

Diagnosis of Cerebral Venous Thrombosis With Echo-Planar T2*-Weighted Magnetic Resonance Imaging

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Background: Magnetic resonance (MR) signal changes suggestive of cerebral venous thrombosis (CVT) on T1- and T2-weighted images may be subtle and their identification requires a high degree of suspicion. Magnetic resonance venography remains essential for definitive diagnosis. Recent reports have shown that T2*-weighted MR sequence is more sensitive than T1-weighted, T2-weighted, and fluid-attenuated inversion recovery (FLAIR) images in detecting subarachnoid and intracerebral hemorrhages, both of which can be seen in association with CVT. The value of T2*-weighted magnetic resonance imaging (MRI) in diagnosing CVT has not been well studied.

Objectives: To investigate and describe T2* (susceptibility-weighted) MRI findings in 5 patients with CVT.

Methods: We reviewed our stroke database from May 1, 1997, through May 31, 2001. The diagnosis of CVT was made in 6 patients, 5 had an MRI with T2* sequence. We

examined T2*/susceptibility-weighted images for these 5 patients to determine their ability, relative to T1-weighted, T2-weighted, and FLAIR sequences, to detect CVT.

Results: On T2*-weighted images, we were able to detect areas of hypointensities in the affected veins and/or sinuses in all 5 patients. Thrombosed veins and/or sinuses were more easily seen on T2*-weighted images than on any other MR sequence. The T2* sequence also allowed visualization of associated hemorrhagic venous infarcts, which were considerably less obvious on other MR sequences.

Conclusions: The T2*-weighted MR sequence can be useful in rapid detection of CVT and may enable the diagnosis to be made prior to MR venography. This is particularly important in clinically unsuspected patients, in whom MR venography is rarely obtained.

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CEREBRAL VENOUS thrombosis (CVT) can lead to devastating disability, and even death, if not timely diagnosed and treated.¹ Diagnosing CVT often challenges physicians owing to the nonspecific symptoms and the broad spectrum of presentation.² Some cases of CVT may be unrecognized. Radiological studies are crucial in establishing the diagnosis. Computed axial tomography (CT) cannot reliably diagnose CVT in many cases, especially if contrast is not given. A nonenhanced CT shows no abnormality in about 20% of the patients with CVT^{3,4}; and CT findings of CVT may be misinterpreted as subarachnoid hemorrhage or intraparenchymal hemorrhage.^{3,5} Alterations in blood flow and hemoglobin degradation products in thrombosed veins may produce signal changes on magnetic resonance (MR) T1- and T2-weighted images, which may suggest the diagnosis of CVT.⁶⁻⁸ However, conventional T1- and T2-weighted MR images (MRIs) are relatively insensitive since

such signal changes are often subtle.⁵ Gadolinium administration can increase the sensitivity of the MRI,⁹ but cerebral angiography remains essential for the definite diagnosis of CVT. Of late, MR venography (MRV) has surpassed conventional angiography as the imaging modality most widely used to establish the diagnosis of CVT.^{5,10}

Thus, the diagnosis of CVT can be missed, particularly in clinically unsuspected cases, if only routine nonenhanced T1- and T2-weighted MRI sequences are performed without angiography. Because MRV and gadolinium enhancement are not routinely performed in most MRI protocols, delays of serious consequences can occur in the diagnosis of CVT. Recent reports have confirmed high sensitivity of echo-planar T2* (susceptibility)-weighted MRIs (SWI) for detecting the magnetic susceptibility effect of blood products such as deoxyhemoglobin, in patients with acute subarachnoid hemorrhage and intraparenchymal hemorrhage.^{8,11} The utility of T2*/SWI for detecting CVT is unknown. A T2*-weighted se-

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SUBJECTS AND METHODS

PATIENT SELECTION

We reviewed our computerized stroke database from May 1, 1997, through May 31, 2001. Over this period, the diagnosis of CVT was made in 6 patients who all had brain MRI, MRV, and CT. Two patients also had conventional angiography (DSA). Five of the 6 patients had T2*-weighted sequences as a part of their MRI. These 5 patients were included in this study.

MRI PROTOCOL

The MRI protocol used in our institution routinely includes diffusion-weighted MRI (DWI), SWI, and T1- and T2-weighted images, non-echo-planar FLAIR images, and MR angiography of the intracranial vessels. The imaging parameters for SWI, echo-planar imaging gradient echo are as follows: repetition time, 0.8 milliseconds; echo time, 60 milliseconds; flip angle, 60°; number of slices, 20; slice thickness, 7 mm; acquisition matrix, 96 × 128 pixels; field of view, 240 cm; and acquisition time, 2 seconds. Parameters for other sequences have been previously reported.⁸

quence has been a routine part of our stroke MRI protocol for several years. We have performed a retrospective analysis of MRI findings in patients with CVT to assess the feasibility of T2*/SWI sequence for the detection of CVT.

REPORT OF CASES

CASE 1

Figure 1 highlights MRI findings in patient 1 and shows signal loss (darkening) in the sagittal sinus, vein of Galen, left transverse sinus, and straight sinus confluence on T2*-weighted images. This patient is a 38-year-old man who presented with acute change in mental status in the setting of a 4-day history of “flu-like illness,” headaches, vomiting, and lethargy. On examination, he was inattentive, abulic, and had papilledema. The findings from the remainder of his neurological and general physical examinations showed no abnormality. The National Institute of Health Stroke Scale (NIHSS) score was 4. A CT of the head, plain and contrasted, suggested “subarachnoid hemorrhage vs cortical venous occlusion in the left posterior occipital region.” Diffusion-weighted MRI showed restricted diffusion abnormalities in frontal regions, a right-sided thalamic infarct, and a left-sided occipital hemorrhagic infarct. Magnetic resonance venography showed poor flow in the sagittal sinus, internal cerebral veins, vein of Galen, septal and thalamic veins, transverse sinuses, and straight sinus confluence (Figure 1D). Conventional angiography confirmed thrombosis in these veins and showed occlusions of both internal jugular veins. He was initially treated with intravenous heparin sulfate but rapidly became somnolent. He received intrasinus recombinant tissue-type plasminogen activator (rt-PA), followed by stenting of the left internal jugular vein and systemic an-

ticoagulation. His condition rapidly improved. He was diagnosed as having polycythemia vera.

CASE 2

Figure 2 highlights MRI findings in patient 2 and shows susceptibility effect in the vein of Galen, sagittal sinus, and left-sided lateral sinus complex on T2* images. He was a 36-year-old man who had left-sided facial pain for 1 week, then suddenly developed severe headache, nausea, and vomiting. He was found “unresponsive” and had urinary incontinence. On examination, he was intubated and comatose with decerebrate posturing. Brainstem reflexes were intact. His pupils were equal and reactive to light. Fundoscopic examination showed papilledema. Neurological examination showed no focal signs; NIHSS score was 37. The findings of his general physical examination showed no abnormality. A CT of the head showed multiple foci of high signal in the left temporoparietal-occipital junction and outlining gyri; this was interpreted as intraparenchymal and subarachnoid hemorrhages (Figure 2D). Brain MRI revealed similar findings on T1-weighted, T2-weighted, and FLAIR images; MRV revealed absent flow in the superior sagittal, straight, and left transverse sinuses. Conventional angiography confirmed the presence of diffuse CVT involving the sagittal, bilateral transverse, and deep venous systems and thrombosis of the left internal jugular vein. He was treated with intrasinus rt-PA, followed by systemic anticoagulant therapy. His condition rapidly improved, with a near-complete recovery. His evaluation for possible underlying cause was normal except for an elevated serum homocysteine level.

CASE 3

Figure 3A depicts the T2*/SWI findings in patient 3 and shows a susceptibility effect within the vein of Galen and left sinus complex. This 62-year-old woman presented with new onset of right-sided focal motor seizure with secondary generalization after a 3-day history of worsening headaches. Her medications included estrogen replacement therapy. On examination, she was inattentive and hypophonic. She had a right Babinski sign and a slow shuffling gait; NIHSS score was 0. Plain head CT showed “an unusual increased signal at the inferior sagittal sinus”; a contrast-enhanced MRI did not support CVT. Brain MRI showed restricted diffusion abnormalities in the basal ganglia and thalami; MRV confirmed CVT involving the internal cerebral veins, vein of Galen, and straight, sigmoid, and left transverse sinuses. Her symptoms resolved with the administration of systemic anticoagulant therapy and the cessation of hormonal replacement therapy.

CASE 4

Figure 3B shows T2* areas of hypointensities within the left transverse and sigmoid sinuses of patient 4. 42-year-old man, he had presented with acute onset of severe headache. Neurological and general physical examination findings showed no abnormality; NIHSS score was 0. A CT of the head showed a left posterior temporal hyperdensity, interpreted as “hemorrhage vs vascular malforma-

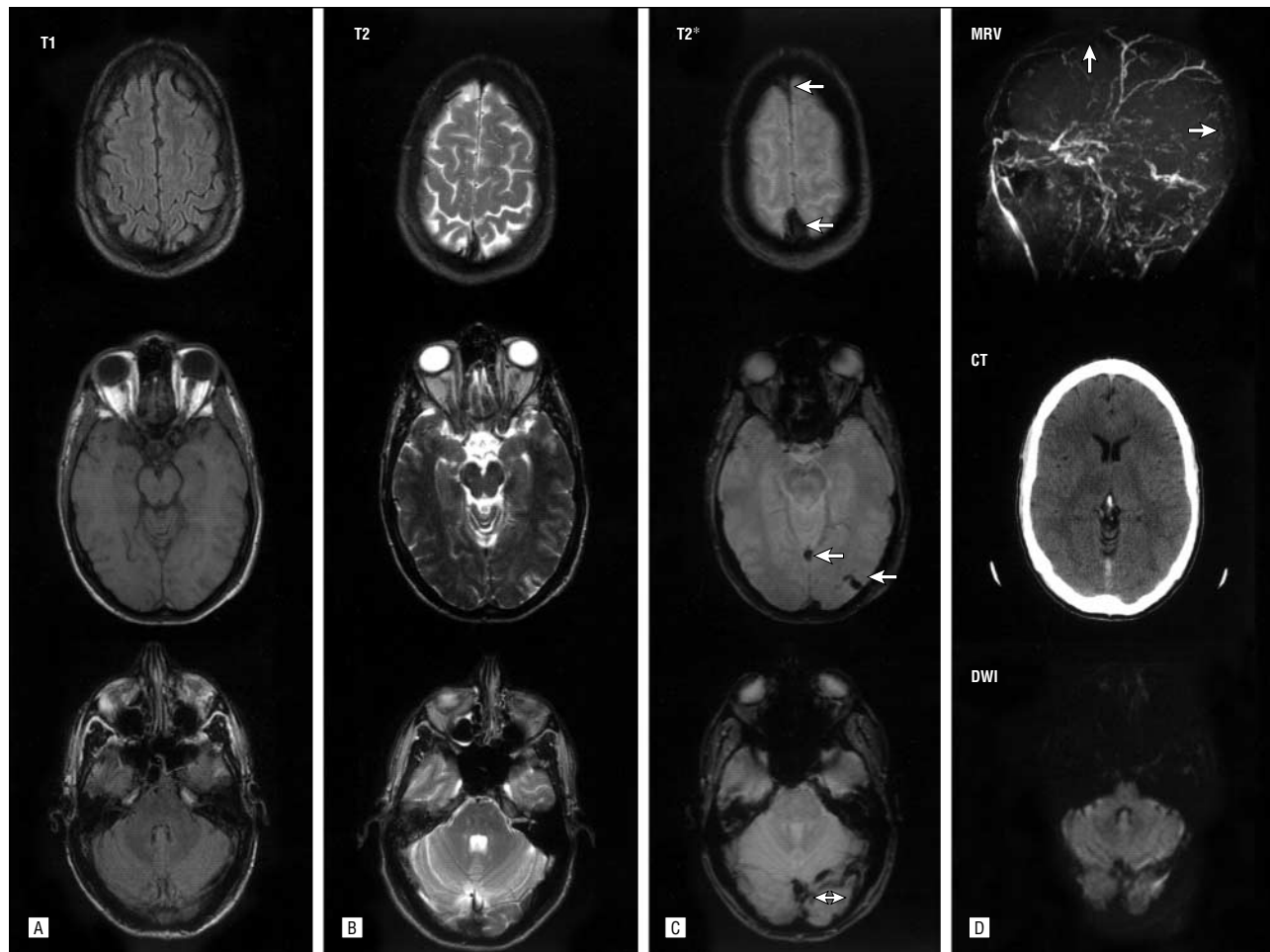


Figure 1. Case 1. Magnetic resonance image (MRI). C, T2*/susceptibility-weighted MRI with the arrows pointing to blood products (darkening) in the sagittal sinus, vein of Galen, left transverse sinus, and straight sinus confluence, which is not easily seen on comparable T1-weighted (A) and T2-weighted (B) MRI slices. D, Views of the MR venography (MRV), nonenhanced computed tomographic scan (CT), and diffusion-weighted image (DWI) of the same patient. Note the filling defects in the superior sagittal sinus (arrows) on MRV in comparison to that in Figure 4 from a healthy control subject.

tion.” Brain MRI, T1- and T2-weighted images, suggested the presence of a hyperintense signal within the left transverse and sigmoid sinuses; MRV confirmed occlusion of the left transverse and sigmoid sinuses. He was treated with heparin, then warfarin sodium. His headache rapidly resolved.

CASE 5

Figure 3C shows a large area of susceptibility effect in the right temporoparietal region and within the right transverse sinus of patient 5. A 53-year-old woman, she had had sudden onset of severe headaches and vomiting. She had 2 witnessed generalized tonic-clonic seizures en route to our hospital. On physical examination, she was somnolent; had bilateral papilledema, left visual field cut, and left-sided hemiparesis. The NIHSS score was 6. A CT of the head showed a right parietal hemorrhage, interpreted as “amyloid angiopathy vs hypertensive hemorrhage.” Brain MRI showed “a large area of hemorrhage with edema within the right temporoparietal cortex” on T1-weighted and T2-weighted images. Gadolinium administration showed a thrombus within the right transverse sinus; MRV confirmed occlusion of the right transverse and sigmoid si-

nuses. She was found to have persistent protein C deficiency. She was treated with systemic anticoagulant therapy that resulted in the improvement of her condition.

RESULTS

The diagnosis of CVT was made by stroke-experienced neurologists and neuroradiologists on the basis of history, clinical examination results, and radiological findings. The definite diagnosis was confirmed by MRV in all 5 patients.

We were able to detect areas of hypointensities in the affected veins and/or sinuses, indicating the presence of intravenous clots, on T2*-weighted sequence. In all 5 patients, thrombosed veins and sinuses were more easily seen on T2*-weighted images than on any other nonangiographic MR sequence. In patients 1 and 2, the associated hemorrhagic venous infarcts were easily visualized on T2*-weighted images, but not T1- or T2-weighted images.

Figure 4 shows MRV and T2* MRI of a healthy control subject for comparisons. The results of CT or DSA are not shown for all patients since the purpose of this study is not to compare CT vs MRI or MRV vs DSA.

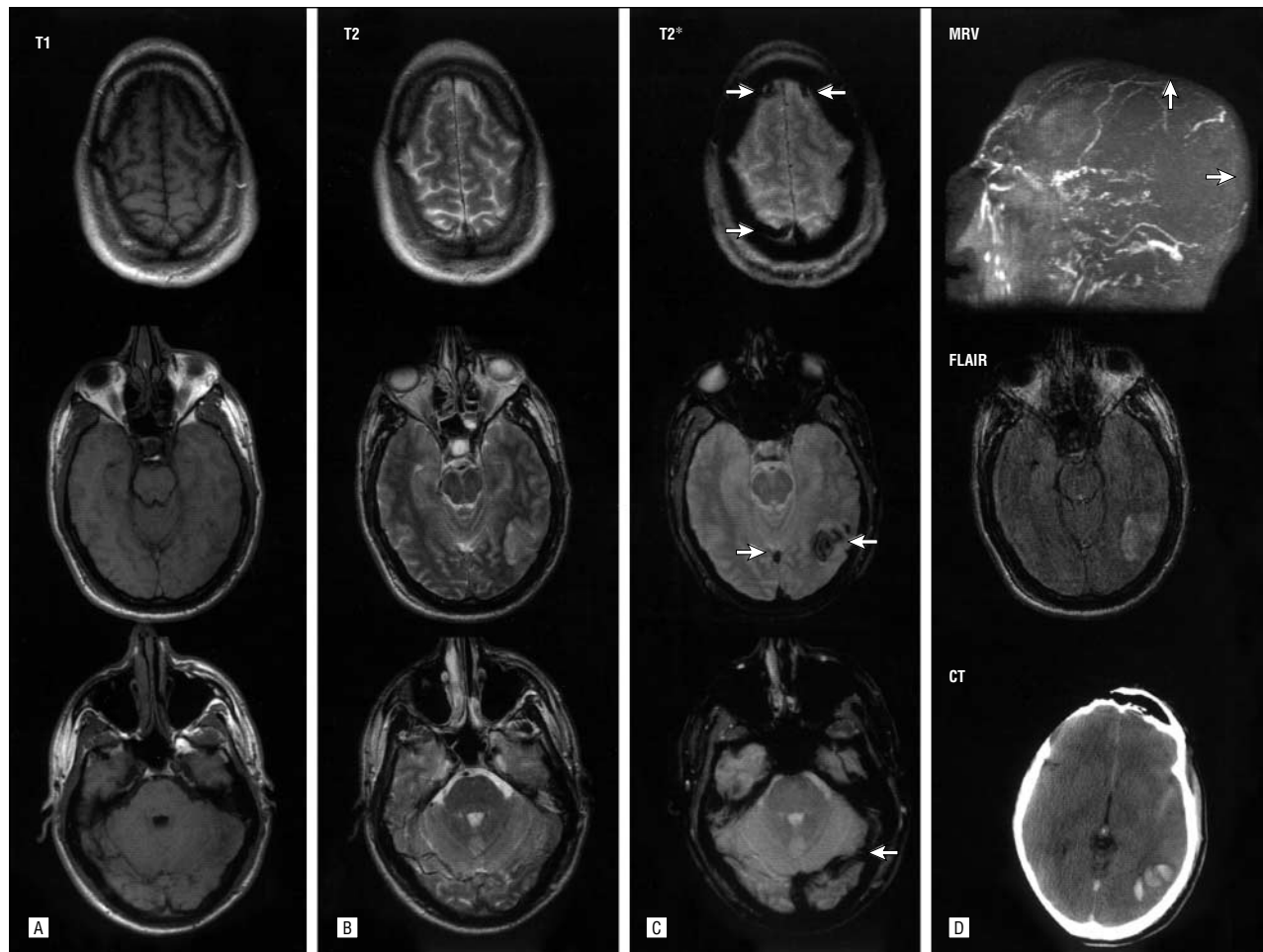


Figure 2. Patient 2. Magnetic resonance image (MRI). C, Note that T2*/susceptibility-weighted MRI shows the abnormalities (arrows), as low signal, within the left parieto-occipital region (hemorrhage) and sagittal, transverse, and straight sinuses (blood degradation products of the intravenous thrombus) more clearly than the the corresponding T1-weighted (A), T2-weighted (B), and fluid-attenuated inversion recovery (FLAIR) (D) images. Magnetic resonance venography (MRV) shows absent flow in the superior sagittal sinus (arrows).

COMMENT

To our knowledge, the use of T2*/SWI in diagnosing CVT has not been previously evaluated. Our study shows that the gradient echo T2*-weighted images are able to detect the presence of the intravenous clot. The clot is directly visualized as an area of hypointensity in the affected vein and/or sinus. Although not quantitatively assessed, the sensitivity of T2*/SWI for detecting CVT far exceeded that of routine T1- and T2-weighted images. Thrombosed veins and sinuses were more easily visualized on SWI than on any other MR sequence in all 5 patients.

Several studies have confirmed the usefulness of MRI for the diagnosis of CVT.^{3,5,9} The MRI features of CVT have been described in detail in numerous reports.^{5,9} The main sign of CVT on a standard MRI protocol is the lack of expected signal flow-void on standard spin echo T1 and T2 sequences. The MR signal relies on proton (hydrogen nuclei) density and T1 and T2 relaxation times.^{10,11} The different chemical products of blood breakdown in thrombosed veins and sinuses result in signal changes on T1- and T2-weighted images. Thus, the actual appearance and signal intensity of the intraluminal thrombus evolve over time depending on the paramagnetic ef-

fects of hemoglobin breakdown products, in a manner similar to that of intraparenchymal hemorrhage.^{6-8,12,13}

The use of standard spin echo T1 and T2 sequences, in isolation, to diagnose CVT has its shortcomings since their sensitivity for detection of CVT is poor, especially in chronic cases, and the lateral and superior sagittal sinuses are not seen well in axial sections.⁵ Magnetic resonance venography is almost always required to confirm the diagnosis of CVT. Absence of flow signal on MRV suggests intraluminal thrombosis. However, MRV is also subject to artifacts, which may result in a false-negative diagnosis.⁵

The MR properties of products of hemoglobin catabolism are well characterized.⁶⁻⁸ Hemoglobin becomes deoxygenated when the arterial blood, with high oxygen saturation, passes into the venous blood with lower oxygen saturation.¹⁴ This results in the formation of deoxyhemoglobin, which possesses paramagnetic properties. Decreased cerebral venous blood flow in CVT promotes a local shift in the hemoglobin oxygenation curve toward the formation of deoxyhemoglobin. Deoxyhemoglobin produces a nonuniform magnetic field and rapid dephasing of proton spins and loss of T2*-weighted signal.¹¹ This property of paramagnetic molecules, such as deoxyhemoglobin, is termed “magnetic susceptibility effect” and results in signal loss

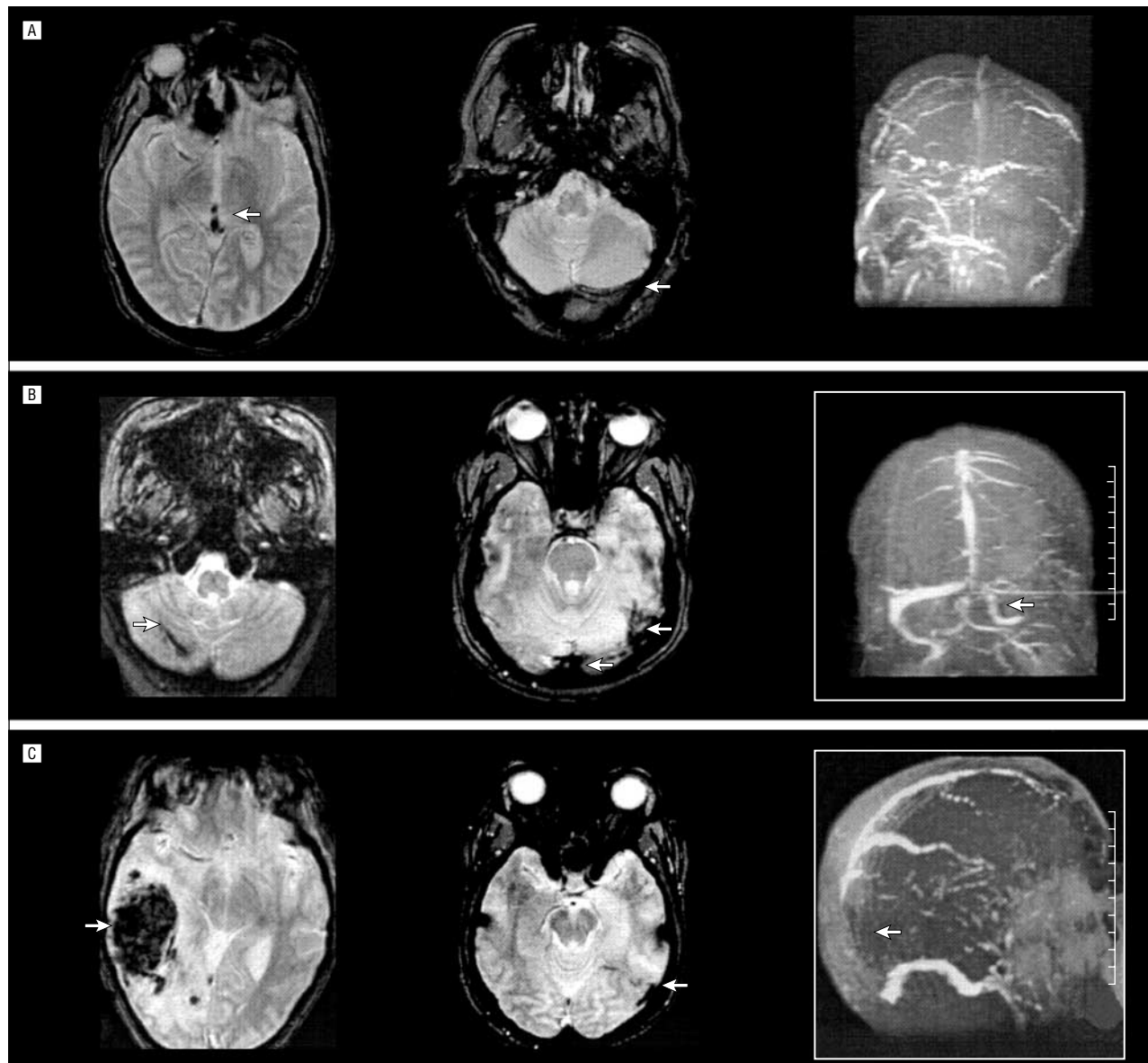


Figure 3. Patients 3 through 5. T2*-weighted magnetic resonance (MR) imaging and MR venography rows A through C. The arrows point to the abnormalities, susceptibility effect on T2*, and filling defects on MR venography.

(darkening) best seen in T2*/SWI.^{13,15,16} This magnetic susceptibility effect of hemoglobin degradation products within the thrombosed veins accounts for our current results, showing that T2*/SWI is the nonangiographic MR sequence that most clearly reveals CVT in all 5 patients. Simultaneous acquisition of MRV in all of our patients, besides establishing the diagnosis of CVT, confirms that the susceptibility effect seen within the veins and sinuses is consistent with blood clots and is not an artifact.

We have previously shown that T2*/SWI is the most sensitive MR sequence for detecting intracerebral hemorrhage.⁸ Thus, T2*/SWI not only allows direct visualization of the involved sinuses that are distended with proton-dense blood clots, but also of associated venous infarcts that are frequently hemorrhagic.

Some have questioned the utility of MRI/MRV in detecting CVT since nonvisualization of a sinus, which may be hypoplastic or absent, is not uncommon in normal in-

dividuals.² The ability of T2* sequence to show an easy-to-visualize susceptibility effect within the involved sinus is of added benefit in such questionable cases.

Although it is impossible to determine the exact time of onset of CVT in all of our patients, the duration of symptoms imply that none could have been longer than 9 days from presentation. Therefore, the sensitivity of T2*/SWI for detecting chronic CVT remains unknown.

It is important to recognize that the susceptibility effect seen on T2*/SWI does not always indicate intravascular thrombosis or blood products. Arterial flow voids or calcifications commonly result in susceptibility artifacts. Therefore, experienced readers, familiar with such artifacts, should interpret signal changes on SWI. Also, the T2* signal may be hard to interpret at the boundaries between tissues of differing magnetic susceptibility, such as bone and soft tissue, where the bone surfaces of the skull causes areas of low signal. Patient 3 (Figure 3A) provides

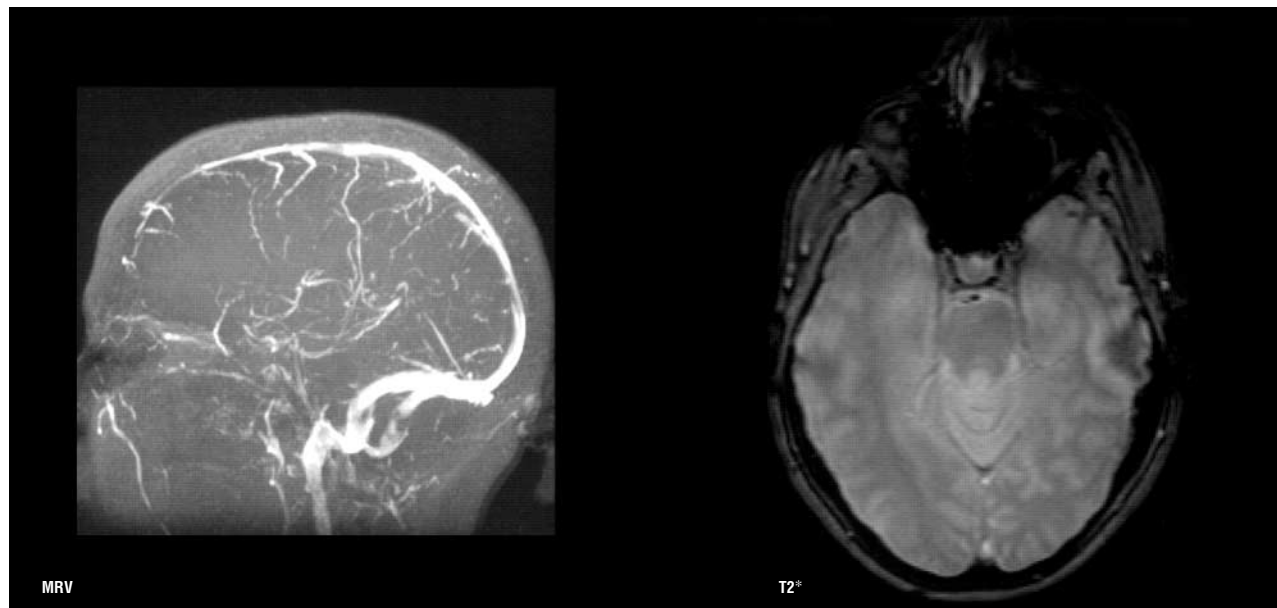


Figure 4. Control subject. Magnetic resonance venography (MRV) and T2*-weighted magnetic resonance imaging sequence of a healthy control subject.

an example where the susceptibility within the left transverse sinus cannot be easily distinguished from the low signal of the nearby bone. In such locations, combining T2* with FLAIR or MRV may be advisable.

CONCLUSIONS

This study shows that T2*/SWI MR sequence can be useful in rapid detection of CVT. It may enable the diagnosis to be made prior to MRV. This is particularly important in clinically unsuspected cases, where MRV is rarely obtained, since early diagnosis will help achieve better outcome. The T2*-weighted sequences can be performed on standard MR scanners, with additional total scan time of only 2 seconds. We recommend adding T2*-weighted sequence to routine MRI protocols to screen for CVT. We recognize the limitations of the retrospective nature and small sample size of this study. However, current observations merit further prospective studies to assess the sensitivity and specificity of T2*/SWIs in diagnosing CVT.

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REFERENCES

1. Bousser MG. Cerebral venous thrombosis. *Stroke*. 1999;30:481-483.
2. Bousser MG, Barnett HJM. Cerebral venous thrombosis. In: Barnett HJM, Mohr JP, Stein BM, Yatsu FM, eds. *Stroke: Pathophysiology, Diagnosis, and Management*. 3rd ed. New York, NY: Churchill Livingstone Inc; 1997:623-647.
3. Lafitte F, Boukobza M, Guichard JP, Reizine D, Woimant F, Merland JJ. Deep cerebral venous thrombosis: imaging in eight cases. *Neuroradiology*. 1999;41:410-418.
4. Virapongse C, Cazenave C, Quisling R, Sarwar M, Hunter S. The empty delta sign. *Radiology*. 1987;162:779-785.
5. Bianchi D, Maeder P, Bogousslavsky J, Schnyder P, Meuli RA. Diagnosis of cerebral venous thrombosis with routine magnetic resonance: an update. *Eur Neurol*. 1998;40:179-190.
6. Hayman LA, Taber KH, Ford JJ, Bryan RN. Mechanisms of MR signal alteration by acute intracerebral blood. *AJNR Am J Neuroradiol*. 1991;12:899-907.
7. Bradley WG Jr. MR appearance of hemorrhage in the brain. *Radiology*. 1993;189:15-26.
8. Linfante I, Llinas RH, Caplan LR, Warach S. MRI features of intracerebral hemorrhage within 2 hours from symptom onset. *Stroke*. 1999;30:2263-2267.
9. Dormont D, Anxionnat R, Evrard S, Louaille C, Chiras J, Marsault C. MRI in cerebral venous thrombosis. *J Neuroradiol*. 1994;21:81-99.
10. Mitchell P, Wilkinson ID, Hoggard N, et al. Detection of subarachnoid haemorrhage with magnetic resonance imaging. *J Neurol Neurosurg Psychiatry*. 2001;70:205-211.
11. Vymazal J, Brooks RA, Baumgarner C, et al. The relation between brain iron and NMR relaxation times: an in vitro study. *Magn Reson Med*. 1996;35:56-61.
12. Gomori JM, Grossman RI, Goldberg HI, Zimmermann RA, Bilaniuk LT. Intracranial hematomas: imaging by high-field MR. *Radiology*. 1985;157:87-93.
13. Edelman RR, Johnson K, Buxton R, et al. MR of hemorrhage: a new approach. *AJNR Am J Neuroradiol*. 1986;7:751-756.
14. Li D, Wang Y, Waight DJ. Blood oxygen saturation assessment in vivo using T2* estimation. *Magn Reson Med*. 1998;39:685-690.
15. Schellinger PD, Jansen O, Fiebach JB, Hacke W, Sartor S. A standardized MRI stroke protocol: comparison with CT in hyperacute intracerebral hemorrhage. *Stroke*. 1999;30:765-768.
16. Patel MR, Edelman RR, Warach S. Detection of hyperacute primary intraparenchymal hemorrhage by magnetic resonance imaging. *Stroke*. 1996;27:2321-2324.