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Brief Communication

Diffusion-weighted Imaging Abnormalities in the Splenium after Seizures

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Summary: *Purpose:* Transient increased T_2 signal in the splenium of the corpus callosum after seizures has been reported and sometimes attributed to a postulated toxicity of anticonvulsant medications (AEDs).

Methods: We describe two patients with bitemporal epilepsy.

Results: Transiently increased T_2 signal (in one) and decreased apparent diffusion coefficient (ADC) (in both) in the splenium appeared to be related directly to acute seizures.

Conclusions: These cases illustrate an unusual acute postictal imaging finding, highlight involvement of an important commissural pathway, and suggest that seizures per se, and not their treatment, are the cause of transient white-matter abnormalities in these cases. **Key Words:** Splenium—Diffusion-weighted imaging—Magnetic resonance imaging.

Magnetic resonance imaging (MRI) has revolutionized the evaluation of patients with seizures over the last two decades. Most MRI is obtained interictally to search for an underlying structural basis for epileptic discharge, recent attention has focused on the potential of MRI to reveal transient physiologic changes associated with abnormal neuronal activity. Here we present two patients who manifested transient changes in the splenium on diffusion-weighted imaging (DWI) after repeated seizures.

METHODS

Patients reported in this study were evaluated by using conventional approaches for possible epilepsy surgery. MRI studies were obtained by using protocols that we have optimized for the evaluation of patients with suspected focal epilepsy. All patients were studied on a GE Signa or Siemens Sonata 1.5-Tesla scanner. The standard epilepsy imaging protocol includes full diffusion tensor imaging [repetition time (ms)/echo time (ms), 6,000/118; field of view (FOV), 40 × 20 cm; matrix, 256 × 256; *b* value, 0 and 1,000 s/mm^2; number of signals acquired, three; gradient directions, six]. Our diffusion sequence automatically processes and displays DWIs and apparent diffusion coefficient (ADC) maps.

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CASE REPORTS

Patient 1

A 23-year-old man with an 11-year history of intractable epilepsy was admitted for presurgical evaluation. An MRI brain study on the day of admission was unremarkable. Antiepileptic medications (AEDs) were discontinued during video-EEG monitoring, which revealed very active independent bilateral anterior temporal interictal spikes, with an approximate ratio of 3:1, right to left. Multiple focal clinical seizures, many with secondary generalization, appeared to arise independently from both temporal lobes. A repeated MRI obtained 24 h after his last seizure to obtain more detailed images of the temporal lobes demonstrated an area of markedly increased signal on DWI and mildly increased T_2signal in the splenium of the corpus callosum. The corresponding ADC map confirmed that there was decreased apparent diffusion of water. Four weeks later, after resumption of AED treatment, a follow-up MRI demonstrated resolution of the lesion (Fig. 1, top).

Patient 2

A 39-year-old man with a history of alcoholism and long-standing seizures presented for presurgical evaluation. Medications were discontinued during an 8-day

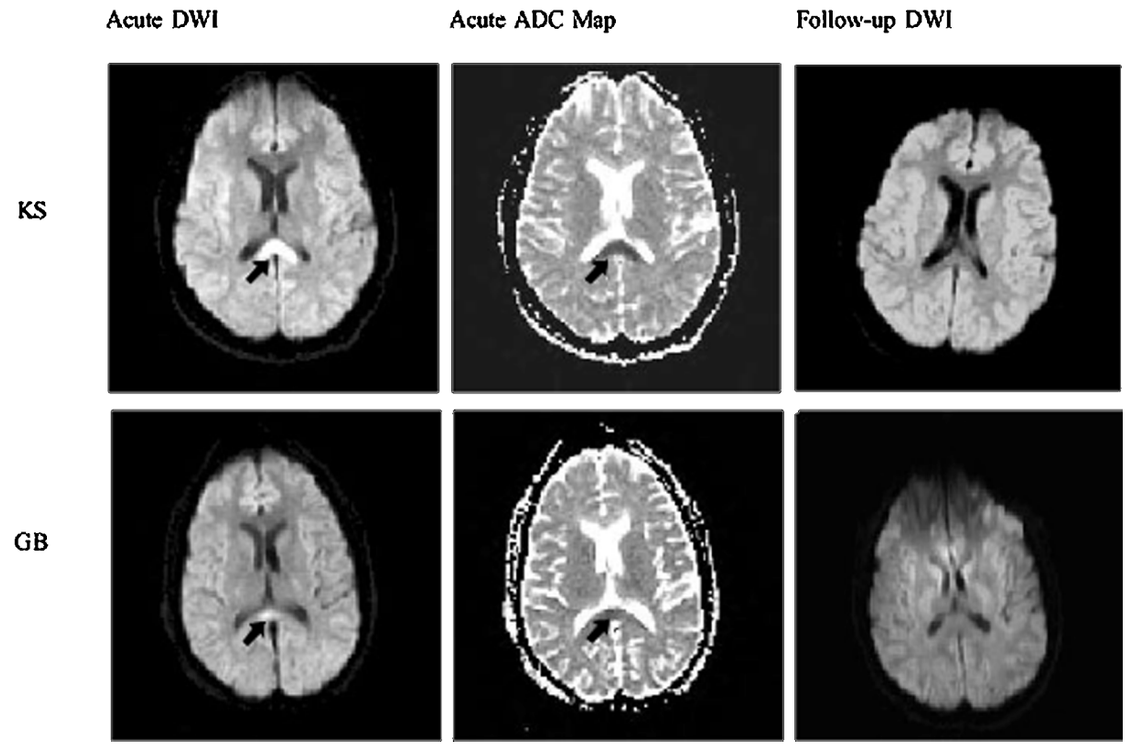

FIG. 1. Transient diffusion-weighted imaging changes in the splenium after seizures. Representative images from patients 1 (top) and 2 (bottom) demonstrate restricted diffusion (left images) with associated decreased apparent diffusion coefficients (center images) that resolved in 4–6 weeks (right images). Arrows, area of abnormality.

video-EEG recording session. Interictal independent bitemporal sharp waves along with rhythmic bitemporal independent slowing were recorded. Nineteen seizures occurred, eight arising from the right temporal lobe, and 11, from the left temporal lobe. Four of these became secondarily generalized. Because the patient had not had previous high-resolution imaging, an MRI was obtained on the day of discharge, 24 h after his last seizure. The study demonstrated an abnormality in the splenium of the corpus callosum, which was bright on a DWI sequence but normal on T_2-weighted imaging. The ADC map confirmed the presence of decreased apparent diffusion of water. AED was restarted, and on follow-up imaging 6 weeks later, the lesion was no longer apparent (Fig. 1, bottom).

DISCUSSION

The main finding in these two patients is that transient lesions of the splenium appeared after recurrent focal seizures in the absence of AEDs and resolved after AEDs had been reintroduced. This finding appears to be related to seizure activity itself, and not the result of medication, as previously suggested (1–3). The mechanism responsible for changes in the splenium is unknown**.** Both mechanisms related to and independent of epilepsy have been hypothesized to cause T_2-weighted changes in the splenium. Transient vasogenic edema has been postulated as a final common pathway underlying white-matter abnormality by some investigators (3). In our patients, however, the presence of decreased ADCs makes this highly unlikely, as vasogenic edema is associated with increased ADCs (11). The decrease in ADC in the splenium described here, as well as its rapid resolution, suggests that a transient disturbance of energy metabolism and ionic transport occurred, resulting in reversible myelin vacuolization or intramyelinic edema. We speculate that this transient disturbance of energy metabolism and ionic transport is the result of repeated excessive activity of commissural projections from temporal structures involved in these patients' seizures. Unfortunately, detailed neuropsychological examination was not performed to document if any clinical accompaniments to the transient splenial lesions existed. The timing of these MRI studies, at the conclusion of monitoring, was unusual but serendipitous and may explain why this finding has not been reported more widely.

One of our patients had both increased T_2 signal and decreased diffusion in the splenium, whereas the other showed only decreased diffusion. Decreased diffusion (viewed as increased signal on DWI) was initially recognized as a sensitive and early indicator of brain ischemia

indicating irreversible cellular injury (4). More recently, it has become clear that transient DWI abnormalities also can occur in association with spreading depression (5), excitotoxic injury (6), and prolonged seizures in animals (7). Several recent reports described DWI and ADC abnormalities in humans in close temporal association with seizures. Wieshmann (8) reported decreased ADC in the motor cortex in a woman in focal status epilepticus affecting the right lower extremity. Lansberg (9) described three additional patients in status in whom DWI abnormalities correlated with the inferred ictal zone but did not respect vascular borders. On the basis of simultaneous leptomeningeal enhancement after gadolinium contrast injection in two of the three, the authors suggested that the findings were most consistent with mixed cytotoxic and vasogenic edema. They further pointed out an increased caliber of vessels on MR angiography, presumably reflecting increased blood flow to the site of seizure activity. Diehl (10) described DWI imaging after single seizures in patients with partial epilepsy undergoing epilepsy monitoring. Of six patients scanned within 150 min of a single short seizure, only one had a focal abnormality. Reversible decreases in white-matter ADC also have been reported in association with seizures and venous sinus occlusion and in association with hemiplegic migraine (12). In most of these reported cases, early diffusion changes were followed by increased T_2 signal, and resolved completely within a matter of weeks. Our patients are unusual in that the transient imaging abnormality was confined to the splenium, a structure that may be involved in seizure propagation but not seizure initiation. Interestingly, both patients had bilateral independent seizure foci. It is possible that robust spread through the splenium may relate to the phenomenon of secondary epileptogenesis with development of a mirror focus. Our patients each had a large number of seizures within a short period, which may have placed a critical burden on energy-dependent ionic transport mechanisms, causing intramyelinic edema and the transient diffusion abnormality.

In our patients, seizure activity per se appears to be the most likely cause of the transient splenial abnormality. In the absence of invasive recording data, it is impossible to assess fully the degree of seizure spread through the splenium, but that structure seems ideally positioned to mediate interhemispheric propagation of ictal discharge. The temporal relation between the seizures, the appearance of the splenial abnormality, and its resolution after medications were restarted and seizures were suppressed argues strongly against the notion that abnormalities of the splenium were related to direct medication toxicity. Similarly, many patients are imaged while taking AEDs, and abnormalities of the splenium are rarely encountered. We cannot eliminate the possibility that transient changes in the splenium are a direct consequence of acute drug withdrawal that, in the absence of apparent seizure activity in previously reported cases, seemed to be the most likely common mechanism (3). However, the unique aspect of this report is the finding of reduced ADC along with the increased T_2 signal, militating against the notion of vasogenic edema in these cases. We propose that the various pathogenic theories relating to splenial changes as well as the general utility of diffusion imaging in acute seizures could be tested in a prospective study of patients who are scanned within 24 h of ictal events. Such a study also would allow one to quantify ADC abnormality and determine whether there is a threshold value at which restricted diffusion predicts the appearance of chronic T_2 signal change.

REFERENCES

1. Kim SS, Chang K, Kim ST, et al. Focal lesion in the splenium of the corpus callosum in epileptic patients: antiepileptic drug toxicity? *AJNR Am J Neuroradiol* 1999;20:125–9.
2. Tennison M. Focal lesion in the splenium of the corpus callosum in epileptic patients: antiepileptic drug toxicity? *AJNR Am J Neuroradiol* 1998;20:131–2.
3. Polster T, Hoppe M, Ebner A. Transient lesion in the splenium of the corpus callosum: three further cases in epileptic patients and a pathophysiological hypothesis. *J Neurol Neurosurg Psychiatry* 2001;70:459–63.
4. Moseley M, Cohen Y, Mintorovitch J. Early detection of regional cerebral ischaemia in cats: comparison of diffusion and T_2-weighted MRI and spectroscopy. *Magn Reson Med* 1990;14:330–46.
5. Hasegawa Y, Latour L, Formato J. Spreading waves of reduced diffusion coefficient of water in normal and ischaemic rat brain. *J Cereb Blood Flow Metab* 1995;15:179–87.
6. Verheul H, Balaz R, van der Sprenkel J. Temporal evolution of NMDA-induced excitotoxicity in the neonatal rat brain measured with H1 nuclear magnetic resonance imaging. *Brain Res* 1993;618:203–12.
7. Zhong J, Petroff OAC, Pritchard J, et al. Barbiturate-reversible reduction of water diffusion coefficient in flurothyl-induced status epilepticus in rats. *Magn Reson Med* 1995;33:253–6.
8. Wieshmann U, Symms M, Shorvon S. Diffusion changes in status epilepticus. *Lancet* 1997;350:493–4.
9. Lansberg M, O'Brien M, Norbash A, et al. MRI abnormalities associated with partial status epilepticus. *Neurology* 1999;52:1021–7.
10. Diehl B, Najm I, Ruggieri P, et al. Post-ictal diffusion-weighted imaging for the localization of focal epileptic areas in temporal lobe epilepsy. *Epilepsia* 2001;42:21–8.11.
11. Schaefer PW, Grant PE, Gonzalez RG. Diffusion-weighted MR imaging of the brain. *Radiology* 2000;217:331–45.
12. Grant PE, He J, Halpern EF, et al. Frequency and clinical context of decreased apparent diffusion coefficient reversal in the human brain. *Radiology* 2001;221:43–50.

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