CASE REPORT

Hemorrhagic Transformation of Stroke Secondary to Spontaneous Internal Carotid Artery Dissection

Ju-Sing Fan[1,4], Feng-Chi Chang[2,4], Han-Hwa Hu[3,4], Li-Chi Hsu[3,4]*

Departments of [1]Emergency Medicine and [2]Radiology, and the [3]Neurological Institute, Taipei Veterans General Hospital, and [4]National Yang-Ming University School of Medicine, Taipei, Taiwan, R.O.C.

The clinical course of patients with hemorrhagic transformation in stroke secondary to spontaneous cervical internal carotid artery dissection (ICAD) has not been elucidated. We report a 36-year-old man with presentation of headache and subsequent left hemiparesis. Magnetic resonance imaging disclosed right ICAD with nearly complete occlusion of the right distal internal carotid artery and infarction over the right basal ganglion with hemorrhagic transformation in its central area. Hemorrhagic transformation can develop early in ICAD patients without preceding treatment with antithrombotic agents. Clinicians are urged to use antithrombotic agents with caution in patients with spontaneous ICAD with ischemic stroke because early hemorrhagic transformation may also be present. Possible pathomechanisms and treatment strategies are also discussed. [*J Chin Med Assoc* 2006;69(12):585–588]

Key Words: hemorrhagic transformation, internal carotid artery dissection

Introduction

Recent studies investigating the effects of administering antithrombotic agents in internal carotid artery dissection (ICAD) to prevent thromboembolic events and to improve prognosis have found that not all ICAD patients are suited to receive antithrombotic agents.[1,2] Antithrombotic agents can be detrimental if the ICAD-induced stroke is accompanied by hemorrhagic transformation. This suggests that the influence of hemorrhagic transformation should be considered in the management of ICAD with ischemic stroke. If they are misadministered because hemorrhagic transformation was not discovered earlier, antithrombotic agents may cause adverse consequences. The clinical course of hemorrhagic transformation has not been comprehensively described, imaging studies of ICAD in patients with hemorrhagic transformation have not been reported, and the treatment and prognosis of ICAD have not been amply discussed.[1–4] Hence, to promote further discussion of ICAD treatment and prognosis, we report this case.

Case Report

A 36-year-old man suffered from sudden onset of a throbbing headache over his right parietal region while walking on December 25, 2004. The man presented to the emergency department (ED) within 1 hour. Initial neurologic examination did not reveal any abnormality. The patient was admitted to the ED observation room with the tentative diagnosis of primary headache. No medications except pain killers were prescribed at that time. Ten hours later, the patient suffered from transient left hemiparesis and hemihypesthesia. Computed tomography (CT) of the brain was performed within 30 minutes, and did not disclose any intracranial lesion. His hemiparesis and hemihypesthesia relapsed on the following morning. Early stroke was suspected and

*Correspondence to: Dr Li-Chi Hsu, Neurological Institute, Taipei Veterans General Hospital, 201, Section 2, Shih-Pai Road, Taipei 112, Taiwan, R.O.C.
E-mail: lchsu@vghtpe.gov.tw • Received: April 18, 2006 • Accepted: October 18, 2006

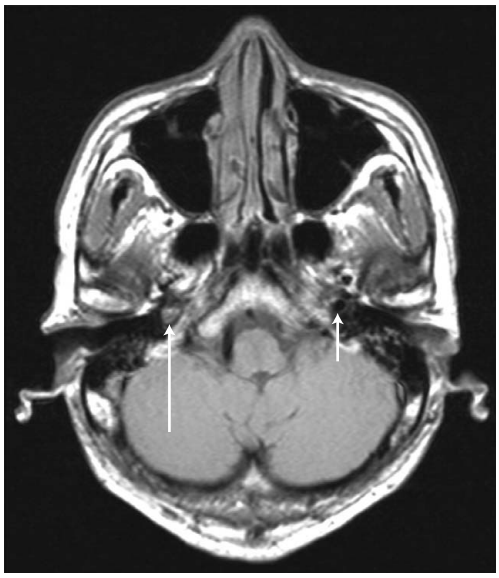

Figure 1. Axial T1-weighted magnetic resonance imaging of the brain shows nearly total occlusion of the right petrous internal carotid artery with soft tissue signal around the stagnant flow (long arrow). The left distal internal carotid artery is normal (short arrow).

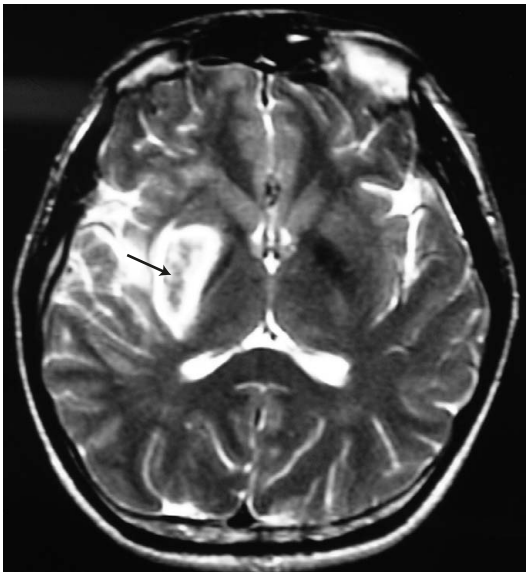

Figure 2. Axial T2-weighted magnetic resonance imaging of the brain shows infarction over the right basal ganglion with central hemorrhagic transformation (arrow).

magnetic resonance imaging (MRI) was arranged. The symptoms presented with undiminished sensation over the right parietal and right retro-orbital areas. MRI disclosed nearly complete occlusion of the right distal internal carotid artery, with soft tissue signal around the region of stagnant flow (Figure 1) and infarction over the right basal ganglion with hemorrhagic transformation in its central area (Figure 2).

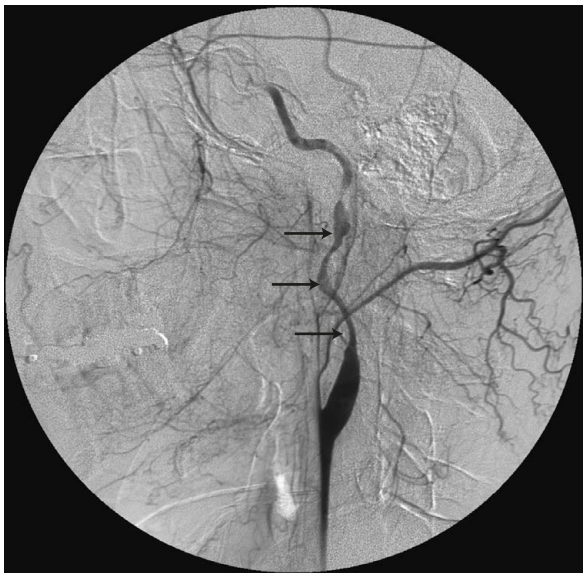

Figure 3. Right carotid angiography showed segmental narrowing over the distal cervical and petrous portions of the right internal carotid artery (arrows).

Conventional angiography showed a long segmental narrowing over the distal cervical and petrous portions of the right internal carotid artery (Figure 3). Hemorrhagic transformation of ICAD-induced stroke was diagnosed. Upon providing informed consent, the patient was enrolled as a case in our study. He was then admitted to the neurologic ward for further evaluation and intervention.

The patient denied having a history of head or neck trauma, cervical manipulation, chronic migraine, illicit drug use, or any other known systemic disease. On admission, neurologic examination showed clear consciousness, isocoric pupils with partially limited eye movement, left hemiparesis and hemihypesthesia, increased tendon reflex, and positive Babinski response on the left. The National Institutes of Health Stroke Scale (NIHSS) score was 13. Laboratory studies, including hemogram, biochemistry, α1-antitrypsin, VDRL (venereal disease research laboratory slide test), coagulation, autoimmune and inflammation profiles, were all within normal limits. Electrocardiogram and transthoracic echocardiography were normal. During the admission period, the patient experienced progressive hemiplegia and headache in the first 2 days. Follow-up brain CT showed enlarged hematoma without midline deviation. Symptomatic hemorrhagic transformation was impressed. Without significant sign of increased intracranial pressure, the patient received only conservative management such as maintaining adequate vital signs and use of nonsteroidal anti-inflammatory drugs for pain relief. After that, no other adverse event

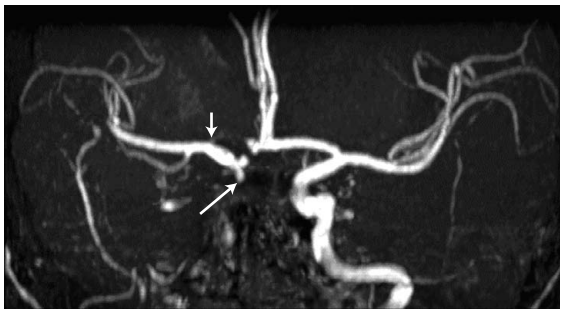

Figure 4. Brain magnetic resonance angiography shows no flow in the distal cervical carotid artery (long arrow) and normal flow in the intracranial carotid artery (short arrow).

occurred during the admission period. He was discharged 1 month later in a stable condition with satisfying neurologic recovery. His NIHSS score was 7 on discharge.

Follow-up brain magnetic resonance angiography (MRA) 4 months later showed no flow in the distal cervical internal carotid artery but relatively normal blood flow in the intracranial carotid artery (Figure 4). The patient's neurologic deficits improved gradually despite the unresolved internal carotid artery occlusion. He did not receive any antithrombotic agent during the admission period. His NIHSS score was 2 and modified Rankin Scale score was 1 (minor sequelae) 1 year later, representing a satisfactory neurologic outcome.

Discussion

Hemorrhagic transformation develops in about 1-third of all stroke patients within the first week of symptom onset, but its incidence is much lower in patients with stroke secondary to cervical ICAD.[3–5] This difference may be due to younger age at onset and fewer predisposing factors of intracranial hemorrhage (such as hypertension, diabetes, and atherosclerotic vessels) in patients with cervical ICAD.[3,4] In ICAD patients with or without cerebral ischemic events, the long-term neurologic prognosis is good.[1,2,6,7]

Most authors agree that ICAD is probably the endpoint of a complex and possibly heterogeneous group of vasculopathies developing under the influence of various genetic and environmental factors.[1,2,6–8] The subsequent hemorrhagic transformation is considered to be related to ischemia and reperfusion injury to vessel walls and capillaries.[5] Like most patients with ICAD, the stroke pattern of our patient was thromboembolic type because the infarcted area on MRI was territorial rather than border-zoned.[1,2,9,10] Although controlled studies of the treatment of cervical artery dissections have not been performed, most clinicians agree that antithrombotic therapy is a reasonable choice.[1,2,7] More invasive treatments like surgical or catheter-based revascularization are allowed in selective cases.[1,2] However, the standard treatments of hemorrhagic transformation of stroke caused by ICAD have not been documented. Most authors agree that anticoagulants should not be used in patients with hemorrhagic transformation or those at high risk for hemorrhagic transformation.[1,2] In our patient, antithrombotic therapy was not done because the intracranial hemorrhage and ICAD were noted concurrently. Due to the symptomatic enlarging cerebral hematoma, we also withheld antiplatelet agent, although there was no evidence that antiplatelet agents worsen the hemorrhagic transformation.

In addition to young age, our patient exhibited 2 features of the carotid artery dissection triad (i.e. pain on 1 side of the head, face, or neck, partial Horner's syndrome, and oculosympathetic palsy, which was then followed by cerebral or retinal ischemia hours or days later).[1,2,7] Some authors describe symptoms resembling migraine attack with aura.[11] Although differentiating between migraine with aura and ICAD in the early stage can be difficult, unusual headaches in patients with or without previous history of migraine need further investigation.[11] The treating physician should maintain a high level of suspicion even if the warning signals are subtle or subclinical.[5] In our patient, the follow-up brain CT was not done because MRI could be performed quickly (within 10 minutes after it was arranged). Although it was incidental, the finding of hemorrhagic transformation on MRI shows that hemorrhagic transformation can develop in the early stage of spontaneous ICAD even before administration of antithrombotic agents.

MRI techniques are replacing conventional angiography as the best imaging modality for diagnosing ICAD.[12] MRI can also identify patients who are at increased risk of secondary hemorrhagic transformation following acute ischemic stroke.[13,14] To find the best treatment plan in a timely fashion, we recommend that MRI be arranged as soon as possible to diagnose carotid artery dissection in all young stroke patients and patients with migraine-like unusual headache with aura, and that before administering antithrombotic agents, the treating physician should carefully look for signs of hemorrhagic transformation. Once the signs of hemorrhagic transformation arise, immediate brain CT is needed. Our patient's condition improved gradually during his month-long admission and the ensuing 1 year. The neurologic outcome indicated that the brain tissue supplied by the occluded internal carotid artery

remained viable. Most authors believe that the ischemic territory is rescued by collateralization from the part of the Circle of Willis,[15] and the follow-up MRA (Figure 4) in our patient showing the normal flow of the right intracranial internal carotid artery supports this belief. These results challenge the need for surgical or catheter revascularization in ICAD patients with persistent deficits. However, studies comparing the outcomes of different management strategies might be useful.

In conclusion, hemorrhagic transformation can occur in young stroke patients secondary to spontaneous cervical ICAD even in the early stage before administration of antithrombotic agents. Physicians should be more cautious in the routine use of anticoagulants in patients with ICAD. Early MRI study facilitates early diagnosis of spontaneous ICAD, and follow-up brain CT in patients with clinical suspicion of hemorrhagic transformation can help in its early recognition. Conservative management may be an alternative approach for ICAD patients with proven stroke with hemorrhagic transformation.

References

1. Schievink W. Spontaneous dissection of the carotid and vertebral arteries. *N Engl J Med* 2001;344:898–906.
2. Zetterling M, Carlström C, Konrad P. Internal carotid artery dissection. *Acta Neurol Scand* 2000;101:1–7.
3. Steinke W, Schwartz A, Hennerici M. Topography of cerebral infarction associated with carotid artery dissection. *J Neurol* 1996;243:323–8.
4. Pelkonen O, Tikkakoski T, Pyhtinen J, Sotaniemi K. Cerebral CT and MRI findings in cervicocephalic artery dissection. *Acta Radiol* 2004;45:259–65.
5. Moulin T, Crepin-Leblond T, Chopard JL, Bogousslavsky J. Hemorrhagic infarcts. *Eur Neurol* 1994:34:64–77.
6. Kasner SE, Hankins LL, Bratina P, Morgenstern LB. Magnetic resonance angiography demonstrates vascular healing of carotid and vertebral artery dissections. *Stroke* 1997;28:1993–7.
7. Kremer C, Mosso M, Georgiadis D, Stockli E, Benninger D, Arnold M, Baumgartner RW. Carotid dissection with permanent and transient occlusion or severe stenosis: long-term outcome. *Neurology* 2003;60:271–5.
8. Brandt T, Grond-Ginsbach C. Spontaneous cervical artery dissection: from risk factors toward pathogenesis. *Stroke* 2002;33:657–8.
9. Lucas C, Moulin T, Deplanque D, Tatu L, Chavot D. Stroke patterns of internal carotid artery dissection in 40 patients. *Stroke* 1998;29:2646–8.
10. Benninger DH, Georgiadis D, Kremer C, Studer A. Mechanism of ischemic infarct in spontaneous carotid dissection. *Stroke* 2004;35:482–5.
11. Duyff RF, Snijders CJ, Vanneste JA. Spontaneous bilateral internal carotid artery dissection and migraine: a potential diagnostic delay. *Headache* 1997;37:109–12.
12. Kirsch E, Kaim A, Engelter S, Lyrer P, Stock KW, Bongartz G, Radu EW. MR angiography in internal carotid artery dissection: improvement of diagnosis by selective demonstration of the intramural hematoma. *Neuroradiology* 1998;40:704–9.
13. Fiehler J, Remmele C, Kucinski T, Rosenkranz M, Thomalla G, Weiller C, Zeumer H, et al. Reperfusion after severe local perfusion deficit precedes hemorrhagic transformation: an MRI study in acute stroke patients. *Cerebrovasc Dis* 2005;19:117–24.
14. Tong DC, Adami A, Mosely ME, Marks MP. Relationship between apparent diffusion coefficient and subsequent hemorrhagic transformation following acute ischemic stroke. *Stroke* 2000;31:2378–84.
15. Bisschops RH, Klijn CJ, Kappelle LJ, van Huffelen AC, van der Grond J. Collateral flow and ischemic brain lesions in patients with unilateral carotid artery occlusion. *Neurology* 2003;60:1435–41.