Diffusion-Weighted Imaging of Intravascular Clots in Cerebral Venous Thrombosis

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Background and Purpose—Hyperintensities on diffusion-weighted MRI at the site of venous occlusion have previously been reported in cerebral venous thrombosis (CVT). The frequency of these signal changes according to late venous recanalization was not determined yet.

Methods—In a series of 28 patients with recent CVT, the frequency of hyperintense signals as seen on diffusion-weighted MRI in vein(s) or sinus(es) (HSVdwi) was assessed at the time of diagnosis, as was rate of recanalization 2 to 3 months after anticoagulation.

Results—HSVdwi was detected in 20 occluded vein(s) or sinus(es) in 12 patients (41%) with recent CVT. The mean apparent diffusion coefficient measured in 5 patients within HSVdwi in the superior sagittal sinus was $4.88 \pm 1.49 \times 10^{-4}$ mm$^2$/s. The delay since clinical onset was larger in the presence than in the absence of HSVdwi as detected at the time of diagnosis. No HSVdwi was visible at the second MRI although some vessels remained occluded. Complete recanalization of the vessel was less frequent when HSVdwi was observed on the first MRI (35% versus 88%, $P=0.005$).

Conclusions—Results of this study suggest that the movements of water molecules are more or less restricted within the venous clot according to the stage of thrombus formation in CVT. The presence of HSVdwi in occluded veins at the time of diagnosis might be predictive of a low rate of vessel recanalization 2 or 3 months later. (Stroke. 2004;35:99-103.)

Key Words: magnetic resonance imaging, diffusion-weighted occlusion sinus thrombosis

Cerebral venous thrombosis (CVT) is usually diagnosed with MRI on both T1- and T2-weighted images in association with MR venography. Selim et al recently observed that thrombosed cerebral veins were detected on T2*-weighted MRI as a loss of signal resulting from the susceptibility effects of deoxyhemoglobin within the blood clots at the site of venous occlusion. The rate of vessel recanalization in CVT, according to the type or number of thrombosed sinuses, has been rarely investigated prospectively. On diffusion-weighted imaging (DWI), some authors previously reported an increased signal corresponding to the presence of intravascular clots in cases of CVT in the presence or absence of cerebral tissue lesions. The corresponding low value of the apparent diffusion coefficient (ADC) suggested important restrictions of the movements of water molecules at the site of occlusion. Both the frequency and diagnostic value of venous diffusion signal changes in CVT are unknown. For this purpose, in a large series of CVT, we investigated the frequency of both diffusion signal changes in sinuses or veins at the time of diagnosis and vessel recanalization at the corresponding site.

Subjects and Methods

Patients

From our database of CVT, among 37 cases diagnosed between November 1999 and July 2001, we selected all patients who had had both a first MRI at the time of diagnosis and a second MRI 2 to 3 months later obtained with identical imaging parameters.

CVT was diagnosed on the basis of the following criteria: (1) absence of flow or partial flow void in thrombosed sinuses or veins in the presence of visible and normal flow in other veins on MR venography and (2) typical signal abnormalities corresponding to the intraluminal clot on T1- and/or T2-weighted MRI as previously reported in CVT (high or isosignal according to the type of sequence and stage of thrombosis).

Twenty-eight patients (25 female, 3 male patients; age range, 15 to 59 years; mean age, 33 years) were selected. Clinical onset was subacute (48 hours to 30 days) in 19 cases, acute (<48 hours) in 8 cases, and chronic (>30 days) in 1 case. At the time of diagnosis, 25 patients complained of headache, which was the only symptom in 16 (associated with papilledema in 7 patients). Other clinical manifestations were focal neurological deficits ($n=9$), seizures ($n=7$), and drowsiness ($n=4$).

A complete clinical and laboratory workup was performed in all subjects as previously detailed. An associated condition already known to increase the risk of venous thrombosis was detected in 23 of the 28 patients.
The delay between clinical onset and the first MRI investigation (MRI 1) ranged from 1 to 30 days (mean delay, 9.2 ± 9 days). CVT involved only the superficial system (cortical vein, superior sagittal sinus [SSS], or lateral sinus [LS]) in 20 patients (right LS, n = 15), both the superficial and the deep venous systems (vein of Galen, straight sinus, or internal cerebral veins) in 5 patients, and only the deep venous system in 2 patients. Anticoagulation was started immediately after the diagnosis of CVT in all subjects. No patient was treated by in situ thrombolysis. In 1 patient, an extensive hemorrhagic lesion was removed by surgery (patient 4).

At time of the second MRI (MRI 2), all patients were headache free; 26 patients were asymptomatic and had a modified Rankin Scale score of 0. Neurological sequelae were present in 2 patients (patients 4 and 17) whose modified Rankin Scale scores were 4 and 2, respectively, and who had an extensive hemorrhagic lesion at the MRI 1.

**MR Imaging**

MRI examinations were obtained with a 1.5-T MR unit (GE Medical System) with the following parameters: (1) T1-weighted sequence: imaging time, 1.44 minutes; sagittal or axial slices, 5-mm thickness with a 1.5-mm gap; matrix, 256 x 192; field of view, 24 x 24 cm; repetition time (TR)/echo time (TE)/excitations, 500/14/1; and bandwidth, 15.6 kHz; (2) fluid-attenuated inversion recovery (FLAIR); imaging time, 4.16 minutes; axial interleaved sections, 5 mm with 1.5-mm gap; matrix, 256 x 192; field of view, 24 x 24 cm; TR/effective TE (TEeff)/TI/excitations, 8002/155/2000/2; and bandwidth, 31.2 kHz; (3) 2-dimensional time-of-flight imaging sequence: imaging time, 4.54 minutes, MIP reconstruction; interleaved sections, 121 x 1.5 mm; matrix, 256 x 128; field of view, 24 x 18 cm; TR/TR, 24/4.9; flip angle, 50°; and bandwidth; 16 kHz; and (4) diffusion-weighted imaging: imaging time, 30 seconds; multisection single-shot spin-echo diffusion echo-planar with a pair of diffusion gradients centered around the 180° pulse; axial section thickness, 5 mm with 1.5-mm gap; matrix, 128 x 128; field of view, 24 x 24 cm; TR/TEeff, 7500/99; and 20 sections acquired with echo-planar T2 imaging acquisition (b = 0 s/mm² and b = 1000 s/mm²) (diffusion gradient, G = 22 mT/m; duration, 32 ms; separation time, 39 ms). The diffusion gradients were successively and separately set in 3 orthogonal directions, and isotropic images were generated. Dedicated software was used to generate quantitative ADC maps (FuncTool, GE Systems).
Image Analysis

The MRI data obtained at the time of diagnosis were reviewed by a board-certified neuroradiologist (J.-P.G.) blinded to the subject’s clinical condition using a structured assessment for (1) the site of each occluded vein or sinus as detected on both MR venography and conventional MRI, (2) the presence (and location) or absence of an increased signal in veins or sinuses by visual inspection on DWI, (3) the presence (and location) or absence of signal abnormalities on T1-weighted and FLAIR images at the same level, and (4) the presence or absence of signal modifications within the cerebral tissue by visual inspection of T1, FLAIR, and DWI. The data obtained at MRI 2 were reviewed similarly; the presence or absence of recanalization was evaluated for each occluded vein or sinus as detected on both MR venography and conventional MRI 1. Recanalization was defined as complete (blood flow without any interruption), partial (small interruptions of continuous blood flow and/or narrowing of the venous lumen), or absent (interrupted blood flow).

ADC was measured within hyperintense signals as seen on diffusion-weighted MRI in vein(s) or sinus(es) (HSVdwi) only in the occluded SSS because the close vicinity of cerebrospinal fluid (CSF) in other locations might alter the exact evaluation of water diffusion. A unique circular region of interest of 45 mm² was positioned on the ADC map at the corresponding site for quantification.

Student’s t test or χ² tests were used for comparisons of MRI data obtained between groups. Values of P<0.05 were considered statistically significant.

Results

Our main clinical and MRI results are presented in the Table. On MRI 1, the presence of HSVdwi was detected in 20 vessels (17 sinuses, 3 veins) of 12 patients (41%); 7 of 17 in SSS, 9 of 20 in LS, 1 of 6 in the deep venous system, and 3 of 8 in cortical veins, in association with HSVdwi in SSS (Figure 1). When HSVdwi was present, an abnormal (high or iso) signal was always observed at the same level on conventional MRI sequences (T1 and/or FLAIR). On MRI 2, HSVdwi was always absent in veins or sinuses. The ADC values corresponding to HSVdwi were calculated in 5 cases in thrombosed SSS. The mean ADC was $4.88 \pm 1.49 \times 10^{-4}$ mm²/s in these cases, which was 6 times lower than the ADC value of CSF (24.0 to $32.4 \times 10^{-4}$ mm²/s) and 2 times lower than the mean ADC value measured in the normal-appearing tissue ($8.4 \times 10^{-4}$ mm²/s) using identical regions of interest.

The frequency of associated conditions and clinical symptoms at time of diagnosis did not differ in the presence or absence of HSVdwi. In contrast, the delay since clinical onset was larger in patient with HSVdwi than in patients without HSVdwi as detected on MRI 1 (13.5±9.5 versus 5.9±7.5 days, respectively; P=0.027). HSVdwi was also less frequent in the presence of an isolated thrombosed sinus (4 of 15) than in CVT involving at least 2 thrombosed sinuses (8 of 13; P=0.06). In our 13 cases with extensive CVT, HSVdwi was observed in all thrombosed sinuses in only 3 cases (patients 11 through 13). Signal changes within the cerebral tissue were less frequent in the presence of HSVdwi as seen on MRI 1 than in its absence (HSVdwi present, 2 of 12, patients 10 and 11; absent, 11 of 16) (P=0.006).

Among the 17 thrombosed sinuses with HSVdwi on MRI 1, recanalization was complete in 6 sinuses (35%), partial in 6 (35%), and absent in 5 (30%). Twenty-six occluded sinuses were found without any HSVdwi on MRI 1; recanalization was complete in 23, partial in 2, and absent in 1 (Figure 2). Therefore, complete recanalization was less frequent in the presence (6 of 17, 35%) than in the absence (23 of 26 88%) of HSVdwi as seen on MRI 1 (P=0.005; Figures 3 and 4).

Discussion

In this series of 28 patients with CVT who had repeated MRI examinations, all classic neurological features of CVT, including focal neurological deficits, seizures, drowsiness, and intracranial hypertension, were observed.1,11 Only the pattern of presentation as headache in the absence of focal neurological deficits was found more frequently than previously reported (57% compared with 44% in the 110 cases described by Ameri et al1). The inclusion of one third of patients from our emergency headache center is probably responsible for this discrepancy.

On the MRI 1, the presence of HSVdwi was detected in 41% of the cases with CVT. This frequency is close to that reported by Lovblad et al4 (7 of 18, 39%) but larger than that observed by Chu et al9 (2 of 14, 14%). Therefore, this sign is
of low sensitivity for the acute detection of clot in CVT. Moreover, HSVdwi was always found in the presence of signal changes in thrombosed veins on either T1 or FLAIR images, which suggests that the presence of HSVdwi is not actually of complementary value for the diagnosis of CVT when T1 and FLAIR images are already obtained.

The ADC value measured within the clot was 6 times lower than diffusion measured in the CSF in the presence of HSVdwi. This supports the view that movements of water molecules are strongly restricted within the venous clot at the site of increased signal on DWI. These results are in line with previous experimental data. Ex vivo, MRI measurements of water diffusion in fresh thrombi showed important modifications of ADC values, depending on the time elapsed after clot formation.12 The initial decrease preceding the large increase in water diffusion detected in the thrombus was presumably related to important ultrastructural modifications of the clot occurring over time.13 In the present study, obtained in vivo, the delay from clinical onset to MRI 1 was longer in patients with HSVdwi (2 to 30 days; mean, 13.5 days) than in patients who did not have these signal abnormalities. Furthermore, HSVdwi was absent on MRI performed later, 2 to 3 months after the first examination. Therefore, signal modifications on DWI are transient in vivo within thrombosed sinuses, which indicates that diffusion changes are actually related to the evolving stages of the thrombus formation.

In this series, we observed that recanalization of occluded vein(s) or sinus(es) was less frequent when HSVdwi was present at the corresponding site on the initial MRI. This suggests that the microstructure of the clot in CVT, as reflected by the signal changes on DWI, might influence the effectiveness of clot dissolution under heparin treatment. Some authors have suggested that the migration of fibroblasts into the clot and incorporation of collagen may render the fibrin less accessible to fibrinolytic enzymes.13 Others argue that this resistance may be related mainly to an abnormal fibrin polymerization.14 Whatever the interpretation, our results suggest that an increased signal on DWI might be of value in the prediction of the risk of persistent venous occlusion at 3 months. This result might be useful in some cases with initial unfavorable evolution for whom heparin continuation or early in situ thrombolysis is considered, although the rate of recanalization and/or the frequency of HSVdwi are not actually correlated to the risk of tissue lesions, as confirmed in the present study. Larger follow-up studies are warranted to confirm the predictive value of HSVdwi for vessel recanalization and to assess its clinical value in CVT.

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References

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