capacity for cerebral vasodilation exceeds, CBF begins to decrease, and cerebrovascular autoregulation is disrupted.[21]

In patients with carotid NTO, CBF in the ipsilateral intracranial circulation is reduced. In response to CBF reduction, the cerebral vessels may be dilated to maintain cerebral perfusion. Likewise, autoregulation may be impaired in proportion to the severity of the stenosis. Immediately after CAS, a large amount of blood flows into the cerebral vessels, where autoregulation is impaired. We thought that cerebral vessels become uniformly constricted under normal autoregulation. Nevertheless, as in our cases, multifocal vasoconstriction may occur because of partial disruption of the autoregulation. Therefore, asymptomatic vasoconstriction in our cases is considered as a type of autoregulation or the boundary between autoregulation and pathological condition. If the autoregulation is completely disrupted, the cerebral vessels cannot constrict and are dilated. This condition is thought to be more vulnerable to hyperperfusion syndrome (HPS).

In our study, vasoconstriction occurred more frequently in patients with isolation of the cerebral circulation, which is consistent with the finding of Reinhard et al. that autoregulation is further impaired in patients without Willisian collaterals.[19] This is probably because the cerebral hemodynamic reserve is further reduced, and autoregulation is subsequently further impaired in patients with isolation of the cerebral circulation. These changes are expected to return to normal when autoregulation is restored over time after CAS.

Six case reports of cerebral vasoconstriction after CAS have been published so far (Table 3). In these reports, cerebral vasoconstriction occurred immediately after CAS to 1 month after CAS. In our study, we observed only the development of cerebral vasoconstriction immediately after CAS.

Table 3. Previous cases of cerebral vasoconstriction after CAS

	Age	Sex	Laterality	Onset from CAS	Infarction	Outcome
Arai[7]	72	M	R	13 hours	Present	No deficit
Shiraga[12]	62	M	R	1.5 days	Present	No deficit
Soltanlkotachi[11]	49	F	L	14 days	Present	No deficit
Aghaebrahim[8]	60	M	R	1 month	Not available	No deficit
Watanabe[9]	74	M	R	17 days	Present	No deficit
Higashi[10]	73	M	L	Immediately	Present	Right hemiparesis, cognitive dysfunction

CAS: carotid artery stenting, M: male, F: female, R: right, L: left

Arai et al. reported a case of cerebral vasospasm following right CAS.[7] A 72-year-old man presented with severe asymptomatic stenosis in the right proximal ICA. CAS was performed for stenosis of right proximal ICA using an open cell stent. However, left hemiparesis, left hemianopsia and hemispatial neglect occurred 13 hours after procedure. Diffusion-weighted image 17 hours after CAS showed high signal spots in the right cerebral hemisphere. MRA 17 hours after the procedure showed diffuse vasospasm of the distal portion of the right MCA, and perfusion CT image indicated hypoperfusion in the right cerebral hemisphere. His symptoms were temporary, and he was discharged without any neurological deficit. Perfusion CT image 6 days after procedure showed normalized mean transit time, and MRA 4 weeks after procedure showed improvement of the diffuse vasospasm.

Cerebral vasoconstriction was solitary in Arai's case report, but multifocal in our study. In our study, post-procedural perfusion image was not performed in the patients with cerebral vasoconstriction, because the patients were asymptomatic and we thought that these changes were physiological response.

Aghaebrahim et al. reported a case of cerebral vasoconstriction after right CAS.[8] A 72-year-old woman presented with headache and left side hemiparesis 1 month after CAS. Trans-femoral cerebral angiography showed vasoconstriction of the right anterior cerebral artery and right MCA. The cerebrospinal fluid study for investigating vasculitis was unremarkable. The vasoconstriction and symptoms improved after intra-arterial verapamil infusion.

Higashi et al. reported a case of cerebral vasoconstriction.[10] A 73-year-old female underwent CAS for a symptomatic high-grade left proximal ICA stenosis. Immediately after CAS, he had consciousness disturbance and right hemiparesis. The authors first suspected HPS, but antihypertensive therapy exacerbated the patient's symptoms. On repeated postoperative angiography, the MCA appeared to become progressively narrower. Diffusion-weighted image showed acute small infarction in the left watershed zone, and perfusion CT showed hypoperfusion in the left MCA territory. The authors diagnosed the patient with cerebral hypoperfusion associated with MCA vasoconstriction. Although cerebral vasoconstriction improved, right hemiparesis and cognitive dysfunction were permanent and

caused severe disability. The authors noted that vasoconstriction after CAS may result in a poor outcome, so it must be promptly distinguished and properly treated.

Soltanolkotabi et al. reported a case of vasoconstriction following left CAS.[11] A 49-year-old female underwent CAS for a symptomatic severe left proximal ICA stenosis. After the procedure, the patient complained of left frontal headache. However, brain CT and neck computed tomography angiography (CTA) revealed a patent left ICA stent with no evidence of in-stent stenosis, thrombosis, or intracranial hemorrhage and the patient was discharged. The patient returned to the emergency department 14 days later due to transient right side weakness and right facial numbness. Brain MR showed 2-3 punctuate foci of restricted diffusion in the left fronto-parietal area, and brain perfusion MR showed a delayed mean transit time. Although subsequent head and neck CTA re-demonstrated stent patency with no residual stenosis. Catheter-based cerebral angiography revealed cerebral vasoconstriction in the distal braches of the left anterior, middle, and posterior cerebral arteries. The cerebral vasoconstriction resolved immediately following the administration of intra-arterial verapamil and follow-up perfusion MR showed normalization of mean transit time. The patient's symptoms improved, and the patient was discharged. The authors noted that presence of headache was correlated well with patient's cerebral perfusion status.

In the abovementioned six reports, the symptoms were mild in some cases and severe in the other cases. However, in our study, all patients with vasoconstriction were asymptomatic. This may be attributed to the difference in location and degree of vasoconstriction, and difference in susceptibility between individuals. Vasoconstriction following CAS has a broad spectrum of manifestations depending on the severity of autoregulation impairment. If the autoregulation impairment is mild, vasoconstriction is not prominent and the patients are asymptomatic. It may be a physiological response, which is a type of autoregulation. Otherwise, if autoregulation impairment is severe, vasoconstriction is prominent and may cause severe symptoms. It may be a pathological condition causing severe headache or stroke.

After CAS, impaired autoregulation of CBF also causes HPS.[22] Both cerebral vasoconstriction and

HPS are caused by abrupt increased blood flow into the cerebral vessels that are dilated by a compensatory response to severe carotid stenosis. Cerebral vasoconstriction probably occurs because the cerebral artery constricts abnormally. On the other hand, HPS probably occurs because the cerebral arteries cannot constrict and are dilated. Both are caused by impairment of cerebral autoregulation. There has been no reports or study on the morphological changes of intracranial vessels in HPS following CAS.

After CAS, aside from HPS, cerebral vasoconstriction may occur. In the previous case report, the patient's symptom deterioration after CAS was misdiagnosed as HPS and antihypertensive medications were administered. Left MCA vasoconstriction was later observed. This has caused severe disability in the patient.[10] Therefore, when the patient's symptoms worsen after CAS, the possibility of cerebral vasoconstriction should be considered. It should be differentiated and treated appropriately. In previous reports, administration of calcium channel blockers such as oral lomerizine hydrochloride[10] or intra-arterial verapamil[8,11] was effective in the treatment of vasoconstriction after CAS.

This study has some limitations. First, this is retrospective study. Second, the sample size is small. Therefore, there are no imaging such as TCD sonography and single-photon emission computed tomography to evaluate the vascular reactivity. Third, there is no follow up angiography.

CHAPTER 5

CONLUSION

Cerebral vasoconstriction after CAS occurs in about one third of patients with NTO of proximal ICA, and it occurs more frequently in patients with isolation of the cerebral circulation. A large-scale study

is necessary to assess the clinical implication of cerebral vasoconstriction after CAS.

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