

Assessment of Focal Parenchymal Abnormalities in Cerebral Venous Thrombosis with Diffusion Weighted Imaging

M R Shashikumar¹, Berton Craig Monteiro², N L Rajendrakumar¹, C P Nanjaraj³

¹Associate Professor, Department of Radiodiagnosis, Mysore Medical College & Research Institute, Mysore, Karnataka, India,

²Senior Resident, Department of Radiodiagnosis, Father Muller Medical College, Mangalore, Karnataka, India, ³Professor and Head, Department of Radiodiagnosis, Mysore Medical College & Research Institute, Mysore, Karnataka, India

Abstract

Introduction: Parenchymal swelling without abnormalities in attenuation or signal intensity on images may occur in as many as 42% of patients with cerebral venous thrombosis (CVT). Sulcal effacement, diminished cistern visibility, and a reduction in ventricular size may occur. Focal brain abnormalities have been identified in as many as 57% of patients with CVT.

Materials and Methods: A 30 patients who were found to have CVT on magnetic resonance imaging (MRI) and magnetic resonance venography during the period from August 2013 to November 2014 were included in this study. All patients were evaluated with a 1.5T MRI 8 channel GE BRIVO MRI Machine. Sequences used were axial and sagittal T1, axial and coronal T2, axial fluid-attenuated inversion recovery (FLAIR), axial T2*, two-dimensional time-of-flight, and axial diffusion weighted imaging (DWI). DW images and apparent diffusion coefficient (ADC) maps were evaluated for increased, decreased, or unchanged signal intensity.

Results: 22 (73.3%), out of 30 patients, were found to have focal parenchymal changes in the form of T2 and FLAIR hyperintensity and T1 hypointensity affecting gray matter/white matter/or both. They were characterized conventionally as hemorrhagic venous infarcts in 16 (53.3%) patients and as non-hemorrhagic venous infarcts in 6 (20%) patients with above-mentioned sequences and also T2* weighted images based on presence or absence of hemorrhage. Using DWI and ADC maps, these focal parenchymal abnormalities were characterized as either cytotoxic or vasogenic edema. 12 (40%) patients were found to have both cytotoxic and vasogenic edema, 9 (30%) patients purely vasogenic edema, and 1 (3.3%) patient purely cytotoxic edema. Hemorrhage was associated with both cytotoxic and vasogenic edema.

Conclusion: Focal parenchymal changes in CVT may be secondary to cytotoxic edema, vasogenic edema, or intracranial hemorrhage. Vasogenic and cytotoxic edema patterns may coexist. Hemorrhage may occur with both types of edema, and various patterns may coexist in the same region.

Key words: Cytotoxic edema, Magnetic resonance imaging, Vasogenic cerebral edema, Venous thrombosis

INTRODUCTION

Parenchymal changes in cerebral venous thrombosis (CVT) could be either diffuse cerebral edema cases or focal parenchymal changes. The focal parenchymal changes

have conventionally been labeled as venous infarcts and further classified as hemorrhagic or non-hemorrhagic based on the presence of hemorrhage. The predominant conventional magnetic resonance imaging (MRI) findings of CVT are hyperintense parenchymal abnormalities on a T2-weighted image that involve gray matter, white matter, or both in approximately 50-60% of patients and intraparenchymal hematoma in approximately 35-40%. The pathophysiology of CVT remains unclear. Both vasogenic and cytotoxic edema are thought to occur in the setting of CVT. Increased venous pressure may cause breakdown of the blood-brain barrier and vasogenic edema or may cause reduced cerebral blood flow and cytotoxic edema.

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Corresponding Author: Dr. M R Shashikumar, Department of Radiology, K.R.Hospital, Mysore, Karnataka, India. Phone: +91-9845813137. E-mail: drmrshashikumar@gmail.com

Unlike conventional MR images, diffusion weighted (DW) MR images can differentiate between vasogenic and cytotoxic edema. DW images are sensitive chiefly to the molecular diffusion of water molecules. Cytotoxic edema is characterized by markedly decreased diffusion. Vasogenic edema, with increased interstitial water, demonstrates increased diffusion. We sought to characterize focal parenchymal changes associated with CVT with DW imaging (DWI) and to determine whether this technique could differentiate lesions that would resolve from those that would lead to permanent injury.

MATERIALS AND METHODS

The study was performed in the Department of Radiodiagnosis, Mysore Medical College and Research Institute, Mysore on patients who were found to have CVT on MRI and magnetic resonance venography (MRV).

Sample size: 30 cases

Type of study: Explorative study.

Study period: 15 months from August 2013 to November 2014.

Imaging

All patients were evaluated with a 1.5T MRI 8 channel GE BRIVO MRI Machine. Sequences used were axial and sagittal T1, axial and coronal T2, axial fluid-attenuated inversion recovery (FLAIR), axial T2*, two-dimensional time-of-flight (2D-TOF), and axial DWI. DW images were obtained by using single-shot, spin-echo echo-planar imaging with a sampling of the entire diffusion tensor with six non-linear directions. Six high-b-value images corresponding to the six non-linear directions were acquired followed by a single low-b-value image. Imaging parameters included 6000/92 (TR/TE), a field of view (FOV) of 22 cm × 22 cm, image matrix of 128 × 128 pixels, section thickness of 5 mm and 2 signal averages. Apparent diffusion coefficient (ADC) maps were also generated. T1-weighted sagittal images were acquired with 340/10, 20 cm × 20 cm FOV, an acquisition matrix of 256 × 192 pixels, section thickness of 5 mm, and 2 signal averages. FLAIR axial MR images were obtained with 8013 × 80.5 (TR/TE), 22 × 25 cm FOV, acquisition matrix of 288 × 224 pixels, section thickness of 5 mm, and 2 signal averages. Fast spin-echo T2-weighted MR axial images were obtained with 3732/90, 22 × 22 cm FOV, acquisition matrix of 256 × 256 pixels, section thickness of 5 mm, and 2 signal averages. T2* axial images were obtained with 680 × 26 (TR/TE), 22 cm × 16.5 cm FOV, section thickness of 5 mm, and acquisition matrix of 256 × 192 pixels. The 2D TOF sequence was done in the sagittal plane, and then the

source images were reconstructed into three-dimensional maximum intensity projection images.

Image Analysis

The presence of CVT in the cases was confirmed by loss of flow void in the sinuses on conventional sequences and absence of flow on MRV. Focal parenchymal abnormalities were detected on the basis of increased signal on T2 weighted and FLAIR images. The presence of hemorrhage was assessed using both conventional and T2* images. DW images and ADC maps were inspected visually, and signal intensity of focal parenchymal changes was assessed as increased, decreased, or unchanged in comparison to that of the contralateral, normal appearing brain.

RESULTS

In the present study, there was found to be a slight female preponderance with 53.3% of the patients being females (Chart 1). The mean age of the patients was found to be 35.3 years, with the mean age of the female patients being 29 years, whereas the mean age of the male patients was 42.5 years. 22 (73.3%), out of 30 patients, were found to have focal parenchymal changes in the form of T2 and FLAIR hyperintensity and T1 hypointensity affecting gray matter/white matter/or both. They were characterized conventionally as hemorrhagic venous infarcts in 16 (53.3%) patients and as non-hemorrhagic venous infarcts in 6 (20%) patients (Table 1) with above-mentioned sequences and also T2* weighted images based on presence or absence of hemorrhage. Using DWI and ADC maps these focal parenchymal abnormalities were characterized as either cytotoxic or vasogenic edema (Table 2). 12 (40%) patients were found to have both cytotoxic and vasogenic edema (Figure 1), 1 (3.3%) patient had purely cytotoxic edema (Figure 2), and 9 (30%) patients purely vasogenic

Table 1: Distribution of patients with CVT depending on parenchymal changes

Focal parenchymal changes	Number of cases	Percentage
Absent	8	26.6
Hemorrhagic infarct	16	53.3
Non-hemorrhagic infarct	6	20
Total	30	100

CVT: Cerebral venous thrombosis

Table 2: Distribution of patients with CVT depending on DWI

Type of Edema	Number of cases	Percentage
Pure vasogenic	9	30
Co-existent	12	40
Pure cytotoxic	1	3.3

CVT: Cerebral venous thrombosis, DWI: Diffusion weighted imaging

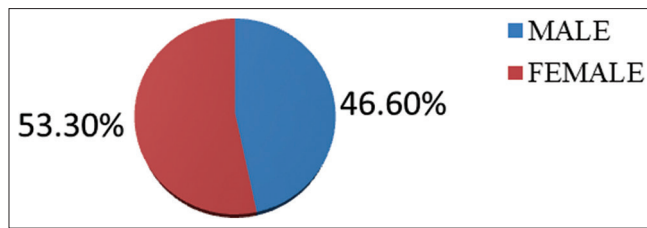


Chart 1: Sex distribution

edema (Figures 3 and 4). Hemorrhage was associated with both cytotoxic and vasogenic edema.

DISCUSSION

The conventional MRI findings of CVT hyperintense parenchymal abnormalities on a T2-weighted image that involve gray matter, white matter, or both in approximately 50-60% of patients and intraparenchymal hematoma in

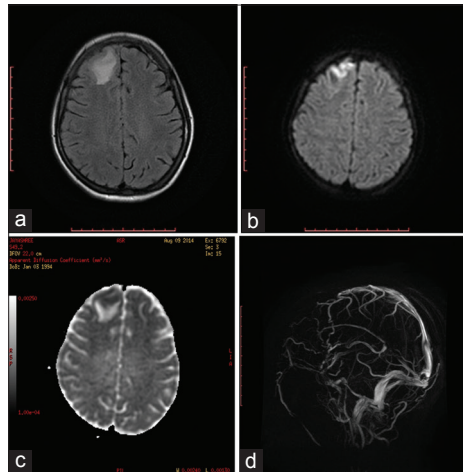


Figure 1: (a-d) Axial fluid-attenuated inversion recovery image showing hyperintense signal involving both gray and white matter in right frontal lobe. Diffusion weighted images show hyperintense signal involving only the gray matter. The white matter appears isointense to a corresponding white matter of left hemisphere. Apparent diffusion coefficient map shows hypointense signal involving gray matter implying cytotoxic edema, whereas hyperintense signal is seen to involve the white matter suggestive of vasogenic edema. Magnetic resonance venography maximum intensity projection image showing thrombosis of anterior part of superior sagittal sinus

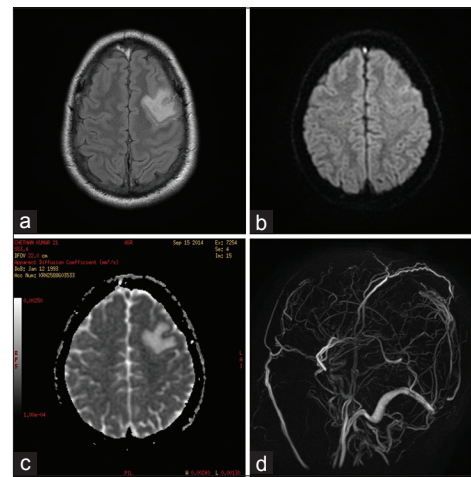


Figure 3 (a-d): Axial T2-fluid-attenuated inversion recovery image showing hyperintensity involving white matter in left frontal lobe region. Diffusion weighted images show no altered signal intensity in corresponding region. Hyperintensity noted in corresponding region in apparent diffusion coefficient map suggestive of pure vasogenic edema. Magnetic resonance venography maximum intensity projection showing absence of flow in superior sagittal sinus

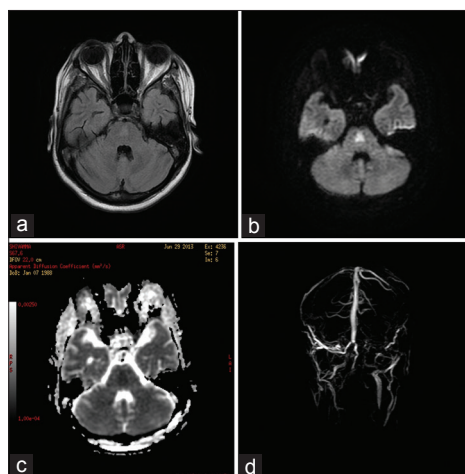


Figure 2: (a-d) Axial T2-fluid-attenuated inversion recovery image showing hyperintense signal in pons. Diffusion weighted images show hyperintense signal in corresponding region with apparent diffusion coefficient map shows hypointense signal in corresponding region suggestive of pure cytotoxic edema. Magnetic resonance venography maximum intensity projection image shows thrombosis of left transverse sinus

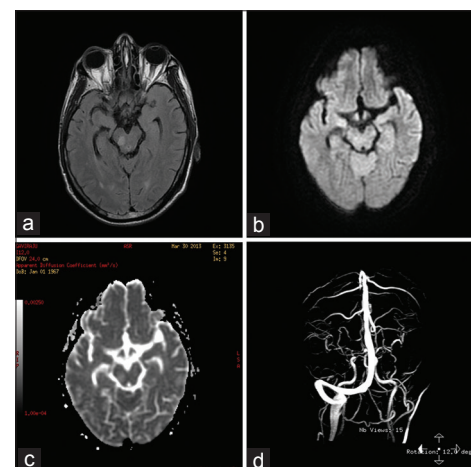


Figure 4: (a-d) Axial T2-fluid-attenuated inversion recovery image shows focal hyperintense signal in midbrain on right side. Diffusion weighted images show no alteration of signal in corresponding region with apparent diffusion coefficient map showing hyperintense signal in corresponding region suggestive of pure vasogenic edema. Magnetic resonance venography maximum intensity projection image shows thrombosis of right transverse sinus

approximately 35-40%.¹ Simonds and Truwit² observed non-hemorrhagic infarction in 40% and hemorrhagic infarction found in 26.7%. In a study conducted by Khandelwal *et al.*,³ hemorrhagic infarcts were the most frequent parenchymal lesions, seen in 60% of cases; non-hemorrhagic infarcts were seen in 13.3% of cases.

In the present study, the most common focal brain abnormality was a hemorrhagic infarction found in 53.3% cases followed by non-hemorrhagic infarction in 20% of cases.

In contrast with arterial ischemic states, many parenchymal abnormalities secondary to venous occlusion are reversible.

Although some T2 hyperintense parenchymal abnormalities resolve, others persist and indicate permanent tissue injury. Lesion distribution does not differentiate between these two lesion types. T2 hyperintensities maybe secondary to cytotoxic edema or vasogenic edema. Vasogenic and cytotoxic edema patterns may coexist.⁴

Hemorrhage may occur with both types of edema, and various patterns may coexist in the same region. In view of the variable nature of the parenchymal abnormalities that may occur in CVT, the use of the term venous infarct in reference to these lesions should be discouraged because that term implies irreversibility.⁵

Unlike conventional MR images, DW MR images can differentiate between vasogenic and cytotoxic edema. As cytotoxic edema due to acute stroke develops, ADC values decrease. The current predominant theory to describe this phenomenon involves loss of ionic gradients with net translocation of water from the extracellular to the intracellular space where water movement is more restricted. Cytotoxic edema produces hyperintensity on DW images and hypointensity on ADC images. In contrast, vasogenic edema leads to increased water in the extracellular space where water is less restricted and is characterized by ADC values that are increased compared with those of normal brain tissue. Because DW images have both T2 and diffusion components, vasogenic edema may appear hypointense, isointense, or slightly hyperintense on DW images, but it always produces hyperintensity on ADC images.⁶

In a study by Mullins *et al.*, they found that found that DWI, in combination with the clinical history (i.e. seizure), may be useful in differentiating parenchymal lesions that resolve from those that progress to permanent injury in the setting of acute CVT. In their retrospective cohort, lesions with elevated diffusion resolved, lesions with decreased diffusion resolved when the patient had seizures, and

lesions with decreased diffusion in the absence of clinical seizure demonstrated abnormality on follow-up images. The ADC values were similar between the lesions with low ADC values that resolved and the lesions with low ADC values that persisted. Lesions characterized by elevated diffusion that showed essentially no abnormality on follow-up images were likely to represent vasogenic edema that is produced in CVT owing to increased pressure in the post-capillary venules and the opening of tight junctions. Lesions characterized by decreased diffusion that showed no abnormality on follow-up images in patients with seizure activity was possibly due to cytotoxic edema. The decreased ADC values in these patients may have resulted from the seizure activity. Animal and human studies have demonstrated decreased ADC values in cortical and white matter lesions in subjects with status epilepticus. The pathophysiology for decreased ADCs in epilepsy is not completely clear. Wang *et al.*⁷ reported an increase in sodium concentration in rat pyriform cortex during status epilepticus. They suggested that this might result from energy failure of the Na⁺/K⁺ - ATPase pump, and consequent Na⁺ and water influx.

Alternatively, reversibility of ADC values in these patients could have been unrelated to the seizures. Based on an animal model of CVT in rats, Röther *et al.*⁸ noted that an initially decreased ADC was followed by an increased ADC in some parenchymal lesions.

They hypothesize that the major pathophysiologic event in the first 1-2 h is cytotoxic edema. Cytotoxic edema is produced in CVT when increased venous pressure leads to increased intracranial pressure, decreased capillary perfusion pressure, and severely decreased cerebral blood flow. The resultant blood-brain barrier disruption leads to increased extracellular water, rising ADC values, and increasing lesion volumes. Subsequently, recanalization of thrombosed veins or improvement of collateral drainage and recovering metabolism lead to a decrease in lesion volume. Thus, while cytotoxic edema associated with acute arterial stroke is usually irreversible, cytotoxic edema associated with CVT may be reversible if the blood drains through collateral pathways.⁹ Lesions characterized by decreased diffusion that showed an abnormality on follow-up images were likely to represent persistent cytotoxic edema followed by tissue infarction. In these cases, there was likely severely decreased blood flow without enough collateral blood drainage to maintain adequate perfusion.

We found that DWI may be useful in differentiating parenchymal lesions that resolve from those that progress to permanent injury in the setting of acute CVT. Of the 22 (73.3%), out of 30 patients, were found to have focal parenchymal changes in the form of T2 and FLAIR

hyperintensity and T1 hypointensity affecting gray matter/white matter/or both. Using DWI and ADC maps these focal parenchymal abnormalities were characterized as either cytotoxic edema, i.e. increased signal on DWI and decreased signal on ADC maps or vasogenic edema, i.e. increased signal on ADC maps. 12 (40%) patients were found to have both cytotoxic and vasogenic edema, 9 (30%) patients purely vasogenic edema, and 1 (3.3%) patient purely cytotoxic edema. Hemorrhage was associated with both cytotoxic and vasogenic edema. This helped in the prognosis and management of the patients.

However, they were a few limitations to our study. Follow-up imaging in the patients was not done, and hence persistence of abnormality in cases with cytotoxic edema was not assessed. Also, areas of hemorrhage may have interfered with an assessment of ADC values. However, areas of hemorrhage based on T2* images were excluded as much as possible to keep this interference to the least.

CONCLUSION

Focal parenchymal changes in CVT may be secondary to cytotoxic edema, vasogenic edema, or intracranial hemorrhage. Vasogenic and cytotoxic edema patterns may coexist. Hemorrhage may occur with both types of edema, and various patterns may coexist in the same region. In view of the variable nature of the parenchymal abnormalities that may occur in CVT, the use of the term venous infarct

in reference to these lesions should be discouraged because that term implies irreversibility. Unlike conventional MR images, DW MR images can differentiate between vasogenic and cytotoxic edema. This information may be important in prospectively determining the severity of the injury, in the determination of prognosis, and in patient management.

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