Acute and chronic bilateral internal carotid artery occlusion

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Abstract

Purpose: Occlusion of both internal carotid arteries (ICAs) is rare. Clinical manifestations of stroke vary widely. We conducted a retrospective review to compare acute and chronic bilateral ICA occlusion.

Methods: We retrospectively reviewed records of inpatients with acute ischemic stroke and carotid duplex sonography (CDS) during the period from February 2006 to February 2021.

Results: Bilateral ICA occlusion and acute bilateral ICA occlusion accounted for 0.3% and <0.1% of all ischemic stroke cases, respectively. All five patients with acute bilateral ICA occlusion presented with consciousness disturbance. Three patients died within 1 week, and two patients had a vegetative outcome. Pituitary apoplexy with bilateral ICA occlusion was observed in one patient. Forward bilateral ophthalmic arterial flow (OAF) was detected in all three patients who received CDS. Among 13 patients with chronic bilateral ICA occlusion, five and six had modified Rankin Scale (mRS) scores upon discharge of ≥5 and ≤2, respectively; two patients did not have a stroke. Of the 13 patients, 11 had reversed bilateral OAF. Patients with acute bilateral ICA occlusion had a higher rate of initial consciousness disturbance, Glasgow Coma Scale score of ≤9, National Institute of Health Stroke Scale score of ≥20, and mRS score of ≥5. than that of patients with chronic bilateral ICA occlusion.

Conclusion: Patients with acute bilateral ICA occlusion had higher initial stoke severity, poorer collateral circulation, and worse clinical outcomes than did those with chronic bilateral ICA occlusion. Physicians must pay attention to rare causes of acute bilateral ICA occlusion, including pituitary apoplexy.

Keywords: acute ischemic stroke, bilateral internal carotid artery occlusion, carotid duplex sonography, computed tomography angiography, magnetic resonance angiography, ophthalmic arterial flow.

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INTRODUCTION

Occlusion of both internal carotid arteries (ICAs) is a rare cerebral vascular disorder[(1)]. Most strokes occur when the ICA on one side is occluded and result in various degrees of neurological deficits; this is followed by another stroke episode if occlusion occurs in the ICA on the other side. Clinical manifestations of stroke vary widely

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according to the progress of arterial occlusion. The area of infarction may be life-threateningly large in cases of acute occlusion. However, patients may simply have symptoms of dementia or even nonspecific symptoms when chronic occlusion occurs[2]. Acute bilateral ICA occlusion is rare, usually leads to sudden coma, and resembles occlusion of the basilar artery; it reportedly occurred in fewer than 1% of patients in a stroke series[3,4].

Intravenous thrombolysis (IVT) has a low recanalization rate when applied for large vessel occlusion[5], and no patient has been successfully treated with thrombolysis alone. Patients with a stroke of high severity for whom emergent computed tomography angiography (CTA) reveals large vessel occlusion receive endovascular thrombectomy (EVT) at a comprehensive stroke center. The reported incidence of bilateral large vessel occlusion in patients with stroke treated with IVT or EVT is 0.34%[6]. The outcomes of patients with acute bilateral ICA occlusion remained unsatisfactory, even though recanalization of the carotid arteries was achieved within 32 min through the use of simultaneous bilateral thrombectomy[6].

We conducted a retrospective review of patients with bilateral ICA occlusion and compared the cases of acute and chronic bilateral ICA occlusion.

METHODS

We retrospectively reviewed the records of all registered inpatients with acute ischemic stroke and more than 45,000 carotid duplex sonography (CDS) findings for patients with suspected cerebrovascular disease during the period from February 2006 to February 2021. Patients who had occlusion in both ICAs documented by CTA, magnetic resonance angiography (MRA), or CDS were selected for analysis. The following information was collected from the patients' medical records: age and sex; clinical features, including initial presentation, Glasgow Coma Scale (GCS) score, National Institute of Health Stroke Scale (NIHSS) score, risk factors of stroke, length of hospital stay, modified Rankin Scale (mRS) score upon discharge; and imaging findings.

The study was conducted in accordance with the Declaration of Helsinki. Ethical approval for this study was provided by the Institutional Review Board of Taipei Tzu Chi Hospital, New Taipei City (approval no. 10-XD-046). The need for informed written consent was waived because the study was retrospective in nature. All data collected and analyzed in this retrospective study were derived from clinical records with no intervention or influence on clinical treatment. To fully protect patient privacy and rights, only clinical observation data are used for publication; personal information will not be disclosed to any third party without patient consent.

Patients were divided into acute and chronic bilateral ICA occlusion groups. Patients who had acute infarction in both cerebral hemispheres with absent bilateral ICAs, as identified through either CTA or MRA, were classified as having acute bilateral ICA occlusion. Patients with absent bilateral ICAs, as identified through either CTA or MRA, and without acute infarction in both cerebral hemispheres were classified as having chronic bilateral ICA occlusion. We compared the clinical features, initial stroke severities, imaging findings, risk factors, Trial of Org 10172 in Acute Stroke Treatment classifications[7], and outcomes of these two groups of patients.

Continuous variables are presented as the median (first to third quartile). The Mann–Whitney U test was used for intergroup comparison of continuous variables. Chi-square and Fisher's exact tests were used for categorical comparisons. A P value of less than 0.05 was considered indicative of a significant result. All statistical analyses were performed with SPSS (v. 24, SPSS Inc., Chicago, IL, USA).

RESULTS

A total of 18 patients with bilateral ICA occlusion were identified. Among them, 5 and 13 patients were categorized as having acute and chronic occlusion, respectively. Acute stroke symptoms were noted for 15 patients, who accounted for 0.27% of all 5265 inpatients with acute ischemic stroke during the investigated 15-year period. Acute bilateral ICA occlusion was rare, with such cases accounting for <0.1% (5/5265) of all inpatients.

Table 1 summarizes the clinical features of the five patients with bilateral acute ICA occlusion. All patients presented with consciousness disturbance at the emergency department without dominant lateralization of motor weakness. In the initial brain computed tomography

Table 1. Clinical features of five patients with acute bilateral internal carotid artery occlusion

No	Age/ Sex	Initial presentations	Coma Scale/ NIHSS	Imaging findings	Collate-rals	TOAST classifi-cation	Risk factors	Length of stay (days)	Outcome
1	64/ Female	Severe headache, vomiting, and consciousness disturbance	E1V1M4/ NIHSS: 20	CT (D1): pituitary tumor with mild hemorrhage MRA (D2): pituitary apoplexy; bilateral ICAO with acute infarct at bilateral frontal lobes CTA (D3): bilateral cavernous ICA tight stenosis	None	SE	None	7	mRS: 6
2	32/ Male	Severe headache and consciousness disturbance	E2V1M5/ NIHSS: 23	CT (D1): left F-P lobes low density CT (D3): severe edema in the bilateral F-P-T lobes and brainstem CDS (D5): bilateral ICAO with forward bilateral OAF	None	UD	None	7	mRS: 6
3	57/ Female	Consciousness disturbance with right hemiplegia	E2V1M3/ NIHSS: 28	CT (D1): sign of hyperdense left middle cerebral artery CTA (D1): bilateral ICAO CT (D2): severe edema in the bilateral F-P-T lobes and brainstem	Right PCA	CE	SSS, breast cancer	2	mRS: 6
4	73/ Female	Generalized convulsion and consciousness disturbance	E1V1M4/ NIHSS: 26	CT (D1): no acute lesions MRA (D1): bilateral ICAO with acute infarction at the bilateral F-P lobes CDS (D2): highly resistant flow in the bilateral ICAs with forward bilateral OAF CTA (D3): bilateral ICA occlusion with diffuse edema in the bilateral F-P lobes	None	LAA	HT, DM, HD	16	mRS: 5 Vegetative Loss of FU
5	75/ Male	Speech, gait, and consciousness disturbance	E3V1M5/ NIHSS: 27	CT (D1): no acute lesions MRA (D2): bilateral ICAO with acute infarct at the bilateral F lobes CT (D7): diffuse edema in the bilateral F-P-T lobes CDS (D8): bilateral proximal ICA and forward bilateral OAF	Bilateral ECAs	LAA	HT, DM	34	mRS: 5 Vegetative Loss of FU

CDS: carotid duplex sonography, CE: cardioembolism, CTA: computed tomography angiography, D: day, DM: diabetes mellitus, ECA: external carotid artery, F: frontal, FU: follow up, HD: heart disease, HT: hypertension, ICAO: internal carotid artery occlusion, LAA: large-artery atherosclerosis, MRA: magnetic resonance angiography, mRS: modified Rankin Scale, NIHSS: National Institute of Health Stroke Scale, OAF: ophthalmic arterial flow, P: parietal, PCA: posterior cerebral artery, SE: special etiology, SSS: sick sinus syndrome, T: temporal, TOAST: Trial of Org 10172 in Acute Stroke Treatment, UD: undetermined

(CT), abnormal lesions corresponding to the clinical features were recognized in three patients—a hemorrhagic pituitary tumor, a low-density lesion in the frontoparietal lobes, and a hyperdense arterial sign in the middle cerebral artery (MCA), respectively. Diagnosis of acute bilateral ICA occlusion was confirmed through rapid CTA or MRA

on the day of symptom onset or the following day. Only one patient received IVT treatment. No patients received EVT because it was not yet available or the patients were ineligible according to the relevant guidelines. No collateral circulation for bilateral ICA occlusion was observed in three patients. Three patients died within 1 week, and two patients had a vegetative outcome and received tracheostomy before being discharged. Patient 1 presented with acute onset of severe headache and vomiting followed by consciousness disturbance due to the bilateral cavernous ICAs being compressed during pituitary apoplexy, causing acute occlusion of both ICAs and infarcts involving both frontal lobes (Figure 1). Although CTA on day 3 revealed that the bilateral anterior cerebral arteries (ACAs) and MCAs regained perfusion through the bilateral tight stenotic ICAs, the patient still died. Patient 3 presented with disturbed consciousness with right hemiplegia. Emergent brain CT showed a left hyperdense MCA sign (Figure 2). She received IVT treatment, and brain CTA immediately after thrombolysis revealed the absence of bilateral ICAs and left MCA with collateral flow from the right posterior cerebral artery (PCA) to the right MCA. She did not receive further EVT treatment because she had an Alberta Stroke Program Early CT (ASPECT) score of <6.8,9 Follow-up brain CT revealed diffuse low-density regions with edematous change of the bilateral hemispheres and brainstem, suggesting total occlusion of the bilateral ACAs and MCAs. She died early on the second day of hospitalization. She had previously received pacemaker implantation for sick sinus syndrome. We speculated that she had a cardiogenic embolus causing occlusion of the left ICA and a subsequent embolus causing right ICA occlusion. Patient 4 presented with generalized convulsion and disturbed consciousness. Emergent MRA revealed occlusion of the bilateral ICAs with acute infarcts involving both hemispheres without collateral flow (Figure 3). CDS showed that the patient had patent bilateral proximal ICAs with extremely highly resistant flow and forward bilateral ophthalmic arterial flow (OAF), indicating tight stenosis or occlusion in the bilateral distal ICAs. Brain CTA on day 3 revealed occlusion of the

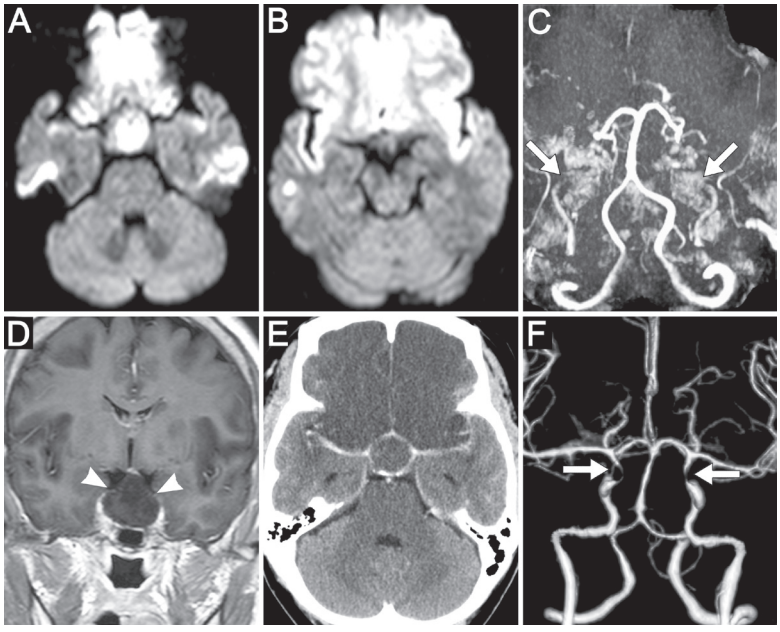

Figure 1. Imaging studies of patient 1 with acute bilateral ICA occlusion. (A, B) Diffusion-weighted MRI on day 2 showed acute infarctions involving the pituitary gland and bilateral frontal lobes. (C) MRA showed interruption of the bilateral ICAs at cavernous portions (arrows). (D) T1-weighted coronal view of brain MRI indicates enlarged pituitary gland (arrowheads). (E) Enhanced axial view of brain CT findings on day 3 revealed enlarged pituitary gland with acute bilateral frontal infarctions and patent bilateral MCAs. (E) Brain CTA on day 3 revealed tight stenosis of the bilateral ICAs at cavernous portions (arrows) with patent bilateral ACAs and MCAs.

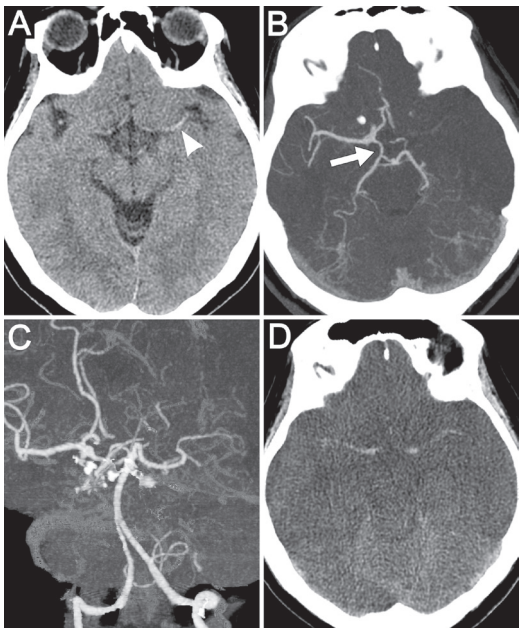

Figure 2. Imaging studies of patient 3 with acute bilateral ICA occlusion. (A) Axial view of brain CT findings on day 1 revealed a sign of hyperdensity of the left MCA (arrowhead). (B and C) CTA on day 1 showed absent bilateral ICAs and left MCA with collateral flow from the right PCA to right MCA (arrow). (D) Brain CT on day 2 revealed acute infarction with diffuse edematous change involving both frontoparietotemporal lobes.

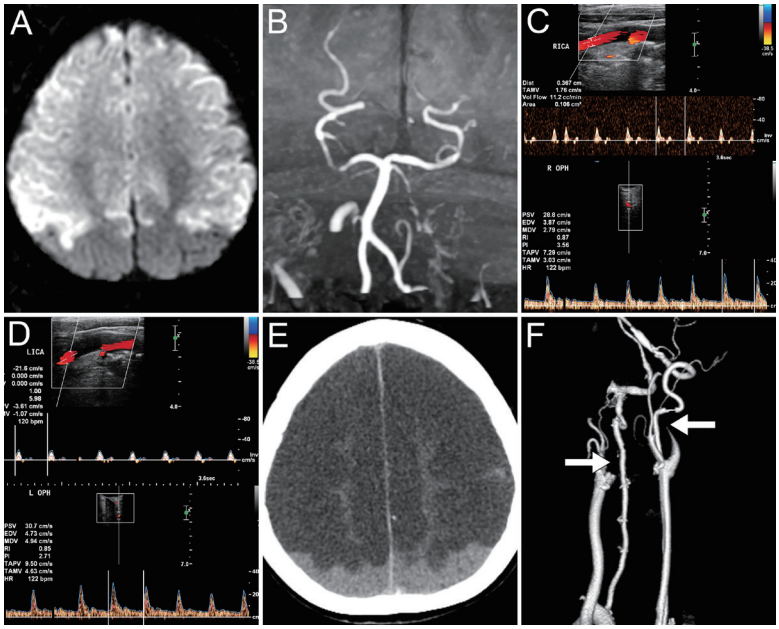

Figure 3. Imaging studies of patient 4 with acute bilateral ICA occlusion. (A) Axial view of diffusion-weighted MRI findings on day 1 indicated acute infarction involving both frontoparietal lobes. (B) MRA revealed absent bilateral ICAs. (C and D) CDS on day 2 showed patent bilateral proximal ICAs with extremely highly resistant flow (upper half) and forward bilateral OAF (lower half). (E) Axial brain CT on day 3 revealed acute infarction with diffuse edematous change involving both frontoparietal lobes. (F) Brain CTA on day 3 showed occlusion of the bilateral proximal ICAs (arrows).

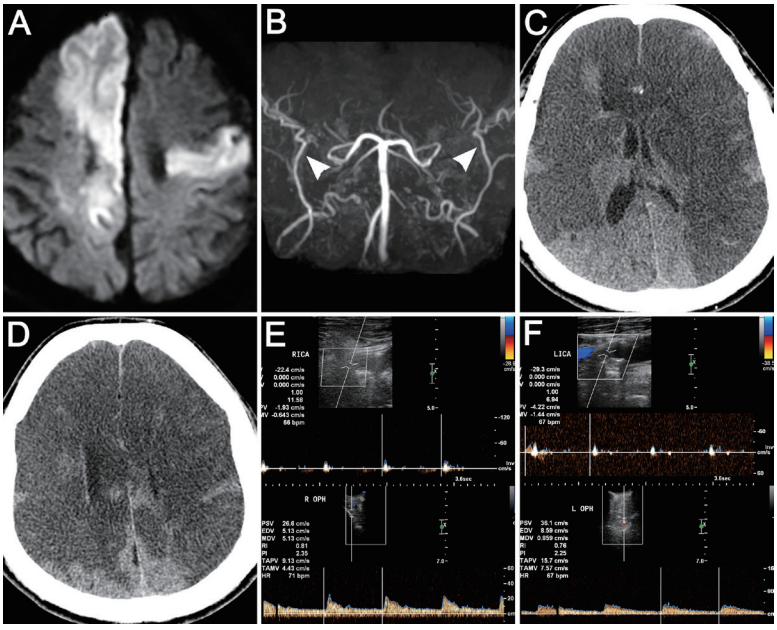

Figure 4. Imaging study results of patient 5 with acute bilateral carotid occlusion. (A) Axial view of diffusion-weighted MRI findings showed acute infarction involving the right high frontal and left frontal lobes. (B) MRA revealed absent bilateral ICAs with collateral flow from the bilateral external arteries (arrowheads) to bilateral MCAs. (C and D) Axial view of the brain CT findings on day 7 revealed acute infarction with diffuse edematous change involving both frontoparietotemporal lobes. (E and F) CDS on day 8 showed occlusion of the bilateral proximal ICAs (upper half) with forward bilateral OAF (lower half).

bilateral ICAs from the proximal ICAs. We speculated that she had distal occlusion of bilateral ICAs with retrograde thrombosis to the proximal ICAs. Patient 5 developed progressive slurred speech and unsteady gait, followed by consciousness disturbance. He was transferred to the emergency department 12 hours later. Although the initial brain CT did not show any acute lesions, brain MRA on the second day revealed absent bilateral ICAs with acute infarcts involving both frontal lobes (Figure 4). His general condition did not improve during hospitalization. Follow-up brain CT on day 7 indicated extensive low densities with edematous change involving the bilateral frontoparietotemporal lobes. Patients 4 and 5 were discharged with a vegetative status and after undergoing tracheostomy.

Table 2 summarizes the details of the 13 patients with chronic bilateral ICA occlusion. Five patients had a history of stroke and an acute infarct on a single side of the brain. Among them, four patients had an initial NIHSS score between 16 and 20 and a discharge mRS score of ≥5. Another five patients had an acute infarct on a single side of the brain without a history of stroke; among them, one patient had an mRS score upon discharge of 5 and the other three had an mRS score upon discharge of ≤2. One patient was found to have bilateral ICA tight stenosis during an acute stroke 10 years previously. He decided on medical treatment without carotid stenting. Bilateral proximal ICA total occlusion was noted during serial follow-up CDS studies, and he has remained stroke free for 10 years. Another two patients with multiple risk factors presented with the nonspecific symptom of intermittent dizziness and were found to have bilateral ICA occlusion. They received medical treatment and have remained in a stable clinical condition for 3 and 10 years, respectively. Of the 13 patients, 11 had reversed bilateral OAF. One patient who had forward bilateral OAF was classified as having cardioembolism from chronic atrial fibrillation and died during hospitalization. The conditions of two patients were classified as having a special etiology due to a history of radiotherapy for oral and laryngeal

Table 2. Clinical features of 13 patients with chronic bilateral internal carotid artery occlusion

No	Age/ sex	Initial presentations	Coma Scale/ NIHSS	Imaging findings	Collate-rals	TOAST classify-cation	Risk factors	Length of stay (days)	Outcome
1	91/ Male	Right limb weakness with aphasia	E3VAM5-6/ NIHSS: 16	CT (D1): multiple old infarcts CT (D7): acute infarct at the left F-P-T lobes CDS (D14): bilateral ICAO with forward bilateral OAF	Right PCA	CE	HT, DM, AF, prior stroke	60	mRS: 6
2	79/ Male	Consciousness disturbance	E1V1M2/ NIHSS: 20	CT (D2): acute infarct at the right F-T lobes and old infarct at the right T-P lobes MRA (D5): bilateral ICAO with acute infarction at the right F-T lobes CDS (D5): highly resistant flow in the right ICA and left ICAO with reversed bilateral OAF	Right PCA	LAA	HT, HD, and prior stroke	30	mRS: 5 Expired 11 months later
3	60/ Male	Left limb twitching with change in consciousness, prior stroke with sequela of left hemiparesis	E2V1M3 NIHSS: 17	CT (D1): acute left subcortical infarct and old right subcortical infarct MRA (D5): bilateral ICAO with left subcortical infarct CDS (D10): bilateral ICAO with reversed bilateral OAF	Right PCA	LAA	Prior stroke	51	mRS: 5 Tracheostomy Loss of FU
4	75/ Male	Left limb weakness with slurred speech	E4V4M6/ NIHSS: 10	CT (D1): no acute lesions MRA (D2): bilateral ICAO with acute infarct at the right F lobe CDS (D3): bilateral ICAO with reversed bilateral OAF	Both PCAs	SE	HT, DM, HL, RT for neck cancer	50	mRS: 5 Tracheostomy Loss of FU
5	67/ Male	Right limb weakness with aphasia, prior stroke with sequela of right hemiparesis	E3VAM5-6/ NIHSS: 20	CT (D1): old right subcortical infarct MRA (D2): bilateral ICAO with acute infarct at the left F-T lobes CDS (D10): right CCAO and bilateral ICAO with reversed bilateral OAF	Right PCA	LAA	HT and prior stroke	30	mRS: 5 Loss of FU
6	60/ Male	Right limb weakness during hospitalization for infection	E4V5M6/ NIHSS: 3	MRA: bilateral ICAO with acute left subcortical infarct CDS: bilateral ICAO with reversed bilateral OAF	Right ECA + left PCA	LAA	HT, DM, HL	8	mRS: 2 FU for 4 years
7	83/ Male	Prior stroke with sequela of right hemiparesis, admitted for pneumonia	E4V5M6	MRA: bilateral ICAO with old infarct at the left F lobe CDS: bilateral ICAO with reversed bilateral OAF	Both PCAs	LAA	HT, HD, prior stroke	8	mRS: 2 Loss of FU

Table 2. Clinical features of 13 patients with chronic bilateral internal carotid artery occlusion (Continue)

No	Age/ sex	Initial presentations	Coma Scale/ NIHSS	Imaging findings	Collate-rals	TOAST classify-cation	Risk factors	Length of stay (days)	Outcome
8	62/ Male	Right limb weakness with aphasia	E3VAM6/ NIHSS: 12	CT (D1): no acute lesions MRA (D3): bilateral ICA tight stenosis with acute infarct at the left F-T lobes CDS (D5): bilateral ICA critical stenosis with reversed bilateral OAF CDS (10 years later): bilateral ICAO with reversed bilateral OAF	Both PCAs	LAA	HT, DM	10	mRS: 1 FU for 10 years
9	64/ Male	Right limb weakness	E4V5M6/ NIHSS: 2	CT (D1): no acute lesions CDS (D2): Right CCAO and left ICAO with reversed bilateral OAF MRA (D5): bilateral ICAO and right CCAO with acute right subcortical infarct	Both PCAs	LAA	HT, DM, HL, AF, SM	15	mRS: 1 FU for 4 years
10	81/ Male	Left limb weakness with slurred speech	E4V5M6/ NIHSS: 4	CT (D1): no acute lesions CDS (D3): bilateral ICAO with reversed bilateral OAF	Both PCAs	LAA	HT, HD	3	mRS: 1 FU for 4 years
11	60/ Male	Prior stroke with sequela of left hemiparesis	E4V5M6	CT: old right putaminal hemorrhage MRA: bilateral ICAO with old right putaminal hemorrhage CDS: bilateral ICAO with forward bilateral OAF	Both ECAs	LAA	HT, DM, HL, SM, prior stroke		mRS: 1 FU for 11 years
12	83/ Female	Intermittent dizziness	E4V5M6	MRA: bilateral ICAO without stroke CDS: bilateral ICAS with reversed right OAF	Right PCA + left ECA	LAA	HT, HL, paroxysmal AF		mRS: 0 FU for 10 years
13	84/ Female	Intermittent dizziness	E4V5M6	CDS: occlusion in the bilateral CCAs and ICAs with reversed left OAF MRA: occlusion in the bilateral CCAs and ICAs	Both PCAs	SE	HT, HL, AF, RT for oral cancer		mRS: 0 FU for 3 years

AF: atrial fibrillation, CDS: carotid duplex sonography, CE: cardioembolism, CTA: computed tomography angiography, D: day, DM: diabetes mellitus, ECA, external carotid artery, F: frontal, FU: follow up, HD: heart disease, HL: hyperlipidemia, HT: hypertension, ICAO: internal carotid artery occlusion, LAA: large-artery atherosclerosis, MRA: magnetic resonance angiography, mRS: modified Rankin Scale, NIHSS: National Institute of Health Stroke Scale, OAF: ophthalmic arterial flow, P: parietal, PCA: posterior cerebral artery, RT: radiotherapy, SE: special etiology, SM: smoking, T: temporal, TOAST: Trial of Org 10172 in Acute Stroke Treatment.

Table 3. Comparison of clinical features between patients with acute versus chronic bilateral internal carotid occlusion

Characteristics	Acute ICAO (n = 5)	Chronic ICAO (n = 13)	P value
Age (years)	64 (44.5–74)	75 (61–83)	0.125
Male sex	2 (40%)	11 (84.6%)	0.099
Presentations			
Conscious disturbance	5 (100%)	2 (15.4%)	0.003
Glasgow Coma Scale score ≤ 9	5 (100%)	4 (30.8%)	0.029
NIHSS score ≥ 20	5 (100%)	2 (15.4%)	0.003
TOAST classification			
Large-artery atherosclerosis	2 (40%)	10 (76.9%)	0.268
Imaging findings			
No collateral flow observed	3 (60%)	0 (0.0%)	0.012
Forward ophthalmic arterial flow	3/3 (100%)	2/13 (15.4%)	0.018
Outcomes			
Modified Rankin Scale score ≥ 5	5 (100%)	5 (38.5%)	0.0359

Data are expressed as median (1st -3rd quartile) or n (%); Mann-Whitney U or Fisher's exact test was conducted
ICAO: internal carotid artery occlusion

cancers.

Table 3 compares the clinical features of the patients with acute versus chronic bilateral ICA occlusion. Compared with the patients with acute bilateral ICA occlusion, those with chronic bilateral ICA occlusion were older and more likely to be female, but the results were not significant owing to the small sample size. All the patients with acute bilateral ICA occlusion had a GCS score of ≤9 and NIHSS score of ≥20 as well as higher initial stroke severity and a higher rate of consciousness disturbance compared with the patients with chronic bilateral ICA occlusion. Collateral flow, either from the PCA or the external carotid artery (ECA), was observed in all patients with chronic bilateral ICA occlusion. Forward bilateral OAF was detected in 2 of 13 patients with chronic bilateral ICA occlusion (15.4%) but in 3 of 3 patients with acute bilateral ICA occlusion (100%). Compared with the patients with chronic bilateral ICA occlusion, among whom 38.5% had a poor outcome (mRS score ≥ 5), the patients with acute bilateral ICA occlusion had much poorer outcomes (100% of patients had an mRS score of ≥5).

DISCUSSION

This study discovered that bilateral ICA occlusion is rare, accounting for only 0.28% of all ischemic stroke cases; this percentage is similar to that in a previous report (0.27%) by Kwon et al[3]. Acute bilateral ICA occlusion is even rarer, accounting for <0.1% of all ischemic stroke cases. Patients with acute bilateral ICA occlusion had higher initial stoke severity, poorer collateral circulation, and worse clinical outcomes than did patients with chronic bilateral ICA occlusion.

Fisher described 11 patients with bilateral ICA occlusion in an autopsy patient study conducted in 1954[2]. Among them, six patients presented with bilateral neurological signs and coma, whereas five patients presented with dementia. Although not explicitly stated, 2 of the 11 patients are assumed to have had acute bilateral ICA occlusion. Only a few cases of bilateral ICA occlusion, either acute or chronic, have been reported to date. AbuRahma et al. reported on 21 patients with bilateral ICA occlusion in 1998[1]. Sixteen patients had clinical presentation of transient ischemic attack, and five patients had stroke. None of the five patients with stroke had acute bilateral ICA occlusion. Kwon et al. reported six patients with acute bilateral ICA occlusion presenting with sudden loss of consciousness, quadriplegia, and initially intact brainstem reflexes, but these patients died within three days[3]. In 2011, Kim et al. described two patients with acute bilateral ICA occlusion associated with a variant of aortic arch branching who presented with abrupt coma and quadriplegia[10]. With the development

of EVT treatment for acute stroke, more patients with acute bilateral ICA occlusion can be identified during the hyperacute stage of stroke through brain CTA. A review conducted by Ota et al. in 2018 revealed that of nine patients with acute bilateral ICA occlusion, eight died despite intra-arterial thrombolysis or EVT treatment[10]. A review conducted by Jeromel et al. in 2020 revealed that seven patients with acute bilateral ICA or MCA occlusion received EVT treatment[12]. However, only one patient had acute bilateral ICA occlusion with a fatal outcome. Larrew et al. performed simultaneous bilateral thrombectomy through bilateral groin access in a patient with acute bilateral ICA occlusion and achieved favorable recanalization of both ICAs within 32 min in 2020[6]. However, this patient still died. In the present study, EVT treatment had not yet been developed when patients 1 and 2, who had acute bilateral ICA occlusion, were hospitalized. Additionally, EVT treatment was not administered to patients 3, 4, or 5, who had acute bilateral ICA occlusion, because of a prolonged prehospital delay beyond the recommended therapeutic window and an excessively low ASPECT score according to brain CT.

Pituitary apoplexy refers to acute neurologic symptoms owing to infarction or hemorrhage within the pituitary gland. The reported incidence of pituitary apoplexy ranges from 0.6% to 10%, depending on the definition[13-15]. The main symptoms of pituitary apoplexy are headache, visual disturbance, and altered consciousness. Acute stroke caused by pituitary apoplexy is extremely rare; only 46 cases were reported for the period 1950–2018 in Jiang's review, with the mortality rate being 26.8%[15], and only 29 cases were reported for the period 1990–2019 in Elarjani's review, with the mortality rate being 24%[14]. Compression of adjacent arteries by an enlarged pituitary tumor and vasospasms due to tumor bleeding are the two main pathophysiological mechanisms of stroke[14,15]. The mortality rate was higher in patients for whom multiple intracranial arteries were involved. Acute bilateral ICA occlusion due to pituitary apoplexy was observed in 5 of 46 patients (11%) in Jiang's review and in 7 of 29 patients (24%) in Elarjani's review, with fatal outcomes occurring in 40% (2/5) and 43% (3/7) of patients, respectively. Patient 1 in the present study, who had acute bilateral ICA occlusion, reported experiencing severe headache followed by disturbed consciousness due to pituitary apoplexy with mechanical compression of the bilateral cavernous ICA, causing acute infarction of the bilateral frontal lobes. Early recognition of pituitary apoplexy–induced stroke is crucial for treatment. Neither IVT nor EVT are appropriate treatments in such situations. Surgical treatment, such as transphenoid decompressive surgery, was not performed for patient 1 owing to unstable vital signs. Although follow-up CTA on day 3 revealed recanalization of bilateral ACAs and MCAs through bilateral tight stenotic cavernous ICAs, the patient died of extensive cerebral infarction.

Cardioembolism and large-artery atherosclerosis are the two most common etiologies of acute bilateral ICA occlusion[3,12]. Cardioembolism has been presumed to constitute the majority of causes in previously reported cases. Eight of nine patients in Jeromel's review12 and three of six patients in Kwon's series3 were classified as having cardioembolism. A multicenter review of patients treated with EVT found that in 70% of cases of multivessel occlusion, the cause was cardioembolic[16]. In the present study, only one patient, who had sick sinus syndrome, among five patients with acute bilateral ICA occlusion was classified as experiencing cardioembolism. No definite cause could be recognized in patient 2, who was a young man with no known traditional risk factors or heart disease. Collateral flow for anterior circulation in acute bilateral ICA occlusion is usually inadequate, particular for patients with cardioembolism. No intracranial flow was observed in the ACA or MCA in three patients with acute bilateral ICA occlusion. Patient 3 had collateral flow from the right PCA to the right ACA and MCA (Figure 2B, C). Follow-up brain CT revealed diffuse infarction in both hemispheres, indicating recurrent embolic stroke causing total occlusion of the right MCA. Although patient 5 initially had collateral flow from the bilateral ECAs to bilateral MCAs (Figure 4B), diffuse bilateral hemisphere infarction eventually occurred due to failed collateral flow. A recent study found that large-artery atherosclerosis was the main cause of acute bilateral hemisphere infarction in the anterior circulation[17]. Nevertheless, large-artery atherosclerosis superimposing a cardioembolism may contribute to the etiology in older patients with multiple risk factors and atrial fibrillation.

The most common etiology of chronic bilateral ICA occlusion is large-artery atherosclerosis. In contrast to

patients with acute bilateral ICA occlusion, those with chronic bilateral ICA occlusion may develop more collateral flow. In the present study, 10 of 13 patients (77%) were classified as having large-artery atherosclerosis. Two of our patients with a history of radiation therapy for oral or neck cancer were classified as having a disease with a special etiology, and the long-term effects of radiotherapy could accelerate the progression of atherosclerosis causing thrombotic occlusion of the bilateral ICAs[18]. Only one patient with chronic atrial fibrillation was classified as having cardioembolism despite the coexistence of other traditional risk factors. Four of five patients with first-ever stroke had a favorable outcome with a discharge mRS score of ≤2 and continued to be stroke free under medications for 4–11 years, whereas four of five patients with a history of stroke had a poor outcome with a discharge mRS score of ≥5. This accords with Fisher's report, in which four of six patients had hemiplegia-producing initial occlusion in one carotid system and the final neurological picture resembled thrombosis of the basilar artery due to occlusion on the other side of the carotid artery several years later[2]. Agnoletto et al. reported that in one patient, chronic right ICA occlusion was compensated for by collateral flow, and this patient developed acute left MCA syndrome due to acute occlusion of the left ICA[19]. The patient recovered immediately after successful angioplasty and stenting of the left carotid artery. Huang et al. suggested that in addition to the time window, clinical status, and location of vessel occlusion, the restored capacity of collateral circulation in large-artery atherosclerosis plays a major role in achieving favorable outcomes compared with those of cardioembolism after EVT[20]. Chronic bilateral ICA occlusion can be asymptomatic or present with subtle clinical symptoms other than cerebrovascular events. In Fisher's report, chronic bilateral ICA occlusion was observed in five patients with dementia[2]. In the present study, two patients with multiple risk factors who had been receiving regular medical treatment for several years were incidentally discovered to have chronic bilateral ICA occlusion during a screening study in which CDS was used for intermittent dizziness.

All but two patients with chronic bilateral ICA occlusion had reversed bilateral OAF. Reversed OAF, which is retrograde ophthalmic filling from the ECA, is highly specific to severe ipsilateral ICA stenosis or occlusion[21]. It has been postulated to indicate reduced perfusion of the hemisphere ipsilateral to the stenotic or occluded ICA[21]. Reversed OAF occurred more frequently in symptomatic than asymptomatic patients with stenotic or occluded ICA, and asymptomatic patients with reversed OAF were more likely to experience subsequent ischemic events than were those with forward OAF[22]. In the present study, reversed bilateral OAF implied a progressive atherosclerotic change in the ICA, probably with inadequate collateral circulation. Forward bilateral OAF detected in three patients with acute bilateral ICA occlusion did not indicate better collateral flow but rather a sudden interruption of bilateral ICA flow to both hemispheres at a level distal to the bilateral ophthalmic arteries without the establishment of quick and successful collateral flow.

This study had some limitations. First, considerable progress was made in the treatment for acute ischemic stroke during the 15-year period of patient selection in this study. The development of IVT and EVT treatments may have influenced patient outcomes. Huang et al. reported dramatic reductions in stroke severity after bilateral thrombectomy, as indicated by a decrease in the NIHSS score from 24 to 16 at the 3-month follow-up[20]. Although most patients still have poor outcomes after EVT treatment, EVT is expected to have benefits. Second, the exact incidence of asymptomatic chronic bilateral ICA occlusion was unclear. We reviewed both inpatients with acute ischemic stroke and outpatients who received CDS at our sonographic laboratory. In accordance with the regulations of the National Health Insurance Administration in Taiwan, patients without symptoms of cardiovascular or cerebrovascular disease, such as dementia, were usually not candidates for CDS. Therefore, older patients with multiple risk factors of vascular disease could perhaps warrant CDS for the evaluation of latent stenotic or occlusive carotid disease. Third, given the rarity of bilateral ICA occlusion, the total number of patients was small, resulting in a type II error in statistical analysis. Differences in age of onset and sex distribution may have been underestimated between the acute and chronic bilateral ICA occlusion groups.

CONCLUSION

Bilateral ICA occlusion is rare, accounting for only 0.3% of all cases of ischemic stroke. Acute bilateral ICA occlusion is even rarer, accounting for <0.1% of such cases. In this study, the patients with acute bilateral ICA occlusion had higher initial stoke severity, poorer collateral circulation, and worse clinical outcomes than did patients with chronic bilateral ICA occlusion. Physicians must pay more attention to rare causes of acute bilateral ICA occlusion, including pituitary apoplexy.

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Ethics approval and consent to participate

This study was approved by the Institutional Review Board of Taipei Tzu Chi Hospital, New Taipei City (approval no. 10-XD-046).

Competing interests

The authors declare that they have no competing interests.

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