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Prediction of Hemorrhagic Transformation after Acute Ischemic Stroke Using Hyperintense MCA Sign

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Abstract— **Purpose: The hyperintense appearance of the middle cerebral artery (HMCA) sign consists of a thickened MCA stem with a blurred intense signal on contrast enhanced T1-weighted magnetic resonance imaging (T1W MRI). In this article, we define it and determine its incidence, diagnostic value, and reliability by comparison with magnetic resonance angiography and digital subtraction angiography. Materials and Methods: Non-contrast CT and immediately subsequent MRI were performed on 30 consecutive patients with acute ischemic stroke within 6 hours after symptom onset. All patients underwent at least one follow-up MRI or non-contrast CT within 2-7 days. Initial studies were analyzed for HMCA sign on post-Gd T1WI. Vascular findings on both MRI and CT were compared with findings at MRA and DSA.** Results: **Eleven patients were developed subsequent HT at follow-up studies. The HMCA sign on MRI was found in 6 hemorrhagic patients (P =0.00), and all of them had M1 occlusion on angiography. None of the patients in nonhemorrhagic group had HMCA sign on MRI. Conclusion: HMCA sign on post-Gd T1WI is highly specific and moderately sensitive indicator of acute thrombus with M1 MCA segment, as validated by angiography. Additionally, HMCA sign may be a useful marker of subsequent HT in acute ischemic stroke.**

Keyword—**Stroke, Hemorrhagic Transformation, Magnetic Resonance Imaging, Angiography**

I. INTRODUCTION

INTRAVENOUS tissue plasminogen activator (tPA) remains the only drug and route of administration approved in North America and Europe for acute ischemic stroke treatment [1]. However, one of the most significant problems impending the general use of thrombolytic therapy is concern over the risk of secondary intracranial hemorrhage. It is necessary to develop reliable and accessible noninvasive imaging modalities for predicting hemorrhagic transformation (HT) in acute ischemic stroke.

More recently, multivariable analyses showed that the presence of hyperdense middle cerebral artery (MCA) sign on non-contrast CT was an independent predictor of HT[4]. However, the sensitivity of the hyperdense MCA sign for MCA occlusion is low [2]. By contrast, the hyperintense MCA sign (HMCA) is analogous to the hyperdense MCA sign on non-contrast CT, can be routinely obtained on post-Gd T1WI MRI in patients with acute ischemic stroke. This correlation has not been reported.

We speculated that MRA would provide similar anatomical localization to formal cerebral angiography [3], and the HMCA sign representing MCA occlusion in the main stem of the artery would predict the subsequent HT.

II. METHODOLOGY

A. Patients

All patients undergoing acute stroke imaging were enrolled in this study according to the following inclusion/exclusion criteria:

Inclusion

- The initial MRI was performed within 6 hours of symptom onset
- The follow-up MRI and CT scan were performed within the first week after symptom onset.

Exclusion

- Patients with hemorrhage on the initial MRI or CT scan.

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Patients treated with tPA were eligible for participation. Thirty patients (18 men and 12 women with age range 39-97 years old, mean age 69.1 years old) underwent acute stroke imaging between August 2002 and April 2005 and fulfilled the enrollment criteria. Five of all patients received intravenous tPA treatment all within 3 hours of symptom onset.

B. Imaging protocol

All MRI studies were performed using a 1.5T whole-body MR unit (Signa cv/I; GE Healthcare, Milwaukee) with a single channel quadrature head coil. The typical stroke-imaging protocol included: (1) LOCALIZER (3 plane head and neck) (TR/TE, 27.3/1.6; FOV, 24×24 cm^2; matrix, 256×128), (2) Fast spin-echo T1-weighted (FSE T1) imaging (TR/TE, 833.3/10; FPV. 24×18cm^2 ; matrix, 256× 192), (3) EPI diffusion-weighted imaging (single-shot b=1000) (TR/TE, 10000/99.6; FOV, 22×22 cm^2; matrix, 96×200; Diffusion gradients with a b value of 1000 s/mm^2 applied separately in three orthogonal directions to generate trace images). (4) EPI FLAIR (single shot) (TR/TE, 8800/120; FOV, 24×24 cm^2; matrix, 256 × 192), (5) EPI GRE (multi-shot) (TR/TE, 2616.7/30; FOV, 24×24 cm^2; matrix, 256×224), (6) GRE permeability (31 phases)(TR/TE, 5.9/1.3; FOV, 24×24 cm2; matrix, 128×128), (7) EPI perfusion (single-shot 25 phases; 18 slices) (TR/TE,1766.7/31.5; FOV, 27×27 cm^2; matrix, 96× 64). (8) CEMRA (arch to circle of Willis). (9) gadolinium-enhanced T1-weighted conventional spin-echo imaging (TR/TE,650/20; FOV, 24×18 cm^2; matrix, 256× 192). The total scanning time is 10 minutes and 49 seconds. Our acute stroke protocol utilizes three sequential 15CC doses of magnevist for permeability, perfusion, and 3D triggered MRA acquisition.

Gadolinium-enhanced three-dimensional autotriggered elliptic centric-ordered (ATECO) MR angiography as a part of the stroke protocol was performed in each patients. Details of the fully automated detection and triggering system have been puplished previously [1].

CT studies were performed using a LightSpeed Ultra CT scanner (140 kV, 206-223 mA; GE Medical Systems) by using 5-mm contiguous sections with 5-mm-thick sections through the skull base without contrast enhancement. A subset of 12 patients underwent selective intracarotid DSA, as these patients were thought to possibly benefit from intraarterial thrombolytic therapy.

C. Image analysis

The hyperintense MCA sign on post-Gd T1W MRI was defined as post-gadolinium T1 hyperintensity within the MCA, in which the diameter of the vessel exceeded the contralateral vessel diameter and showed blurred margins with intense signal. The hyperdense MCA sign on CT defined as a MCA denser than its counterpart and any other vascular structure excluding obvious calcification. The MCA dot sign on CT was defined as the hyperdensity of an arterial structure in the Sylvian fissure relative to the contralateral side or to other vessels within the Sylvian fissure (Fig).

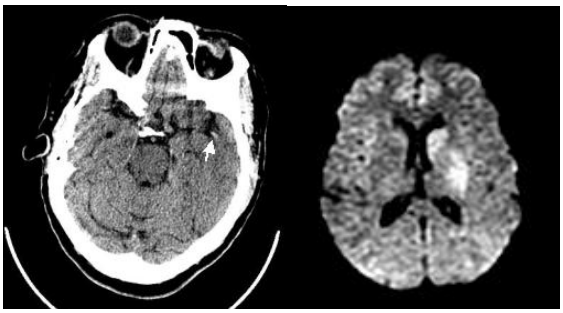
The presence of HT on MR was assessed on initial and follow-up T2*-weighed gradient echo images (EPI GRE) as low signal compared to the brain parenchyma, and on CT as high attenuation compared to the cortex. The presence of acute stroke was assessed on DWI as high signal, and on ADC images as low intensity.

D. Statistic analysis

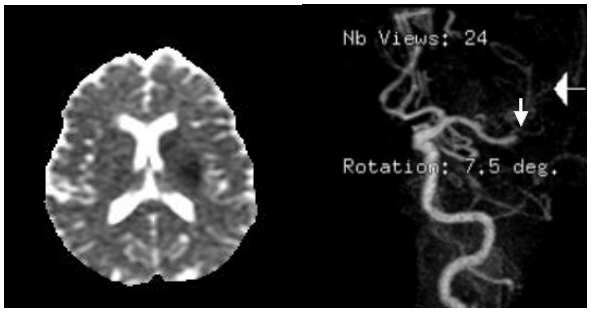
Fisher's exact test was used to determine if the differences in the HMCA on post-Gd T1W MRI, hyperdense MCA sign and dot sign on non-contrast CT observed in patients with and without HT were statistically significant. A p-value of less than 0.05 was considered to indicate a significant difference. Sensitivity, specificity, and positive predictive value of subsequent HT were also calculated for the HMCA sign on MRI.

III. RESULTS

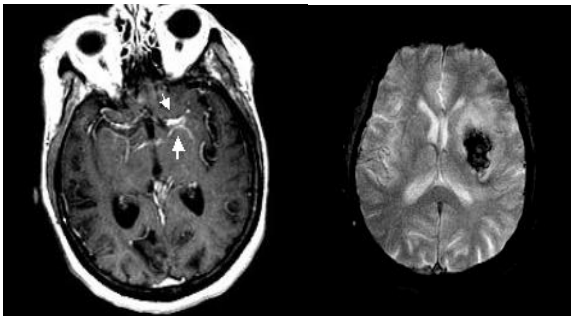
Thirty patients had admission CT and MR imaging obtained within 6 hours from symptom onset (4.3 hours ±1.4 for initial MRI), all without evidence of hemorrhage. Time between admission CT and MRI was 2.4 hours±1.4. Lesions visible on diffusion-weighted images were located within the MCA territory in all patients. ATECO MRA and DSA showed vessel occlusion as follows: 8 in ICA, 9 in M1 segment, 4 within M2 segment.



Admission CT Initial DWI



Initial ADC MRA



Post-Gd T1WI Follow-up EPI-GRE

Figure. A 73-year old female with right hemiparesis and aphasia. The admission CT showed left dot sign in the right Sylvian fissure. The initial DWI and ADC (15 minutes after CT) showed restricted diffusion in the left MCA territory. Post-Gd T1W MRI showed HMCA sign (arrow) in the left MCA stem. MRA showed occlusion in the right MCA stem. Follow-up EPI-GRE image (day 2) depicted hemorrhage in the left MCA territory.

Eleven patients showed HT on follow-up studies (36.7%). The HMCA sign on post-Gd T1W MRI was found in 6 patients (20%), all of whom developed HT. There was no significant age difference between patients with and without HMCA sign in HT group. None of patient without hyperintense MCA sign had subsequent HT. The incidence of HMCA sign on post-Gd T1W MRI in HT group was significant compared with non-HT group ($P = 0.001$). The sensitivity, specificity, and positive predictive values of the HMCA sign for subsequent HT were 54.5%, 100%, and 100% respectively. All of the patients with HMCA sign had MCA occlusion on ATECO MRA (4 in the right, 2 in the left). The hyperdense MCA sign on CT was found in 9 patients (30%), 5 of them in HT group. Four of the 5 patients who had the hyperdense MCA sign on CT in HT group were associated with the HMCA sign on MRI. MCA "dot" CT sign was observed in 7 patients (23.3%), 3 of them within HT group. One of the patients with an MCA "dot" sign on CT was associated with an HMCA sign on MRI, but no hyperdense MCA sign on CT (Fig). One MCA "dot" sign was associated with hyperdense MCA sign on CT only. The incidences of HMCA sign on MRI, hyperdense MCA sign and MCA dot sign on CT in two groups (HT group and non-HT group) were shown in Fig 4. In the study group, 2 of 5 patients treated with tPA developed HT, both of these patients had HMCA sign on Gd-DTPA MRI, as well as 1 hyperdense MCA sign on CT.

IV. DISCUSSION

The goal of this study was to validate the hyperintense MCA sign on post-Gd T1W MRI, including direct comparison with gold standard of MRA and DSA. MR angiography and DSA comparison demonstrated that the HMCA sign on

Gd-DTPA MRI clearly has diagnostic value as a high specific (100%) and moderately sensitive (20%) indicator of acute thrombus within the MCA. Further more, this sign was significant correlation with developing HT (P =0.001). The sensitivity, specificity, and positive predictive values of the HMCA sign on post-Gd T1W MRI for subsequent HT were 54.5%, 100%, and 100% respectively.

Comparison with ATECO MRA and DSA, all patients with HMCA sign on MRI had occlusions on M1 segment of MCA. The thrombosed MCA on Gd-DTPA MRI appeared not only hyperintense but also was larger than the contralateral artery. This likely represents vascular distention at and/or proximal to the obstructing clot [4]. Another possible mechanism may be associated with hypertension in these patients [4]. Hypertension during the first 24h after onset of stroke is an independent factor for predicting HT [4]. The atherosclerotic MCA burdened with elevated blood pressure during the acute phase may result in exudation of RBCs and gadolinium. Consequently, the affected MCA appears thickened and blurred with increased T1 signal. Additionally, these patients with a proximal occlusion experience an immediate fall in blood flow to the territories supplied by the lenticulostriatal arteries, where collaterals are limited. This leads to an increased risk of hemorrhagic transformation where ischemic injury is greatest [4]. It should be mentioned that ischemic-induced stasis of blood may lead to hemolysis. Hemolysates may contribute to parenchymal damage, as well as enhance rtPA activity, which could have been a factor in the exacerbation of hemorrhagic transformation. Two patients with HMCA sign after tPA treatment developed HT on follow-up in our group.

V. CONCLUSION

By comparison with MR angiography and DSA as gold standards, this study demonstrated that HMCA sign on post-Gd T1W MRI clearly has diagnostic value as a high specific and moderately sensitive indicator of acute thrombus within the MCA during the acute phase of ischemic stroke. Further more, the present study found that HMCA sign on Gd-DTPA MRI had a significant correlation with developing HT. The HMCA sign represents a useful addition to the catalog of signs of acute cerebral ischemia evident on early MR studies. For patients in acute phase with hyperdense MCA sign and dot sign on non-contrast CT, the Gad-DTPA MRI is recommended for selecting the tPA candidates.

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