Ipsilateral Sinus Hypoplasia and Poor Leptomeningeal Collaterals as Midline Shift Predictors

Ondrej Volny, MD,*† Petra Cimflova, MD,*‡ and Robert Mikulik, MD, PhD*†

Background: We explore the role of dural sinus morphology, leptomeningeal collaterals, and clot localization in the development of malignant brain edema in acute ischemic stroke in anterior circulation. *Methods:* This is a single-center retrospective study of consecutive stroke patients with acute occlusion (middle cerebral artery M1 ± intracranial internal carotid artery) treated with intravenous thrombolysis (from November 2009 to November 2014). Admission computed tomography angiography data were evaluated for hypoplasia of dural sinuses, leptomeningeal collaterals, and clot location. Primary outcome was midline shift (<5 mm versus ≥5 mm) on follow-up computed tomography. Secondary outcomes were infarct volume and modified Rankin Scale score of 2 or lower at 90 days. Multivariate logistic regression was used. *Results:* Of 86 patients (49 females), 36 (42%) had poor collaterals, 26 (30%) had ipsilesional sinus hypoplasia, and 38 (44%) had proximal clots. A midline shift of 5 mm or higher was diagnosed in 14 patients (16%). Infarct volume was larger in the group with midline shift (median: 318 mL [interquartile range {IQR} = 260-350]) than in the group without midline shift (median: 44 mL [IQR = 28-60]) (P = .007). In multivariate analysis, poor leptomeningeal collaterals (odds ratio [OR] = .11, 95% confidence interval [CI] = .03-.44, P = .002 for good collaterals) and ipsilesional sinus hypoplasia (OR = 6.43, 95% CI = 1.5-46.1, P = .008) were independently associated with a midline shift of 5 mm or higher. *Conclusion:* Patients with poor leptomeningeal collaterals and ipsilesional hypoplasia of dural sinuses are more likely to develop midline shift. **Key Words:** Stroke—anterior circulation—dural sinuses—leptomeningeal collaterals—edema—midline shift.

Introduction

Malignant brain edema is a life-threatening complication of acute ischemic stroke. It develops in up to 10% of stroke patients with occlusion of the middle cerebral artery (MCA) and results in mortality rates reaching almost 80%.[1-4] Disruption of the blood–brain barrier (vasogenic edema) and extensive cytotoxic edema play a role in the pathogenesis of malignant brain edema.[5] Age, sex, admission stroke severity as measured by the National Institutes of Health Stroke Scale (NIHSS), elevated white blood cell count, history of hypertension, heart failure, abnormalities of the circle of Willis, clot in the internal carotid artery, ischemic changes involving more than 50% of MCA territory, and involvement of multiple vascular territories (anterior or/and posterior cerebral arteries) have all been described as being associated with the development of malignant brain edema.[6-9] Nonetheless, the exact pathophysiology and risk factors are still poorly understood.

A previous case–control study indicated the association between hypoplasia of ipsilateral dural sinuses and risk of early brain edema in acute MCA infarction, and the contribution of dural sinuses in the pathophysiology of brain edema development was hypothesized.[10]

From the *Stroke Research Program, International Clinical Research Centre, St. Anne's University Hospital, Brno, Czech Republic; †Department of Neurology, St. Anne's University Hospital and Faculty of Medicine, Masaryk University, Brno, Czech Republic; and ‡Department of Medical Imaging, St. Anne's University Hospital and Faculty of Medicine, Masaryk University, Brno, Czech Republic.

Received February 28, 2016; accepted April 2, 2016.

Disclosure: None.

Address correspondence to Ondrej Volny, MD, Department of Neurology, St. Anne's University Hospital and Faculty of Medicine, Masaryk University, 53 Pekarska, 602 00 Brno, Czech Republic. E-mail: 214565@mail.muni.cz.

1052-3057/$ - see front matter

http://dx.doi.org/10.1016/j.jstrokecerebrovasdis.2016.04.004

In the present study, we seek to explore the relationship between clot location, status of leptomeningeal collaterals, and dural sinus morphology in the development of substantial midline shift. As a secondary outcome, 90 days' clinical outcome was evaluated in this cohort of patients treated only with intravenous thrombolysis. Our hypothesis was that these vascular markers apparent on admission computed tomography angiography (CTA) might be predictive for development of brain edema.

Methods

Data were from an ongoing single-center prospective registry of patients with acute ischemic stroke treated with intravenous tissue plasminogen activator (IV tPA) from November 2009 to November 2014 with CTA documented acute intracranial ICA ± M1 MCA occlusions (M2 was not involved). The local institutional ethical committee approved the present study. Clot location was dichotomized as proximal (the mid-M1 was selected as a borderline) and distal (clot distally to mid-M1).[11] The following baseline parameters were prospectively collected: age, sex, baseline NIHSS score, history of hypertension, history of diabetes mellitus, dose of IV tPA, history of previous stroke, atrial fibrillation, coronary artery disease, and hyperlipidemia.

Imaging

Standard nonhelical and noncontrast computed tomography (CT) was performed on a multislice scanner (120-140 kV, 50-125 mAs; GE LightSpeed VCT 64 Slice CT [General Electric Healthcare, Waukesha, WI, USA)] with 5-mm slice thickness. Noncontrast CT was followed by a CTA with a helical scanning technique. Coverage was from the aortic arch to the vertex with continuous axial slices parallel to the orbitomeatal line with .6- to 2.5-mm slice thickness. Acquisitions were obtained after a single bolus of intravenous contrast injection of 90-120 mL of nonionic contrast medium into an antecubital vein at 3-5 mL/s, autotriggered by the appearance of contrast in a region of interest manually placed in the ascending aorta.

Clot location was assessed as either proximal (intracranial ICA to mid-M1 segment of MCA) or distal (distally from the mid-M1). Dural sinuses (from the confluens sinuum through the transverse sinus and sigmoid sinus to the superior bulbs of the internal jugular vein) were evaluated on 3D-reconstruction and volume rendering CT angiograms in venous phase (in coronal, axial, and sagittal planes if needed, using 24-mm thick slabs) and were scored as follows: score 1, less than 50% of contrast filling of the ipsilesional dural sinus when compared to the opposite normal side; score 2, contrast filling in ipsilesional sinuses 50%-99% of the opposite normal side; score 3, the size of dural sinuses is the same on both sides; and score 4, the dominant sinuses are on the side of occlusion. If the dural sinuses on the normal side were hypoplastic or aplastic, score 4 (ipsilesional dominant sinus) was used. We then classified scores 1 and 2 as dural sinus hypoplasia and scores 3 and 4 as normal. Leptomeningeal collaterals were evaluated according to a previously published score: 1—retrograde filling of pial arteries almost absent or not visible on the side of occlusion, 2—poor but still visible, 3—similar bilaterally, 4—robust on the side of occlusion in comparison with the unaffected side.[12] Scores 1 and 2 corresponded to poor collaterals and scores 3 and 4 corresponded to good collaterals.

One reader read all images blinded to all baseline data and follow-up imaging; a second reader assessed 25 randomly chosen patients to test inter-rater reliability. The clot location was evaluated by the consensus of 2 readers.

Outcomes

Primary outcome was the early midline shift measured as previously described on follow-up noncontrast CT (24-32 hours after admission CT/CTA) at the level of the third ventricle.[10,13] Patients were divided into those with substantial midline shift (midline shift ≥5 mm) and nonsubstantial midline shift (midline shift <5 mm).[14-17] Infarct volume (in milliliter) was measured semiautomatically on follow-up noncontrast CT using TomoCon PACS software (TatraMed, Bratislava, Slovak Republic). Hypoattenuation corresponding to the acute infarct was delineated on each slice and this area was multiplied by a slice thickness to obtain the total acute infarct volume.[18]

Statistical Analysis

Analysis was performed with NCSS (version 2007; NCSS, Kaysville, UT). Data are presented as mean and standard deviation for continuous variables, median and interquartile range for ordinal data, and percentage for nominal variables. Inter-rater agreement was assessed with intraclass correlation coefficient. Multivariate logistic regression was used to test for the presence of an independent association between dural sinus hypoplasia and the presence of midline shift at follow-up imaging. The above model included baseline leptomeningeal collateral status and any other variable that was deemed statistically significant in univariate analysis (at a 2-sided P value <.05).

Results

Of 256 consecutive patients treated with IV tPA during the study period, 88 were excluded (35 with extracranial internal carotid occlusion, 1 with acute carotid dissection, 29 with vertebrobasilar strokes, 6 with posterior cerebral artery strokes, 2 with anterior cerebral artery strokes, and 15 with distal M2 and/or M3 occlusions), an additional 40 patients had no visible MCA ± ICA occlusion on admission CT/CTA, and 42 patients had incomplete personal and/or imaging data (missing demographics, outcome variables, baseline CTA scans, and/