

# Hypoplasia or Occlusion of the Ipsilateral Cranial Venous Drainage Is Associated With Early Fatal Edema of Middle Cerebral Artery Infarction

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**Background and Purpose**—Thrombosis of the cerebral venous sinus may cause venous congestion, cerebral edema, and infarction. The role of cerebrovenous disorders in arterial ischemic stroke is unknown. The objective of this study was to examine the contribution of ipsilateral cranial venous abnormalities to the development of cerebral edema in middle cerebral artery infarction.

**Methods**—This is a retrospective study of consecutive patients with large middle cerebral artery infarction admitted to our neurocritical care unit from January 2007 to October 2008. Medical records, laboratory data, and imaging of cerebral edema and cranial venous sinuses were analyzed.

**Results**—Of the 14 patients identified to have large middle cerebral artery infarction and images of cranial venous drainages, 5 (35.7%) had fatal edema with clinical signs of transtentorial herniation. Four of the 5 patients developed fatal edema within 48 hours of ictus and were found to have abnormal ipsilateral cranial venous drainage, including atresia of the transverse sinus (one), occlusion of the internal jugular vein (one), and hypoplasia of the transverse sinus and internal jugular vein (2). The fifth patient had symmetrical bilateral cranial venous drainages and fatal edema at Day 5. Of the 9 patients with nonmalignant middle cerebral artery infarction, all had ipsilateral dominant or symmetrical bilateral venous drainages.

**Conclusions**—In this small case series, we demonstrated that only the patients with hypoplasia or occlusion of the ipsilateral cranial venous drainage developed early fatal edema after large middle cerebral artery infarction. Our results suggest a role of cranial venous outflow abnormalities in the development of brain edema after arterial ischemic stroke. (*Stroke*. 2009;40:3736-3739.)

**Key Words:** fatal edema ■ cranial venous sinus ■ MCA infarction

Approximately 40% of patients with large middle cerebral artery (MCA) infarction develop fatal edema with a significant midline shift and compression of the basal cisterns, resulting in clinical signs of transtentorial herniation.<sup>1-4</sup> The mortality rate of patients with such a malignant MCA syndrome is as high as 78%.<sup>4</sup> Recently, decompressive hemicraniectomy was shown to improve outcome in controlled clinical trials.<sup>5</sup> It is therefore essential to identify patients at risk of fatal edema for early surgical intervention.

Early predictors of fatal edema include infarct size, young age, female sex, National Institutes of Health Stroke Scale score >20 on admission, elevated white blood cell counts, hypertension, heart failure, an ipsilateral abnormality of the circle of Willis, the involvement of multiple vascular territories, and carotid occlusion.<sup>1-4</sup> A recent meta-analysis showed that size of the infarct >50% of the MCA territory and a perfusion deficit >66% were the major determinants of the

development of fatal edema.<sup>6</sup> Most of these predictors, including infarct volume, lack sufficient predictive value to encourage early surgical decompression before the onset of clinical signs of herniation.<sup>3,6</sup> To date, the factors that contribute to a more malignant course between similar infarct volumes are still poorly understood.

Thrombosis of the cerebral venous sinus may cause venous congestion, cerebral edema, and infarction.<sup>7</sup> The role of cerebrovenous disorders in arterial ischemic stroke is unknown. The objective of this study was to examine the contribution of ipsilateral cranial venous abnormalities to the development of cerebral edema in patients with MCA infarction.

## Patients and Methods

This is a retrospective study of patients with large MCA infarction admitted to the Neurological Critical Care Unit of the University of

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**Table 1. Demographics and Clinical Features**

Patient No.	Age, Years	Sex	Infarction	Etiology	Maximal Midline Shift, mm	Ipsilateral Transverse Sinuses	Ipsilateral Internal Jugular Vein	Modified Rankin Scale Score at Discharge
1	67	M	R MCA	Cryptogenic	2	Dominant	Dominant	3
2	81	F	R MCA	Cardioembolic	3.4	Dominant	NA	4
3	69	M	L MCA	ICA occlusion	16.1	Hypoplastic	Hypoplastic	6
4	60	M	L MCA	Cardioembolic	4.6	NA	NA	5
5	38	M	L MCA	ICA dissection	6.4	NA	NA	3
6	37	M	R MCA	Vasculitis	1	NA	NA	6
7	64	M	R MCA	ICA dissection	16.8	NA	Occluded	6
8	46	M	L MCA	ICA dissection	1.9	Dominant	Dominant	3
9	70	F	R MCA/ACA	Iatrogenic	24.3	Atresic	Hypoplastic	6
10	54	M	R MCA	Iatrogenic	7.2	NA	NA	3
11	60	F	R MCA	ICA occlusion	9.8	NA	NA	5
12	48	F	R MCA	Iatrogenic	12.7	Hypoplastic	Hypoplastic	6
13	67	M	R MCA	ICA stenosis	16.6	NA	NA	4
14	47	M	R MCA	Cardioembolic	6.3	NA	NA	3

M indicates male; F, female; R, right; L, left; ICA, internal carotid artery; ACA, anterior cerebral artery; NA, normal appearance.

Texas Southwestern Medical Center Zale-Lipshy Hospital from January 2007 to September 2008. All patients with hemispheric stroke who fulfilled the following criteria were included in this study: (1) acute large MCA infarction with well-defined onset; (2) proximal arterial occlusion (internal carotid artery, carotid T, or MCA main stem) per MR angiography, CT angiography, or digital subtraction angiography (DSA); (3) serial imaging of cerebral edema; and (4) DSA or CT angiography performed for visualization of cranial venous sinuses and jugular veins. Patient demographics, clinical data, and imaging of the infarction and cerebral venous anatomy were reviewed.

All patients were managed by a multidisciplinary team, including neurointensivists, stroke neurologists, and vascular neurosurgeons. Patients and families were informed about decompressive hemicraniectomy as a life-saving procedure. Midline shift was measured from the septum pellucidum on serial CT scans. Infarct size was estimated by measurement of the 3 largest diameters. DSA and CT venography were reviewed by a vascular neurologist (W.Y.). The abnormalities of the transverse sinuses and internal jugular veins were independently verified by an experienced neuroradiologist (E.S.). Malignant MCA syndrome was defined by large MCA infarction with fatal edema and clinical signs of transtentorial herniation, including ipsilateral pupillary dilation, decreased level of consciousness, and ipsilateral or contralateral hemiparesis. Functional outcome at discharge was estimated using modified Rankin Scales. The Institutional Review Board of the University of Texas Southwestern Medical Center approved the study.

We compared patients who developed malignant MCA syndrome with those who did not (nonmalignant MCA infarction). All patients received maximal medical management. Surgical intervention was considered for patients who had fatal edema and clinical signs of herniation. Statistical analysis was carried out with unpaired *t* test for numeric variables.

**Results**

Nineteen patients were identified to have large MCA infarction. Five patients did not have imaging of the venous anatomy and were excluded from the study. Four of them had embolic stroke from atrial fibrillation (n=1), mitral valve repair surgery (n=2), or carotid dissection from radical neck tumor resection (n=1). They underwent MRI/MR angiography for acute stroke workup. The fifth patient was transferred

from an outside hospital after she developed transtentorial herniation with dilated fixed pupils and extensor posturing.

Fourteen patients had large embolic MCA infarction and imaging of cerebral venous anatomy. The demographics, clinical features, and neuroimaging data of these patients are summarized in Table 1. Patient ages ranged from 37 to 81 years. Infarction appeared to be more common in right MCA distribution (10 of 14). The causes of MCA infarcts were as follows: cardioembolic (3), large artery occlusive disease (3), iatrogenic from clipping of a giant aneurysm or angiography (3), carotid artery dissection (3), vasculitis (one), or cryptogenic (one). Of the 14 patients, 2 had DSA, 11 had CT angiography, and one had both.

Five of the 14 patients (35.7%) had malignant MCA infarction with fatal edema and a midline shift of >10 mm (Table 2). All 5 had significantly larger infarct size with clinical signs of transtentorial herniation, including dilation of

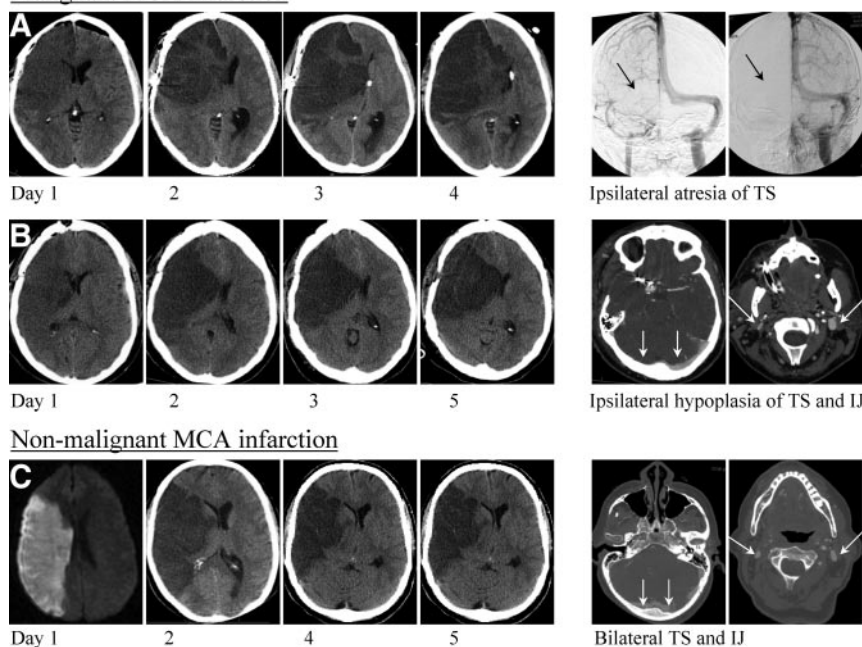
**Table 2. Clinical Features of Malignant and Nonmalignant MCA Infarction**

	Nonmalignant MCA Infarction	Malignant MCA Infarction
No. of patients	9	5
Age, years	54.4±14.9	58.8±10*
Female, n (%)	2 (22.2%)	2 (40%)
Right MCA, n (%)	6 (66.7%)	4 (80%)
Infarct size, cm <sup>3</sup>	196±70	327±36†
Maximal midline shift, mm	4.7±3.1	17.3±4.9†
Ipsilateral transverse sinus or ipsilateral internal jugular vein		
Atresia or occlusion	0	2 (40%)
Hypoplasia	0	2 (40%)
Mortality rate (%)	0%	80%

\*P=0.422.

†P<0.001.

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Malignant MCA infarction

**Figure.** Representative images of cerebral edema and cranial venous sinuses. A, A 70-year-old woman had right MCA/ anterior cerebral artery infarction with fatal edema on Day 2 of ictus. Cerebral angiography showed ipsilateral atresia of the transverse sinus (TS) and hypoplasia of internal jugular vein (IJ). B, A 53-year-old man developed fatal edema on Day 2 from right MCA infarction. CT venography showed hypoplasia of ipsilateral TS and IJ. C, A 60-year-old woman with a large MCA infarction developed moderate edema without herniation. CT venography showed bilateral symmetrical TS and IJ.

ipsilateral pupil, loss of pupillary light reflex, and precipitous onset of decreased levels of consciousness or coma.

Of the 5 patients with malignant MCA infarction, 4 (80%) developed fatal edema within 48 hours of symptom onset (Figure A–B). DSA or CT venography showed abnormal ipsilateral cranial venous drainage, including atresia of transverse sinus and hypoplasia of internal jugular vein (one), occlusion of internal jugular vein from previous surgical ligation for neck tumor resection (one), and hypoplasia of transverse sinus and internal jugular vein (2). After extensive discussions, 4 families declined surgical decompression per the patient's wishes. All 4 patients died from herniation. The fifth patient developed fatal edema and transtentorial herniation at Day 5. CT venography showed symmetrical bilateral venous drainages. He initially responded to osmotic therapy with hypertonic saline but required decompressive hemicraniectomy on Day 8 for recurrent edema and transtentorial herniation. He recovered with moderate severe disability (modified Rankin Scale score 4) at hospital discharge.

Nine patients had mild or moderate edema without significant neurological deterioration (nonmalignant MCA infarction). Three of them had ipsilateral dominant venous drainage and mild cerebral edema with a midline shift of <3.5 mm. They had a favorable outcome (modified Rankin Scale score <4) at hospital discharge. Six patients had symmetrical bilateral venous sinuses and moderate cerebral edema with a midline shift of <10 mm. They all survived with an uneventful hospital course. As shown in Figure C, large infarct size was not associated with fatal edema in a patient with symmetrical bilateral venous drainages.

Three patients had DSA (n=2) or CT angiography (n=1) for aneurysm or transient ischemic attack workup before MCA infarction. Two of them had hypoplasia (n=1) or atresia (n=1) of ipsilateral cranial venous drainage. Eleven patients had CT angiography within 24 hours (n=5), between

Days 3 and 7 (n=5), or DSA (n=1) on Day 5 after symptom onset. Two of them, both in the 24-hour group and including the patient with prior internal jugular veins ligation, had abnormal cranial venous drainage. Therefore, the hypoplasia or occlusion of the cranial venous drainage is not the result of low flow secondary to arterial occlusion or mass effect of the hemispheric stroke.

## Discussion

Postinfarction cerebral edema usually peaks at 3 to 7 days after symptom onset. Most patients with malignant MCA infarction develop fatal edema within 48 hours of ictus.<sup>8</sup> A number of studies have shown that infarct size is the major determinant of the development of fatal edema.<sup>1–4</sup> However, its predictive value is only moderate and other factors may play a role.<sup>6</sup>

In this case series, we showed that in addition to infarct size, hypoplasia or occlusion of ipsilateral cranial venous drainage was associated with early fatal edema of MCA infarction.

It is unlikely that our findings are coincidental. A known association exists between thrombosis of cerebral venous sinuses and venous congestion, intracranial hypertension, cerebral edema, and infarction.<sup>7</sup> Congenital venous sinus stenosis or obstruction has also been implicated in idiopathic intracranial hypertension, presumably by resisting cerebrospinal fluid absorption.<sup>9–12</sup> Increased intracranial pressure (ICP) in some patients with idiopathic intracranial hypertension was associated with either complete or partial obstruction of the internal jugular veins.<sup>11</sup> There is increasing evidence that venous sinus stenting reduces cerebral venous pressure and clinical symptoms of elevated intracranial pressure.<sup>13–16</sup> In addition, a recent study showed that venous outflow abnormalities were frequently associated with cerebral edema of unruptured arteriovenous malformation.<sup>17</sup>

Transverse sinuses and internal jugular veins are commonly asymmetrical with one side being atretic or hypoplastic in 20% to 39% of cases.<sup>18,19</sup> In our small case series, 23% of the patients (3 of 13) had hypoplasia or atresia of the transverse sinus and internal jugular vein.

The intracranial venous compartment occupies approximately 70% of blood volume inside the inflexible cranial cavity. Following volume-targeted rationale, ICP can be regulated effectively by the fluctuation of venous blood volume. Venous hemodynamics passively influence the ICP through a possible key regulator, outflow obstruction. This outflow obstruction contributes to intracranial venous congestion more in patients with high ICP than in patients with normal ICP.<sup>20</sup> In case of normal ICP, venous collaterals may be sufficient to prevent cerebral venous congestion and edema. However, in the setting of large MCA infarction with widespread ischemic injury, pre-existing abnormalities of cranial venous drainage may pose significant resistance to venous outflow, accelerating the development of cerebral edema.

Taken together, our findings suggest a role of ipsilateral venous drainage abnormalities in the development of early fatal edema after large MCA infarction. Because this is a small observational study with potential selection bias, a further larger study would be necessary to verify our findings. Additionally, it is unclear whether a congenital atresia or hypoplasia of a dural sinus and/or internal jugular vein may actually limit ipsilateral venous outflow and contribute to the development of early fatal edema after MCA infarction. As the interest in cerebral venous circulation evolves, we should have a better understanding of the venous collaterals and their role in cerebral edema of arterial ischemia.

**Disclosures**

None.

**References**

1. Oppenheim C, Samson Y, Manai R, Lalam T, Vandamme X, Crozier S, Srour A, Cornu P, Dormont D, Rancurel G, Marsault C. Prediction of malignant middle cerebral artery infarction by diffusion-weighted imaging. *Stroke*. 2000;31:2175–2181.
2. Kasner SE, Demchuk AM, Berrouschot J, Schmutzhard E, Harms L, Verro P, Chalela JA, Abbur R, McGrade H, Christou I, Krieger DW. Predictors of fatal brain edema in massive hemispheric ischemic stroke. *Stroke*. 2001;32:2117–2123.
3. Maramattom BV, Bahn MM, Wijdicks EFM. Which patient fares worse after early deterioration due to swelling from hemispheric stroke? *Neurology*. 2004;63:2142–2145.

4. Hacke W, Schwab S, Horn M, Spranger M, De Georgia M, von Kummer R. ‘Malignant’ middle cerebral artery territory infarction: clinical course and prognostic signs. *Arch Neurol*. 1996;53:309–315.
5. Vahedi K, Hofmeijer J, Juettler E, Vicaut E, George B, Algra A, Amelink GJ, Schmiedeck P, Schwab S, Rothwell PM, Bousser MG, van der Worp HB, Hacke W. DECIMAL, DESTINY, and HAMLET investigators. Early decompressive surgery in malignant infarction of the middle cerebral artery: a pooled analysis of three randomised controlled trials. *Lancet Neurol*. 2007;6:215–222.
6. Hofmeijer J, Algra A, Kappelle LJ, van der Worp HB. Predictors of life-threatening brain edema in middle cerebral artery infarction. *Cerebrovasc Dis*. 2008;25:176–184.
7. Stam J. Thrombosis of the cerebral veins and sinuses. *N Engl J Med*. 2005;352:1791–1798.
8. Qureshi A, Suarez J, Yahia A, Mohammad Y, Uzun G, Suri M, Zaidat O, Ayata C, Ali Z, Wityk R. Timing of neurologic deterioration in massive middle cerebral artery infarction: a multicenter review. *Crit Care Med*. 2003;31:272–277.
9. Karahalios DG, Rekatte HL, Khayata MH, Apostolides PJ. Elevated intracranial venous pressure as a universal mechanism in pseudotumor cerebri of varying etiologies. *Neurology*. 1996;46:198–202.
10. Farb RI, Vanek I, Scott JN, Mikulis DJ, Willinsky RA, Tomlinson G, terBrugge KG. Idiopathic intracranial hypertension: the presence and morphology of sinovenous stenosis. *Neurology*. 2003;60:1418–1424.
11. Alperin N, Lee SH, Mazda M, Hushek SG, Roitberg B, Goddwin J, Lichter T. Evidence for the importance of extracranial venous flow in patients with idiopathic intracranial hypertension (IIH). *Acta Neurochir Suppl*. 2005;95:129–132.
12. Owler BK, Parker G, Halmagyi GM, Johnston IH, Besser M, Pickard JD, Higgins JN. Cranial venous outflow obstruction and pseudotumor cerebri syndrome. *Adv Tech Stand Neurosurg*. 2005;30:107–174.
13. Higgins JNP, Owler BK, Cousins C, Pickard JD. Venous sinus stenting for refractory benign intracranial hypertension. *Lancet*. 2002;359:228–230.
14. Owler BK, Parker G, Halmagyi GM, Dunne VG, Grinnell V, McDowell D, Besser M. Pseudotumor cerebri syndrome: venous sinus obstruction and its treatment with stent placement. *J Neurosurg*. 2003;98:1045–1055.
15. Higgins JNP, Cousins C, Owler BK, Sarkies N, Pickard JD. Idiopathic intracranial hypertension: 12 cases treated by venous sinus stenting. *J Neurol Neurosurg Psychiatry*. 2003;74:1662–1666.
16. Donnet A, Metellus P, Levrier O, Mekkaoui C, Fuentes S, Dufour H, Conrath J, Grisoli F. Endovascular treatment of idiopathic intracranial hypertension: clinical and radiologic outcome of 10 consecutive patients. *Neurology*. 2008;70:641–647.
17. Kim BS, Sarma D, Lee SK, terBrugge KG. Brain edema associated with unruptured brain arteriovenous malformations. *Neuroradiology*. 2009;51:327–335.
18. Alper F, Kantarci M, Dane S, Gumustekin K, Onbas O, Durur I. Importance of anatomical asymmetries of transverse sinuses: an MR venographic study. *Cerebrovasc Dis*. 2004;18:236–239.
19. Lichtenstein D, Saïfi R, Augarde R, Prin S, Schmitt JM, Page B, Pipien I, Jardin F. The internal jugular veins are asymmetric. Usefulness of ultrasound before catheterization. *Intensive Care Med*. 2001;27:301–305.
20. Si Z, Luan L, Kong D, Zhao G, Wang H, Zhang K, Yu T, Pang Q. MRI-based investigation on outflow segment of cerebral venous system under increased ICP condition. *Eur J Med Res*. 2008;13:121–126.



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