Neurologia medico-chirurgica Advance Publication Date: January 5, 2023

Original Article doi: 10.2176/jns-nmc.2022-0249

Current Treatment Results of Intracranial Carotid Artery Dissection Causing Cerebral Ischemia: A Japanese Nationwide Survey

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Abstract

Intracranial carotid artery dissection causing cerebral ischemia is a rare but important cause of cerebral infarction in children and adolescents. Although endovascular therapy has been reported to be effective, questions regarding the indications for intervention are yet to be addressed. Therefore, this study aimed to evaluate factors related to clinical outcomes through a nationwide survey. Overall, 35 neurosurgical centers reported patients within 2 weeks after ischemic onset due to intracranial carotid artery dissection causing cerebral ischemia treated between January 2015 and December 2020. Data on clinical and radiological findings were statistically analyzed. Twenty-eight patients met the inclusion criteria. The median age was 36 years (range, 7-59 years), without sex differences. Headache at onset was documented in 60.7% of the patients. Dissection findings were categorized into stenosis (71.4%) or occlusion (28.6%). Initial treatments, including various antithrombotic agent combinations in 23 (82.1%) patients, effectively improved or prevented aggravation in half of the patients. The patients with stenotic dissection were significantly more likely to experience aggravation during the initial treatment than did those with occlusive dissection (P = 0.03). In addition, the patients with moderate to severe neurological deficits on admission had poorer outcomes at discharge more frequently than did those with mild neurological deficits on admission. Eight patients undergoing endovascular therapy had no procedural complications or further aggravation after intervention. In conclusion, patients with intracranial carotid dissection causing cerebral ischemia who had a stenotic dissection were at risk of further aggravation, and endovascular therapy effectively improved or prevented aggravation.

Keywords: carotid artery, cerebral ischemia, dissection, intracranial, nationwide survey

Introduction

Intracranial carotid artery dissection causing cerebral ischemia (IsICD) is a rare condition, representing approximately 2% of all dissections of the intracranial carotid circulation.[1,2] However, the exact incidence is yet to be assessed. In children, it has been reported that intracranial carotid dissections are not rare and can result in severe ischemic neurological deficits.[3] Oka et al.[4] reviewed sporadic case reports and series and revealed that IsICDs occurred in relatively healthy adolescents and worsened even during medical treatments, resulting in severe neurological

Received August 5, 2022; Accepted October 11, 2022

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deficits. Furthermore, recent case reports and series have shown the effectiveness of endovascular treatments using percutaneous transluminal angioplasty (PTA) or stent placement.[5-15] However, the precise indication and timing for such interventions are yet to be evaluated in a larger population of patients.[16]

Therefore, this study aimed to evaluate the current treatments and outcomes of IsICDs in Japan, primarily focusing on factors of aggravation and poor outcomes through a nationwide multicenter survey.

Materials and Methods

Patients

This nationwide survey was conducted after obtaining authorization from the Japanese Society of Surgery for Cerebral Stroke. The study protocol was approved by the Institutional Review Board (IRB) of the Akita University Graduate School of Medicine (No. 2640). A letter of invitation to participate in this study was sent to 870 centers that served as training hospitals for the Board Certification Program of the Japanese Neurosurgical Society. Overall, 35 neurosurgical centers reported relevant cases and participated in this retrospective study after the approval of the IRBs of each center. The requirement for informed written consent from the included patients was waived because of the retrospective and noninvasive nature of this study.

The inclusion criteria were the following: (i) first-ever patients with IsICD admitted between January 2015 and December 2020 and (ii) within 2 weeks after ischemic onset due to IsICD lesions. No age or sex restrictions were imposed. Furthermore, no exclusion criteria were established.

In this study, IsICD was defined to represent spontaneous intracranial and intradural carotid dissections distal to the ophthalmic artery. Carotid dissections determined to originate from the cavernous, petrous, or cervical portion and possibly caused by trauma, vasculitis, or iatrogenic procedures were not regarded as the IsICD in this study. At least one of the following findings was required on magnetic resonance angiography (MRA), computed tomography angiography, or conventional angiography: double lumen, pearl and string sign, intimal flap, tapering stenosis or occlusion, and intramural hematoma.[10,17]

Data collection

The patients' medical information was anonymized in the participating hospitals and collected via an encrypted online system. The collected information included baseline patient characteristics (age; sex; past medical history, including head trauma; history of smoking and alcohol consumption; and modified Rankin scale (mRS) before onset).

Data on the time between onset and hospital arrival; headache at onset; exercise associated with onset; neurological findings on admission, including the National Institutes of Health Stroke Scale (NIHSS); radiological features of the dissection (side, findings to diagnose as dissection, and beginning and ending portions of the dissection); radiological features of the infarction; initial medical treatments and their results; additional treatments (medical or endovascular therapy or bypass surgery) and their results; and NIHSS and mRS on discharge were also collected. The sizes of the infarctions before treatment and at discharge were compared visually.

Statistical analysis

Baseline patient characteristics, clinical and radiological findings, treatments, and outcomes were summarized descriptively. In addition, values were expressed as counts and percentages (%) or median with range.

The primary outcome of this study was the clinical outcome evaluated using the mRS at discharge. Favorable and poor clinical outcomes were defined as mRS scores ranging from 0 to 2 and from 3 to 6, respectively. Any aggravation of neurological symptoms, size of infarction, or degree of steno-occlusive findings due to dissection were evaluated as a secondary outcome.

The patients with or without primary (or secondary) outcomes were compared statistically regarding their age, sex, NIHSS score on admission, and imaging findings of the dissection using the Mann-Whitney U test or Fisher's exact test. Factors related to the primary (or secondary) outcomes were analyzed statistically using univariate and multivariate logistic regression analyses.

All statistical analyses were performed using Easy R (EZR; Saitama Medical Center, Jichi Medical University, Saitama, Japan), a graphical user interface for R (R Foundation for Statistical Computing, Vienna, Austria). Primarily, it is a modified version of the R commander designed to add statistical functions that are commonly used in biostatistics.[18]

Results

Overall, 58 patients were initially reported from the 35 participating centers. Thirty cases did not meet the inclusion criteria: nine, dissection of the petrous portion; two and one dissection of M1 and A1 portions, respectively; three, admission later than 2 weeks after the onset; two, possible iatrogenic dissection after mechanical thrombectomy; one each, possible vasculitis and traumatic origin; and 11, insufficient data to confirm diagnoses of IsICD and/or locations of the dissections. Data of the remaining 28 patients met the inclusion criteria and were enrolled for further analysis.

Baseline characteristics, imaging findings, initial treatments, and interventions

The baseline characteristics of the patients and imaging findings are presented in Table 1. The median age of the

Table 1 Baseline characteristics, treatments, and outcomes

Number of patients = 28	Median (range) or n (%)
Baseline characteristics	
Age	36 (7–59 years old)
Male	16 (57.1%)
mRS 0 before onset	28 (100)
Hypertension	2 (7.1%)
Diabetes mellitus	1 (3.6%)
Dyslipidemia	5 (17.8%)
Smoking	8 (28.6%)
Excessive alcohol drinking	2 (7.1%)
Prior head trauma	1 (3.6%)
Exercise or movement related to the onset	7 (25.0%)
Headache at onset	17 (60.7%)
Findings on admission	
Time between the onset and admission	5.0 (0.8–240 hours)
NIHSS on admission	8 (0–34)
Japan coma scale on admission	1 (0–100)
Glasgow coma scale on admission	15 (15–10)
DWI-ASPECTS on admission	9 (11–1)
Side of Dissection (right)	15 (53.5%)
Dissection with stenosis	20 (71.4%)
Dissection with occlusion	8 (28.6%)
Initial medical treatment	
rtPA	4 (14.3%)
SAPT	9 (32.1%)
Argatroban	4 (14.3%)
Heparin	2 (7.1%)
Heparin+SAPT	2 (7.1%)
Heparin+DAPT	2 (7.1%)
No antithrombotic agent	5 (17.9%), including one case with PTA
Effect of the initial treatment on symptoms and imaging findings	
Improved	5 (17.9%)
No change	9 (32.1%)
Worsened (including temporary ones)	14 (50.0%)
Intervention	9 (32.1%)
Endovascular therapy	8 (28.6%): stenting in 6 and PTA in 2 cases
STA-MCA bypass	1 (3.6%)
Infarction size (on admission vs. at discharge)	
Reduced	4 (14.3%)
No change	14 (50.0%)
Enlarged	10 (35.7%)
Clinical outcome	
NIHSS at discharge	1 (0–18)
Japan coma scale at discharge	0 (0–1)
Glasgow coma scale at discharge	15 (13–15)
mRS at discharge	1 (0–4)

mRS, modified Rankin scale score
NIHSS, National Institutes of Health Stroke Scale
DWI, diffusion-weighted imaging
ASPECTS, Alberta Stroke Program Early Computed Tomography Score
rtPA, recombinant tissue plasminogen activator
SAPT, single antiplatelet therapy
DAPT, dual antiplatelet therapy
PTA, percutaneous transluminal angioplasty
STA, superficial temporal artery
MCA, middle cerebral artery

patients was 36 years (range, 7-59 years). No sex differences were observed. The common risk factors for cerebrovascular disease were less frequent. Headache at onset was reported in 60.7%. Although most patients showed mild to moderate neurological deficits on admission, a few exhibited severe deficits.

Regarding dissection findings, the reported characteristics included tapering stenosis/occlusion in 12, double lumen in seven, pearl and string signs in six, mural hematoma in five, and intimal flap in one case (multiple counts allowed). However, for further statistical analysis, dissection findings were categorized into stenosis (20 cases, 71.4%) or occlusion (8 cases, 28.6%) after confirming available images and/or interviewing the corresponding hospitals. Among 20 patients with stenotic dissections, the distal side of the lesion involved the M1 and/or A1 in 13 cases.

The details of the treatments are presented in Table 1. Various antithrombotic drugs were used as initial medical treatments. In four cases, recombinant tissue plasminogen activator (rtPA) was initially administered under suspected diagnoses of embolic occlusion. In one case, PTA was performed as the initial treatment.

These initial treatments improved or prevented aggravation in 14 patients (50.0%). However, 14 (50.0%) patients showed a degree of aggravation, including temporary aggravation, regarding their symptoms and/or imaging findings (size of infarction or degree of steno-occlusive dissection).

Interventions were performed in nine (32.1%) patients: eight and one were treated with endovascular therapy and with superficial temporal artery-middle cerebral artery (STA-MCA) bypass, respectively. Two patients were treated before the aggravation of symptoms or imaging findings. In addition, seven patients were treated after some aggravation. These interventions led to no complications, and aggravation was stopped or prevented by endovascular therapy. One patient (Case 11) who underwent STA-MCA bypass after aggravation experienced significant postoperative brain edema due to presurgical infarction, necessitating external and internal decompression.

Infarction sizes on admission MRI were compared with those at discharge. Half of the cases showed no change during the course: 10 (35.7%) showed expansion and 4 (14.3%) were judged to have slightly reduced infarction size.

Clinical course of each patient

Table 2 summarizes the clinical course of each patient after admission.

In eight patients whose imaging findings of dissection at diagnosis indicated occlusion, one showed aggravation of symptoms and the other seven showed no aggravation of symptoms or imaging findings. One patient (Case 2) underwent stent placement on day 15 after admission because of asymptomatic partial recanalization with dissection characteristics. A poor outcome of mRS >2 was observed in one patient (Case 5) who had relatively severe neurological deficits on admission and was treated conservatively.

Thirteen of the 20 patients with stenotic dissections showed aggravation of symptoms and/or imaging findings. Six and two of these patients underwent stent placement and PTA, respectively, without procedural complications. The time between onset and admission for 11 of the 13 patients experiencing aggravation was within 6.5 h, whereas only one case showed aggravation in six admitted later than 10 h after onset.

Five of the eight patients with an mRS >2 at discharge (Cases 10, 13, 14, 16, and 27) demonstrated moderate to severe neurological deficits on admission and were treated medically with or without subsequent aggravation. Although three other patients (Cases 11, 19, and 22) underwent intervention (one bypass surgery and two stent placements) after aggravation was confirmed, two showed only mild symptoms on admission.

Thirteen patients showed mild symptoms (NIHSS <4) on admission, 10 of which were uneventful with no aggravation (n = 8) or only temporary aggravation (n = 2) during the course, resulting in good outcomes. After aggravation, three patients (Cases 11, 15, and 19) underwent bypass surgery or endovascular therapy, and two of these resulted in poor outcomes.

Conversely, 15 patients showed moderate to severe symptoms (NIHSS ≧8) on admission, and 9 of these experienced aggravations of symptoms or imaging findings. Five of these patients with aggravation underwent endovascular therapy (stent or PTA), four had good outcomes, and one had poor outcomes at discharge.

Factors related to aggravation in symptoms and/or imaging findings and poor outcomes

Comparisons were performed for various factors between a group of 14 patients without aggravation and another group of 14 who had some aggravation (Table 3). Notably, only dissection imaging findings (stenosis or occlusion) showed a statistically significant difference.

The comparisons between patients with good and poor clinical outcomes are presented in Table 3. The NIHSS and diffusion-weighted imaging (DWI)-Alberta Stroke Program Early Computed Tomography Score (ASPECTS) on admission showed statistically significant differences. However, imaging findings of dissection showed no difference.

Furthermore, univariate and multivariate logistic regression analyses were performed to evaluate factors related to aggravation after admission and clinical outcome at discharge. Using univariate analysis, dissection with stenosis was a predictor of aggravation (odds ratio (OR), 13.0; 95% confidence interval (CI), 1.32-128; p = 0.028) and NIHSS and DWI-ASPECTS on admission were predictors of poor

Table 2 Clinical course of each patient after admission

Case No.	Age	Sex	NIHSS	Side	DWI-ASPECTS	Dissection findings	Timing of admission, aggravation, and intervention (if any)				mRS at discharge
							≦24h	Day 1–3	Day 4–7	Day 8–15	
1	16	F	11	R	9	occlusion	◎ 1 h	Agg.→medication			2
2	57	M	12	R	11	occlusion	◎ 1 h			Stent	0
3	36	M	10	R	11	occlusion	◎ 1.5 h				1
4	16	M	2	L	9	occlusion	◎ 9 h				2
5	45	M	18	L	1	occlusion	◎ 18.5 h				4
6	7	F	12	L	9	occlusion	◎ 23 h				1
7	42	F	0	L	11	occlusion	◎ 24 h				0
8	48	F	0	R	10	occlusion			◎ 10 d		0
9	16	M	9	R	6	stenosis	◎ 1 h		Agg.→Stent		1
10	14	M	10	R	6	stenosis	◎ 1 h	Agg.→ Medication			4
11	13	M	2	R	8	stenosis	◎ 2 h		Agg.→Bypass		4
12	28	F	8	R	10	stenosis	◎ 2 h Agg.#→PTA				1
13	39	F	14	R	3	stenosis	◎ 2 h				3
14	27	M	16	R	7	stenosis	◎ 2.5 h	Agg. (temporary)			3
15	54	F	2	L	8	stenosis	◎ 3 h	Agg.→PTA			2
16	48	F	34	L	7	stenosis	◎ 3 h	Agg. (temporary)			3
17	59	M	2	L	8	stenosis	◎ 4 h	Agg. (temporary)			1
18	47	F	12	R	9	stenosis	◎ 4.5 h	Agg.→Stent			2
19	28	M	1	R	10	stenosis	◎ 4.9 h	Agg.→Stent			3
20	34	F	1	L	10	stenosis	◎ 5 h				0
21	36	M	13	R	8	stenosis	◎ 5 h	Agg.→Stent			0
22	9	M	14	L	7	stenosis	◎ 6.5 h	Agg.→Stent			4
23	43	F	3	L	7	stenosis	◎ 10 h				0
24	41	M	3	R	7	stenosis	◎ 16 h				0
25	13	F	1	R	7	stenosis	◎ 17 h				1
26	34	M	1	L	10	stenosis		◎ 3 d			1
27	48	M	8	L	9	stenosis			◎ 7 d		3
28	40	M	3	L	8	stenosis				◎ 10 d Agg. (temporary)	1

NIHSS, National Institutes of Health Stroke Scale on admission
DWI, diffusion-weighted imaging
ASPECTS, Alberta Stroke Program Early Computed Tomography Score
Aggravation (Agg.), aggravation in clinical symptoms and/or imaging findings (infarction size or degree of stenosis)
mRS, modified Rankin scale
◎ n h: Admission to the index hospital n hours after the onset
PTA: percutaneous transluminal angioplasty
#Case 12 was treated with PTA immediately after the initial diagnosis with NIHSS 8 and was considered during aggravation.

Table 3 Factors associated with aggravation after admission and clinical outcomes

		Aggravation*			Clinical outcome at discharge		
		no (n = 14)	yes (n = 14)	*p*-value	mRS 0-2 (n = 19)	mRS 3-5 (n = 9)	*p*-value
Age (median, range)		40 (7–57)	28 (9–59)	0.45**	36 (7–59)	28 (9–48)	0.46**
Sex	Male	7	9	0.70†	9	7	0.22†
	Female	7	5		10	2	
NIHSS on admission		3.0 (0–18)	9.5 (1–34)	0.20**	3 (0–13)	14 (1–34)	0.030**
Side	Right	6	9	0.45†	10	5	0.10†
	Left	8	4		9	4	
Dissection finding	Occlusion	7	1	0.033†	7	1	0.21†
	Stenosis	7	13		12	8	
DWI-ASPECTS on admission		9 (1–11)	8 (6–10)	0.23**	9 (6–11)	7 (1–10)	0.019**
Initial antithrombotic therapy	None	2	3	0.42†	2	3	0.56†
	Antiplatelet	7	2		6	3	
	Anticoagulant	2	4		4	2	
	Antiplat/coag	1	3		4	0	
	Alteplase	2	2		3	1	
Aggravation*	No				11	3	0.42†
	Yes				8	6	
Any surgical therapy	No				14	6	1.0†
	Yes				5	3	

*, aggravation in clinical symptoms and/or imaging findings (infarction size or degree of stenosis).
mRS, modified Rankin scale
NIHSS, National Institutes of Health Stroke Scale
DWI, diffusion-weighted image
ASPECTS, Alberta Stroke Program Early CT Score
Antiplat/coag, both antiplatelet and anticoagulant therapy
**, Mann-Whitney U test.
†, Fisher's exact test.

clinical outcomes (OR, 1.19; 95% CI, 1.01-1.40; p = 0.037 and OR, 0.53; 95% CI, 0.29-0.96; p = 0.037). Using multivariate analysis, none of these factors showed statistically significant independence.

Representative cases

Case 11: A 13-year-old boy presented with a headache and left hemiparesis. He was transferred to the emergency department 2 h after onset with an NIHSS score of 2. DWIs performed on admission revealed small hyperintense lesions in the right cerebral hemisphere (Fig. 1A). MRA performed on admission revealed stenosis of the right supraclinoid internal carotid artery (ICA) and M1 segment (Fig. 1B). A right carotid angiogram on the same day demonstrated tapering stenosis of the right C2 portion, immediately distal to the ophthalmic artery (Fig. 1C, D). Stenoses and wall irregularities were observed in the right M1 and A1 segments. Therefore, the patient was treated with heparin. DWI performed 5 days after onset showed infarct expansion (Fig. 1E). In addition, MRA showed aggravation of the right ICA and middle cerebral artery (MCA) stenosis. Medical management was continued because his symptoms were stable. However, he experienced an intractable headache the next day, which was followed by a sudden aggravation of left hemiparesis and consciousness. An emergency right superior temporal artery (STA)-MCA bypass was performed (Fig. 1F). Intraoperatively, the ipsilateral M2 to M4 were confirmed intact without dissection and the bypass was successful. DWI (Fig. 1G) showed infarct expansion on the day after surgery, reflecting acute aggravation that occurred before surgery. Although the bypass effectively prevented further infarct expansion, external and internal decompression was necessary because of brain edema. Finally, the patient was discharged with an mRS score of 4 for rehabilitation.

Case 22: An 8-year-old boy presented with left eye pain, followed by right hemiparesis and aphasia. DWI (Fig. 2A) and MRA (Fig. 2B) at a previous hospital 1 h after onset showed a hyperintense lesion in the left basal ganglia and wall irregularities of the left supraclinoid ICA (arrow) starting from the C2 to the left M1 and A1 portions. He was transferred to our hospital 6.5 h after onset. Although his

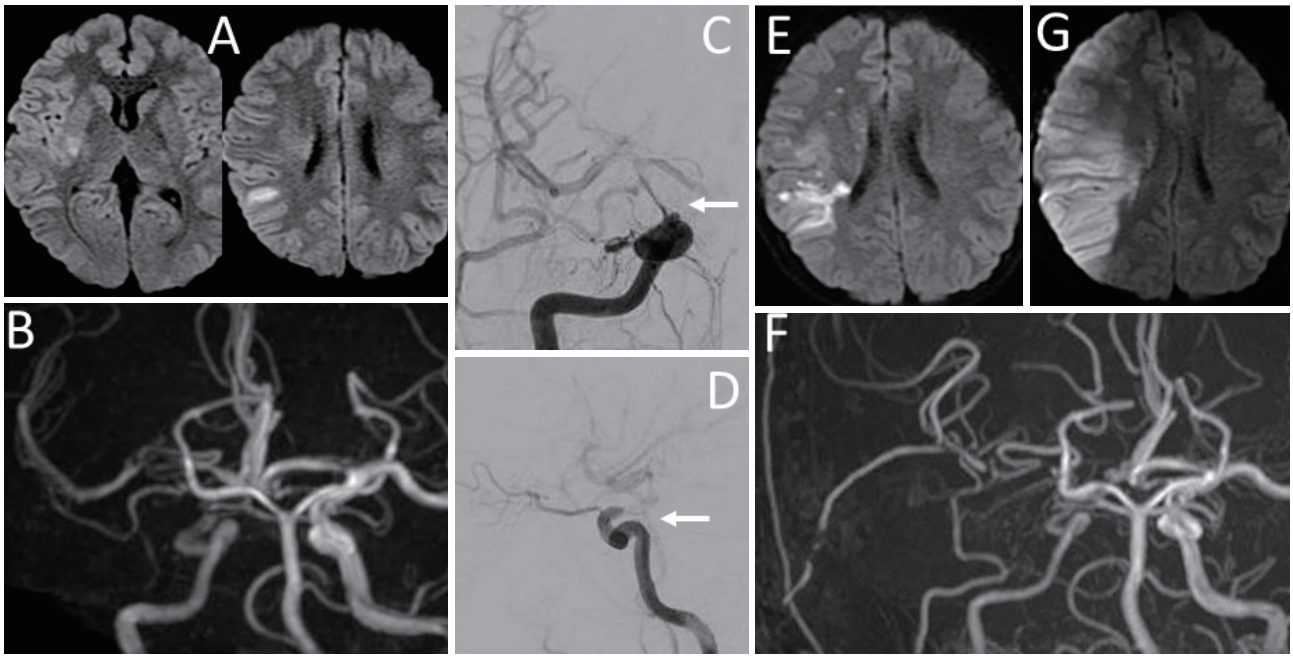

Fig. 1 Case 11. A 13-year-old boy presented with a headache and left hemiparesis. A: DWIs on admission showing small hyperintense lesions in the right cerebral hemisphere. B: MRA on admission demonstrating stenosis of the right supraclinoid ICA and M1. C, D: AP (C) and lateral (D) views of the right carotid angiogram on the same day showing tapering stenosis at the right C2 portion (arrow) just distal to the ophthalmic artery. Stenoses and wall irregularities were found in the right M1 and A1. E: DWI 5 days after the onset showing enlargement of the infarction. MRA at the same time showed some aggravation of the stenosis due to the dissection. F, G: MRA (F) and DWI (G) on the next day after surgery showing good patency of the bypass and enlarged infarction reflecting the preoperative aggravation of the symptoms, respectively.

symptoms were moderate with an NIHSS score of 14, they were stable during the prehospital period. The patient was treated with edaravone. However, the next day, the stenosis of the distal ICA and M1 segments aggravated on MRA (Fig. 2C), and the left carotid angiogram on the same day showed a pearl and string sign starting at the left C2 portion involving M1 and A1 (Fig. 2D). Although his symptoms showed no significant changes after admission, endovascular therapy was prophylactically administered. The angiogram at the end of stenting using Enterprise2™ showed improvement in stenosis (Fig. 2E). The left A1 was iatrogenically occluded. However, the anterior communicating artery provided collateral flow. DWI on the next day (Fig. 2F) revealed infarction, which was similar to that shown in Fig. 2A, except for some edema. The postoperative course was uneventful, and the patient was discharged with an mRS score of 4 for further rehabilitation.

Discussion

The major findings of this study included: First, 14 cases (50%) of the patients experienced some aggravation during initial medical therapies with various combinations of antithrombotic agents. Second, stenotic dissection was a statistically significant risk factor for further aggravation. Third, the endovascular therapies performed in eight patients were effective in improving symptoms or preventing further aggravation.

A possible reason that stenotic dissection was more plausible to be aggravated than did occlusive dissection may be the subsequent thrombotic or thromboembolic formation due to dissection, progression of the degree of stenosis at the site of dissection, or propagation of dissection to more distal sites such as the C1, M1, and/or A1 portions. Oka et al. described a case who underwent bypass surgery after aggravation, demonstrating that not only the ICA but also M1 to M4 portions were involved with dissected intramural hematoma.[4)]

In patients with poor outcomes (mRS at discharge >2, n = 9), the NIHSS and DWI-ASPECTS on admission were more severe than in those with good outcomes. Ten of the 13 patients with mild symptoms (NIHSS on admission <4) were discharged with good outcomes. However, two of the remaining three patients who underwent interventions after aggravation resulted in poor outcomes. Owing to the nature of retrospective studies, it was difficult to extract the effect of interventions compared with the medical therapy alone in patients who showed any degree of aggravation. However, at least when interventions were performed, they would be recommended to be performed before severe aggravation.

Recently, the effectiveness of endovascular therapy using

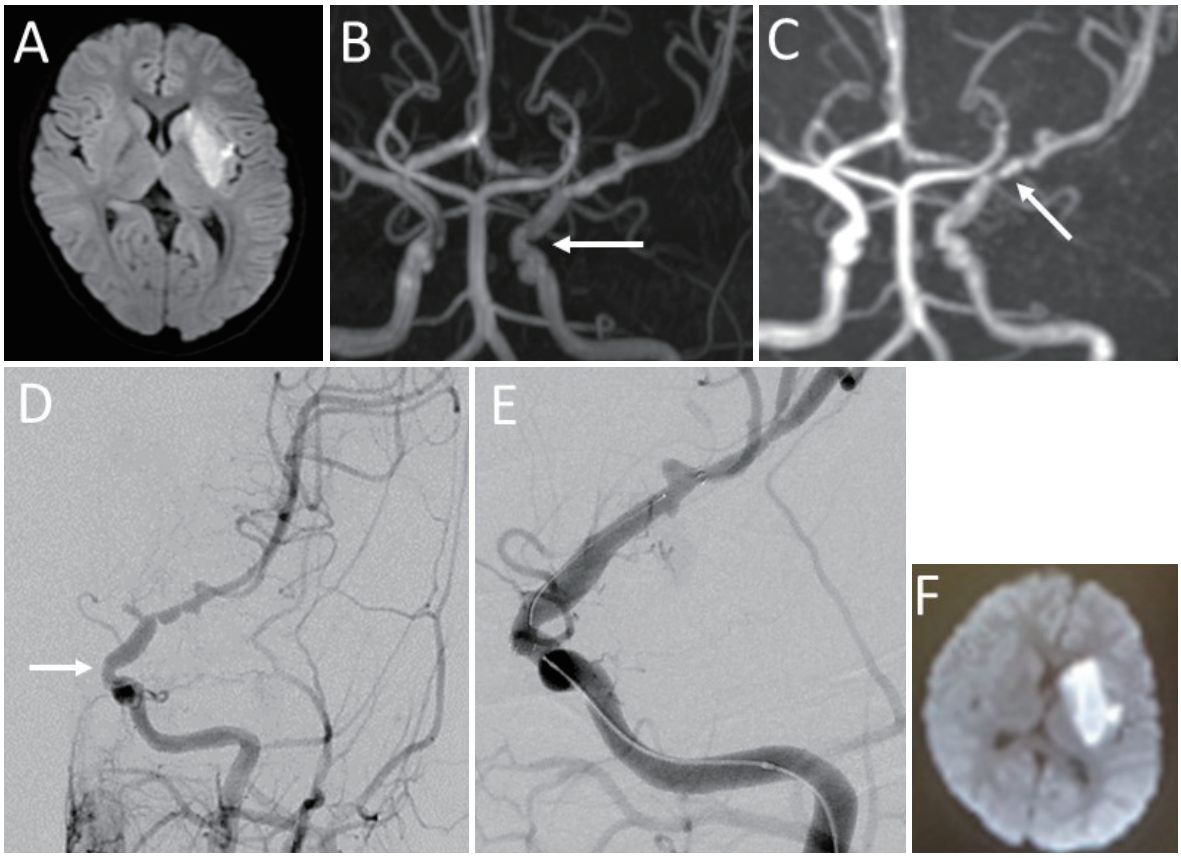

Fig. 2 Case 22. An 8-year-old boy presented with pain in the left eye and subsequent right hemiparesis and aphasia. A, B: DWI (A) and MRA (B) at the previous hospital 1 h after the onset showed a hyperintense lesion in the left basal ganglia and wall irregularities starting from the C2 portion of the left supraclinoid ICA (arrow) to the left M1 and A1 portions. C: MRA on the next day showing an aggravation of the stenosis of distal ICA and M1 (arrow). D: An AP view of the left carotid angiogram on the same day showing a pearl and string sign starting at the left C2 portion (arrow) involving M1 and A1. E: The same angiogram as D at the end of stenting using Enterprise2™ showed an improvement in the stenosis. The left A1 was iatrogenically occluded. However, the anterior communicating artery provided a collateral flow. F: DWI on the next day of the intervention demonstrated infarction in the left basal ganglia, which was similar to that shown in A, except for some edema.

stents has been repeatedly reported.[5-15] In addition, recent guidelines from America[19] and Europe[20] positively have mentioned the use of endovascular therapy. However, questions regarding which timing should be selected for intervention are yet to be addressed. The current results showed that endovascular therapies were effective in improving or at least preventing aggravation with no procedural complications, which may tentatively support an early intervention before or immediately after any aggravation in patients with stenotic dissection. However, further research using prospective studies is required to draw conclusions.

Half of the patients in this cohort responded well to initial medical treatment, primarily with antithrombotic agents. Notably, none of the patients had an mRS score of 5 or 6. This is inconsistent with the results of an early study by Fullerton et al.[3] that evaluated 118 children with dissection of cerebral arteries and reported high mortality (as high as 51%) in those with intracranial ICA dissection. Advance in modalities for early diagnosis and improved medication use were the primary reasons for this improvement. Owing to the lack of hemorrhagic complications in this study, initial treatments of IsICDs may include antithrombotic agents. However, this study could not determine whether antiplatelet or anticoagulant agents were better. In addition, neither the American nor European guidelines[19,20] could specify which was superior to the other. Therefore, more research is warranted in this area.

In this series, four patients (Cases 2, 3, 20, and 21) were initially treated with rtPA, with no hemorrhagic complications and varying outcomes. According to an extensive review[16] and guidelines,[19,20] the use of rtPA for IsICDs is debatable and requires further investigation.

This study has several limitations. First, although this was a nationwide survey, the recruited cases were limited to 28.

Second, 30 initially reported cases were excluded in the final analysis owing to the reasons described in the results

section, most of which were due to dissections in the petrous portion. Different authors' definitions of IsICDs have been published. Some include only intradural lesions,[4,10] whereas others include extradural lesions (petrous and cavernous portions).[16,21] This confusion was encountered in this study because only "intracranial" and not "intradural" were mentioned in the inclusion criteria. Further studies are needed to clarify the precise definition of IsICDs.

Third, owing to the retrospective nature of the study, selection of medications and indications for interventions depended on each hospital. Therefore, this may have resulted in difficulties in statistical power. In addition, the details of the PTAs, stents used, and time course of morphological changes in the dissections were not obtained in this study, which may be a target for further studies.

In conclusion, patients with IsICD who showed stenotic dissection were at risk of further aggravation, and endovascular therapy was effective in improving or preventing aggravation in this study. A prospective study is necessary to evaluate whether early intervention before aggravation could improve the clinical outcomes in patients with IsICD.

Acknowledgments

We want to express our deep gratitude to the following neurosurgery institutes for cooperating with the questionnaire survey: Teine Keijinkai Hospital, Gifu University Hospital, National Cerebral and Cardiovascular Center, Kagawa University Hospital, Asahikawa Medical University Hospital, Red Cross Asahikawa Hospital, Sapporo Medical University Hospital, Hakodate Shintoshi Hospital, Iwate Prefectural Central Hospital, Akita Cerebrospinal and Cardiovascular Center, Kohnan Hospital, Red Cross Nagaoka Hospital, Red Cross Maebashi Hospital, The Jikei University Hospital, Kofu Neurosurgical Hospital, Juntendo University Shizuoka Hospital, Noto General Hospital, Tosei General Hospital, Shiga University of Medical Science Hospital, Ohnishi Neurological Center, Red Cross Himeji Hospital, Shimane Prefectural Central Hospital, Nagasaki University Hospital, Sapporo Teishinkai Hospital, Nakamura Memorial Hospital, Sendai Medical Center, South Miyagi Medical Center, Yamagata City Hospital Saiseikan, Tokyo Metropolitan Geriatric Hospital and Institute of Gerontology, Kitazato University Hospital, Tominaga Hospital, Ainomiyako Neurosurgery Hospital, Okayama University Hospital, and Steel Memorial Yawata Hospital.

Abbreviations

IsICD, intracranial carotid artery dissection causing cerebral ischemia

mRS, modified Rankin scale score

NIHSS, National Institutes of Health Stroke Scale

DWI, diffusion-weighted imaging

ASPECTS, Alberta Stroke Program Early Computed Tomography Score

rtPA, recombinant tissue plasminogen activator

PTA, percutaneous transluminal angioplasty

STA, superficial temporal artery

MCA, middle cerebral artery

Conflicts of Interest Disclosure

All authors have no conflict of interest in this study.

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