Treatment and Outcome of Intracranial Hemorrhage after Carotid Artery Stenting

A Ten Year Single Center Experience

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Summary

Intracranial hemorrhage following carotid artery stenting (CAS) is a rare but potentially devastating complication. The present study reviewed intracranial hemorrhage cases from patients undergoing CAS in ten years to find the methods to rescue patients from this fatal complication.

Patients with postoperative intracranial hemorrhage following CAS were retrospectively selected, and clinical features, treatments and outcomes were studied.

Ten patients with intracranial hemorrhage were identified. The mean onset time of hemorrhage was 6.1 ± 7.1 h. Intracerebral hemorrhage occurred in eight patients and SAH in two patients. The patients were treated by stopping anti-platelet and anticoagulant for at least three days, and surgical drainage of the hematoma/ventricle drainage or conservative treatment. Six patients survived, two had left moderate paralysis, four had a good recovery at four week follow-up, and four patients died. No patients underwent thrombosis in stent after withdrawing of antiplatelet and anticoagulant.

Intracranial hemorrhage after CAS occurs usually in a few hours and leads to catastrophic results. Once patients have intracranial hemorrhage, good neurocritical care may help to save them. Stopping antiplatelet and anticoagulant for at least three days may avoid thrombosis in the stenting site.

Introduction

Carotid artery stenting (CAS) has been proposed as an alternative technique for revascularization in case of ICA stenosis^{1,2}. Postsurgical intracranial hemorrhage (ICH) has been well described following carotid endarterectomy (CEA), and is associated with significant morbidity and mortality. Systemic analyses of large series of patients with ICH after CAS have demonstrated that this post-CAS disorder occurs in about 0.7% of patients³. Although there have been multiple reports of ICH following CAS⁴⁻¹⁵, none of these study focused on how to rescue these patients from the fatal disorders and outcome was not studied. The present study reviewed ten intracranial hemorrhage cases from patients undergoing CAS to find the methods to rescue patients from this fatal complication.

Clinical Material and Methods

We reviewed a retrospectively collected database of all patients who underwent CAS in Beijing Xuan Wu hospital from January 1997 to June 2008 to find patients who had ICH. The database included demographic information, clinical history, symptomatic status of the internal carotid artery (ICA), angiographic findings, procedure details, adjunctive antithrombotic/anticoagulant agents used, and peri-procedural events. Peri-operative and follow-up data on

neurological events including any transient ischemic attack, stroke, seizure, or change in neurological status were collected. Treatments of every ICH patient were reviewed in detail.

Intracranial hemorrhage was defined by computed tomography evidence of punctuate or confluent hyperdensity consistent with blood within the parenchyma of the cerebral hemispheres or within the subarachnoid space^{3,4}.

The technique of CAS has been described elsewhere¹⁶, but evolved over the ten years of this study. Patients were pretreated with aspirin 300 mg/d and clopidogrel (Plavix) 75 mg/d for at least three days. All patients were treated with heparin intra-operatively with a bolus of

50 U/kg with additional doses as necessary to achieve an activated clotting time (ACT) of 250 to 325 s. Procedural success was defined as a post-stent luminal narrowing of <30% using the North American Symptomatic Carotid Endarterectomy (NASCET) method¹⁷. All patients underwent CAS as part of institutional review board-approved protocols. All patients with postoperative ICH were hospitalized for at least two weeks after the surgical procedures and underwent serial CT examinations to detect the development of intracranial hemorrhage. Stenting site ultrasonography was performed on the first postoperative day and on the seventh day. The treatment protocol is

Figure 1 Protocol for treatment of ICH after CAS.

shown in Figure 1. GOS recovery scores were evaluated by follow-up neurological examination at four weeks. Descriptive statistics were expressed as the means $\pm$ SDs.

Results

Out of 832 patients undergoing CAS, ten patients (1.2%) experienced postoperative intracranial hemorrhage, including eight intracerebral hemorrhages and two SAHs. Characteristics of patients with postoperative intracranial hemorrhage after CAS are listed in detail in Table 1. Eight out of the ten were male and the stenosis rate range from 90% to 99%. The mean time between the last ischemic episode to procedure was 54 ± 20 days (Table 1). None of the patients had major infarction before treatment. Table 2 shows the statistics of risk factors related to the development of intracranial hemorrhage. Most of the patients had baseline hypertension and all were symptomatic ICA stenosis cases. Sixty per cent of them had bilateral ICA stenosis.

Table 3 details the location of hemorrhage and clinical details peri-procedure. Four of the ten cases were treated under general anesthesia (Nos. 5,6,7,8) and two were extubated 5h and 19h before hemorrhage occurred. One patient was not extubated, and could not recover from anesthesia and one pupil dilated 2h after

the procedure. One patient lost consciousness 30 min after wake up and extubation (No. 8). Most of the patients had hypertension when the hemorrhage symptom occurred (mean $163 \pm 18/77 \pm 8$ mmHg).

All the anti-platelet and anticoagulation drugs were stopped once symptoms were found. Protamine was injected for anti-heparin purposes if necessary. When hemorrhage was confirmed by CT scan, depending on the volume of hemorrhage neurosurgeons would decide whether hemorrhage drainage should be performed. If severe SAH occurred, and ventricles enlarged, ventricle drainage would be performed. Treatment and clinical outcome is described in Table 4. Anti-platelet drugs would be given at least three days after the hemorrhage if the patient's condition was stable. No stenting thrombosis occurred according to follow-up ultrasonography. One patient with 40 ml hemorrhage in the temporal-occipital lobe and one patient with 70 ml hemorrhage in the basal ganglia survived with left paralysis, and one patient with severe SAH who survived with hydrocephalus and underwent ventriculoperitoneal shunt had a good recovery at four week follow-up. Three patients with mild or moderate hemorrhage also recovered with good results.

Figures 2 and 3 are two case presentations (Case No. 8 and Case No. 10).

Table 1 Clinical characteristics of patients with intracranial hemorrhage after CAS.

Patient	Sex	Age	Lesions	Stenosis	Last symptomatic and time (d)
1	male	74	RICA	90%	TIA 60
2	female	70	RICA	95%	lacunar infarction 40
3	male	66	LICA	90%	TIA 50
4	male	65	RICA	99%	lacunar infarction 80
5	male	69	LICA	90%	TIA 60
6	male	66	RICA	99%	infarction 60
7	male	74	LICA	99%	Infarction 30
8	female	43	RICA	99%	TIA 40
9	male	52	RICA	90%	infarction 90
10	male	65	RICA	99%	TIA 30
Mean $\pm$ SD		64 ± 10		$95\% \pm 4.5\%$	54 ± 20
TIA: transient ischemic attack					

Table 2 Risk factors of patients with intracranial hemorrhage after CAS.

Risk factors	Intracranial hemorrhage after CAS
Male sex	8 (80%)
hypertension	7 (70%)
Diabetes mellitus	4 (40%)
Hyperlipidemia	5 (50%)
Symptomatic lesion	10 (100%)
Preop admin of 2 antiplatelet drugs	10 (100%)
Preop admin of anticoagulation drugs	0
Mean no. days from last ischemic event (d)	54±20
Mean of ICA stenosis % (±SD)	95%(±4.5%)
Bilateral lesions	6 (60%)
General anesthesia	4 (40%)
Postop admin of anticoagulation drugs	10 (100%)
Strict control of postop blood pressure	4 (40%)
Postop induction of propofol sedation therapy	4 (40%)

Discussion

Characteristics of CAS-associated ICH

Our study disclosed a 1.2% incidence of ICH after CAS in a single medical center, which is slightly higher than recently reported. Grunwald et Al reported three ICH cases out of 417 carotid artery stented cases (0.72%)¹⁸, and Brantly et Al reported a single-operator series of 482 consecutive patients without ICH complications¹⁹. Kang et Al, using a pooled analysis of English language literature (1996-2005), concluded CAS-associated ICH occurred in 0.63% of patients in studies consisting of >100 cases and 2.69% of case series consisting <100 cases²⁰. Our case series comprised all consecutive patients from 1997 to 2008 in our hospital. We did not have a strict blood pressure protocol until five years ago. This higher ICH morbidity indicated physicians must pay more attention to hyperperfusion syndrome prevention.

We concluded our ICH cases were caused by hyperperfusion syndrome. In these cases of intracranial hemorrhage, 80% were cerebral hemorrhage and occurred on the ipsilateral side of stenting. All hemorrhages occurred acutely

(mean 6.1±7.1h), most in seven hours after CAS. The ipsilateral basal ganglia was the most common bleeding place. One cerebral hemorrhage occurred in the cerebral lobe, where there were infarction lesions before. None of the SAH patients had any aneurysms on angiography. This phenomenon may be explained by the current accepted theory that hyperperfusion syndrome occurs because the ischemic cerebral tissue lost normal CBF autoregulation. Long-lasting hypoperfusion distal to a high grade stenosis with maximal vasodilatation and impaired autoregulation might result in high-pressure autoregulation failure. Thus, very high perfusion pressure after CAS overwhelms the vasoconstriction ability of the arterioles, disrupting the tight junctions of the capillary endothelial cells and causing ICH and also SAH⁷.

In the literature, Chamorro et Al²¹ report the only fatal ICH case in which ICH occurred on the contralateral side and did not affect an area that had been considered acutely infarcted before the intervention. Buhk et Al argued that hyperacute intracranial hemorrhage complicating carotid stenting should be distinguished from hyperperfusion syndrome, considering most cases do not have the triple hyperperfusion symptoms (i.e., clinical signs of elevated brain pressure: severe headache, nausea and seizures)²². In the present series of cases, the above triad of symptoms did not exist in most intracerebral hemorrhages. But the single mechanism of hypertension hemorrhage could not explain why significantly most cases developed ipsilateral hemorrhage after CAS. In the current cases, most patients had a history of hypertension and the blood pressures were high when symptoms occurred (mean 163±18/77±8 mmHg). Sometimes hypertension may be a result of increased intracranial pressure after intracranial bleeding. We accepted that both mechanisms may take part in intracerebral hemorrhage development, and more cases should be collected and pathological evidence should be purchased in these patients. Even normal blood pressure may be dangerous for high-risk patients. Some authors mentioned that normal systemic blood pressure ("normotension") after a revascularization procedure is often excessive blood pressure (effective "hypertension") in the susceptible cerebral circulation. Already a low resistance system, the brain can sustain severe barotraumas because of the loss of cerebrovascular tone and reactivity²³. Too

Figure 2 A 67-year-old man with a history of TIA and 99% left ICA stenosis underwent stenting (Precise 8 mm*40 mm) and lost consciousness 3 hours after the procedure. CT showed a 40ml left basal ganglia hemorrhage. Micro-invasive drainage of the cerebral hemorrhage was performed at the bedside. About 70% of the hemorrhage was cleared the first day. The patient woke up on the 2nd day and was discharged one week later. A) DSA revealed severe stenosis of left ICA. B) The ICA territory was supplied partially by an extracarotid artery. C) A 8x40mm Precise stent was planted in the stenosis site. D) Post stenting DSA showed the left ICA supplies increased significantly. E) Three hours later, the patients had severe headache and lost consciousness, CT revealed left basal ganglia hemorrhage. F) The follow-up CT showed 70% blood cleared on the first day. The patient woke up on the second day. G) 7 days later follow-up CT showed most hemorrhage had cleared and absorbed.

Table 3 **Periprocedural for patients with ICH.**

patient	complications	time after op (h)	symptoms of hemorrhage	Initial pressure (mmHg)	Post-op Bp (mmHg)	Bp at symptoms (mmHg)
1	ICH basilar ganglia	3	dizziness, left side paralysis	120/70	140/70	148/69
2	ICH basilar ganglia	2	left side paralysis	110/60	110/60	130/80
3	ICH temporal and occipital lobe with SAH	2.5	severe headache, vomiting, ipsilateral seizure	140/80	123/66	150/70
4	ICH basilar ganglia	19	ipsilateral seizure and paralysis	140/80	135/75	169/82
5	ICH basilar ganglia	2	did not wake up from general anaesthesia, one pupil dilated	160/80	120/60	187/74
6	ICH basilar ganglia	5	suddenly lose of consciousness	230/80	136/55	180/80
7	ICH thalamus breaking into ventricles	19	one under extremity not able to move	160/80	136/55	170/80
8	SAH	0.5	lost of consciousness after awake from general anaesthesia	150/80	120/60	180/80
9	SAH	7	headache, vomiting, dizziness	160/90	180/110	164/94
10	basilar ganglia	1	headache and coma	180/100	110/70	149/64
mean		6.1		SBP	SBP	SBP
±SD		±7.1		155±33	131±20	163±18

Table 4 **Treatment and outcome.**

patient	volume of hemorrhage	treatment	outcome
1	100 ml	hemorrhage drainage and hematoma cavity rinsed with urokinase saline	died 6 days later
2	40 ml	hemorrhage drainage and hematoma cavity rinsed with urokinase saline	awake, left paralysis
3	40 ml, 100 ml at second time	conservative treatment for 3 days, hemorrhage drainage and hematoma cavity rinsed with urokinase saline	awake after 7 day, moved 2 days later and died
4	10 ml	conservative treatment	awake, no complications
5	100 ml	hemorrhage drainage and ventricles drainage	died 7 days later
6	10 ml	conservative treatment	awake, no complications
7	20 ml	conservative treatment	awake, no complications
8	SAH	ventricle drainage	died 1 day later
9	SAH	ventricle drainage	wake up 2 days after SAH, no other complications
10	70 ml	hemorrhage drainage, hematoma cavity rinsed with urokinase saline	wake up 3 days after hemorrhage, left side paralysis

A

B

C

D

E

Figure 3 A 65-year-old man with TIA and severe right carotid artery stenosis underwent stenting. Two hours later he complained of headache and soon lost consciousness. CT showed basal ganglia hemorrhage broken into the lateral ventricles. Micro-invasive drainage of the cerebral hemorrhage was performed at the bedside. About 50% of the hemorrhage was cleared on the first day. He woke up 3 days later and survived with hemiplegia. A) Before CAS DSA revealed 90% stenosis of the right ICA. B) The ICA territory was supplied partially by an extracarotid artery. C) A 8x40 mm Precise RX stent was planted in the stenosis site. D) Post stenting DSA showed the left ICA supplies increased significantly. E) Two hours later, the patients had severe headache and lost consciousness, CT revealed left basilar ganglia hemorrhage. F) The follow-up CT showed 50% blood cleared and the patient woke up three days later.

low blood pressure may lead to ischemic lesions and normal blood pressure may be dangerous, blood pressure control still be a problem in post operation stage of CAS. Theoretically, strict control of blood pressure should be continued until cerebrovascular autoregulation is restored²⁴, but the time of restoration of autoregulation varies among patients²³. In the future, imaging may better guide pharmacotherapy on an individualized patient basis. Four out of ten of our cases were treated under general anesthesia, among them, two hemorrhages occurred 5h and 19h after extubation. One patient was not extubated, and could not recover from anesthesia and one pupil dilated 2h after CAS. One patient lost consciousness 30 min after waking up and extubation. In this case the extubation reaction may be the cause of hypertension and hemorrhage. In our hospital, most stenting procedures are performed under local anesthesia. General anesthesia is considered only when the neurointerventionist believes the patient had a high risk of hyperperfusion hemorrhage. This may be the reason 40% of our patients with intracranial hemorrhage underwent general anesthesia, and obviously, we should pay more attention to blood pressure control during the anesthesia recovery procedure.

Treatments and outcome

Only one paper in the literature mentioned treatment of intracranial hemorrhage⁴, but the authors presented no details of the treatment protocol for the intracranial hemorrhage. In the present study, every patient was treated according to the protocol described in Figure 1. Blood drainage and ventricular drainage could have induced intracranial hyperpressure, and rescue some of the patients from hernia. Antiplatelet and anticoagulation drugs were stopped once hemorrhage occurred, and restarted at least three days later. No stenting thrombosis was found in these cases. Half of the patients survived, including one patient with a 40 ml hemorrhage in the temporal-occipital lobe and one patient with a 70 ml hemorrhage in the basal ganglia survived with left hemiplegia, and one patient with severe SAH had hydrocephalus. Three patients with mild or moderate hemorrhage recovered with good results. The SAH and hydrocephalus patient recovered well after shunting.

In the literature, patients seldom survived with ICH after CAS^{4,18,9,12,15,25}. The antiplatelet and anticoagulant procedure usually resulted in severe diffuse hemorrhage. Some authors mentioned that the ICH after CAS is often devas-

tating and has no effective treatment besides supportive measures²⁶.

In the present cases, outcomes were not so poor. Although severe hemorrhage or diffuse SAH were fatal, three patients with mild hemorrhage recovered without any disability, and two patients with hemorrhage larger than 40ml survived with paralysis. Operators should be encouraged to save patients by good neuro-intensive care.

Conclusions

The pathological mechanism of ICH after CAS remains unsettled. ICH usually occurs a few hours after CAS and leads to catastrophic results. Once patients have had intracranial hemorrhage, good neurocritical care may be life-saving. Stopping anti-platelet and anticoagulant for at least three days may avoid thrombosis in the stenting site.

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