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Quantitative Assessment of Diffusion Abnormalities in Posterior Reversible Encephalopathy Syndrome

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BACKGROUND AND PURPOSE: **Previous studies have shown that lesions in posterior reversible encephalopathy syndrome are often isointense on diffusion-weighted MR images. We hypothesized that 1) apparent diffusion coefficient (ADC) maps using various thresholds would show larger abnormalities in posterior white matter (WM) and 2) isointense appearance of lesions on isotropic diffusion-weighted images results from a balance of T2 prolongation effects and diffusibility effects.**

METHODS: **T2-weighted MR images from 11 patients were reviewed. Hyperintense lesions were located in both anterior and posterior WM in eight patients and solely in posterior WM in three patients. The ADC maps were produced by use of ADC values $\geq$ 3 SD and $\geq$ 10 SD above the mean value of normal WM. Lesions on diffusion-weighted images were classified as isointense or hypointense. ADC values within lesions (ADC_L) were compared with those of normal WM (ADC_N), and compared for isointense lesions and hypointense lesions.**

RESULTS: **The distribution of lesions with ADC values $\geq$ 3 SD was essentially identical to that on T2-weighted images. Regions with ADC values $\geq$ 10 SD were found in both anterior WM and posterior WM in two patients and solely in posterior WM in nine patients. On diffusion-weighted images, lesions appeared isointense in seven patients and hypointense in four patients. Mean ADC_L/ADC_N for all lesions was 1.81; for hypointense lesions, 2.30.**

CONCLUSION: **Vasogenic edema was more severe in posterior WM. Isointense lesions result from a balance of T2 effects and increased water diffusibility. Hypointense lesions have higher ADC values, which are not balanced by T2 effects.**

The term posterior reversible encephalopathy syndrome (PRES) refers to a symptom complex characterized by headache, confusion, visual disturbance, and seizures in the setting of acute rise in blood pressure, eclampsia, or following treatment with a number of therapeutic agents (eg, cyclosporine, tacrolimus, and cisplatin) (1, 2). Lesions associated with this syndrome are typically hyperintense on T2-weighted MR images. Reports depicting diffusion-weighted (DW) images of patients with PRES have shown that lesions are often isointense with normal WM on DW isotropic images (indicating the presence of vasogenic edema) (3, 4). This finding is seen even though apparent diffusion coefficient (ADC) values are elevated (and would be expected to produce decreased signal intensity [SI] on DW images). In a recent report of two cases of this syndrome, ADC maps showing regions of vasogenic edema predominantly in posterior WM were presented (5). However, in our initial experience based on four unpublished cases, we found that regions of vasogenic edema seen on ADC maps were nearly evenly distributed in both anterior and posterior WM regions. We hypothesized that ADC elevations would be higher in posterior WM, even though areas of increased SI were present in both anterior and posterior WM regions. A review of DW images from our four cases also showed that lesions were usually isointense with normal brain tissue. Thus, we also aimed to determine the cause of the isointense appearance of these lesions on DW images, when they would be expected to be hypointense because of the presence of vasogenic edema.

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Methods

Patient Identification

We studied 11 patients (nine women, two men; mean age, 23 years) with PRES who underwent MR imaging during an

18-month period and were identified by means of a computerized data base that recorded diagnosis. Criteria for diagnosis included 1) regions of hyperintense signal primarily within posterior WM; 2) presence of at least one of the following risk factors for PRES: acute sustained rise in diastolic blood pressure to > 100 mm Hg (n = 7), eclampsia (n = 2), or treatment with cyclosporine or tacrolimus following solid organ or bone marrow transplant (n = 7); and 3) absence of another likely cause of WM lesions. The case of one of these patients has been previously reported (6). Typical elevation of systemic arterial blood pressure was between 30 and 50 mm Hg, and typical elevation of diastolic blood pressure was between 10 and 20 mm Hg. All patients underwent imaging within a 4- to 11-day period after onset of symptoms. Because seizure activity has been shown to produce restricted diffusion in the ictal and immediately postictal state (7), presence of seizures and the interval between last seizure and MR imaging were documented; three patients had seizures, and the aforementioned interval was between 2 and 4 days for all three patients.

For six patients, follow-up MR imaging was performed at a mean of 3.5 weeks; in all six, lesions regressed or resolved after removal of the presumed causative factor. No cases were encountered in which hyperintense regions on T2-weighted images were more prominent in anterior WM regions. In five cases, hyperintense regions were relatively equally distributed in anterior and posterior WM regions, but posterior WM involvement was always slightly greater. No cases were found to have involvement of gray matter regions.

MR Imaging Techniques

All patients underwent MR imaging with a 1.5-T imaging system (GE Medical Systems, Milwaukee, WI). In each case, T2-weighted MR imaging and isotropic DW imaging were performed by using diffusion gradients in three orthogonal directions, with a maximal b value of 1000 s/mm^2. The DW imaging was performed by using a single-shot, multisection, spin-echo echo-planar imaging sequence with the following parameters: 12,000/101 (TR/TE); flip angle, 90 degrees; field of view, 40 × 20 cm; and matrix size, 128 × 64 mm. Between 20 and 24 axial sections with a thickness of 5 mm and an intersection gap of 2.5 mm were obtained. An inversion recovery pulse (TI, 2200 ms) was applied to prevent partial volume averaging of brain tissue with cerebrospinal fluid, which would result in falsely elevated ADC measurements (8). For each patient, ADC maps were generated from DW images. The ADC maps served as references to determine whether corresponding lesions present on T2-weighted images had increased diffusibility. The ADC maps were generated by using an image analysis software package (Functool; GE Medical Systems) operating at a separate workstation.

Lesion Identification

Hyperintense lesions were identified on T2-weighted images by two trained neuroradiologists who were not blinded to diagnosis, and decisions were made by consensus. All patients were found to have prominent posterior WM involvement, including three patients in whom solely posterior WM involvement was seen. In the remaining eight patients, involvement of frontal WM regions also was seen, although it was always less extensive than posterior WM involvement. For the sake of this study, posterior WM was defined in the following manner. On an axial image located just above the head of the caudate nucleus, the point at which the outermost walls of the lateral ventricles were closest was identified. WM posterior to a line connecting the walls of the lateral ventricles at this point was considered as posterior WM. Similarly, WM anterior to this line was defined as anterior WM.

Assessment of Severity of Vasogenic Edema According to Brain Region

To assess whether severity of vasogenic edema (as reflected by degree of elevation of ADC values) differed in anterior and posterior WM, ADC maps using various threshold values above normal WM were generated. Use of thresholds based on the SD of mean ADC values is only one means of evaluating degree of ADC elevation. An alternative method would have been to draw regions of interest in various WM regions and compare mean ADC values. We chose the threshold method because it allowed regions of most severe vasogenic edema to be directly mapped on T2-weighted images and provided a visual display that was not evident solely from drawing regions of interest.

The first step in generating threshold ADC maps was to measure the mean ADC value and SD for normal WM (defined by normal SI on T2-weighted images) for each patient using a uniform region of interest placed on ADC maps. To verify that WM regions considered normal on T2-weighted images did not have abnormal diffusibility, ADC values for these regions were compared with values of similar regions in healthy volunteers. Next, window and level settings were prescribed for ADC maps in a standard manner for each case. A window of 80 and a level that showed ADC values ≥ 3 SD above the mean value of normal WM were chosen. The level of 3 SD was chosen, because at lower values small regions of falsely elevated ADC values could be seen at interfaces of brain and cerebrospinal fluid. The level was set by choosing the value that was halfway between the mean value plus 3 SD and a point 80 units above the mean value plus 3 SD. A color-coded map was used to depict all regions having ADC values ≥ 3 SD above the mean, with values at the lower end of the spectrum seen in blue and green and values at the higher end seen in red and orange (Figs 1D and 2D). The images from the color-coded maps then were superimposed directly on corresponding images from the T2-weighted sequence.

From this process, it was apparent that, in each case, the size of lesions on T2-weighted images was essentially identical to that on ADC maps using a threshold of ≥ 3 SD (Figs 1D and 2D). Therefore, ADC values at this threshold did not provide any information regarding severity of ADC elevation. For this reason, the threshold process was repeated with a value of ≥ 10 SD above normal mean ADC value, the maps of which were also superimposed on T2-weighted images (Figs 1E and 2E).

Determination of Cause of Isointense Signal of Lesions on DW Images

Measurement of SI and ADC of Lesions.—To document the isointense nature of lesions in a quantitative manner, SI of lesions on DW images was measured. Regions of interest were drawn on six representative WM lesions and on six control regions of normal-appearing WM on T2-weighted images. Measurement of SI was performed on DW images after superimposition of regions of interest on corresponding DW images. The SI values were obtained from isointense lesions and, when present, hypointense lesions on DW images. The location of lesions on DW images was determined by the site of areas of hyperintense signal on corresponding ADC maps, because T2-weighted images and DW images were generally slightly offset. The ratio of SI of lesions (SI_L) to normal-appearing WM (SI_N) on DW images was calculated. Next, ADC values were measured on ADC maps within the same regions of interest used for SI measurements. For each patient, ADC values of lesions (ADC_L) were compared with ADC values of the patient's normal WM (ADC_N). The ratio of SI_L/SI_N on DW images was compared with ADC_L/ADC_N.

Comparison of Lesion Areas on DW Images and ADC Maps.—The DW images were reviewed for presence of hy-

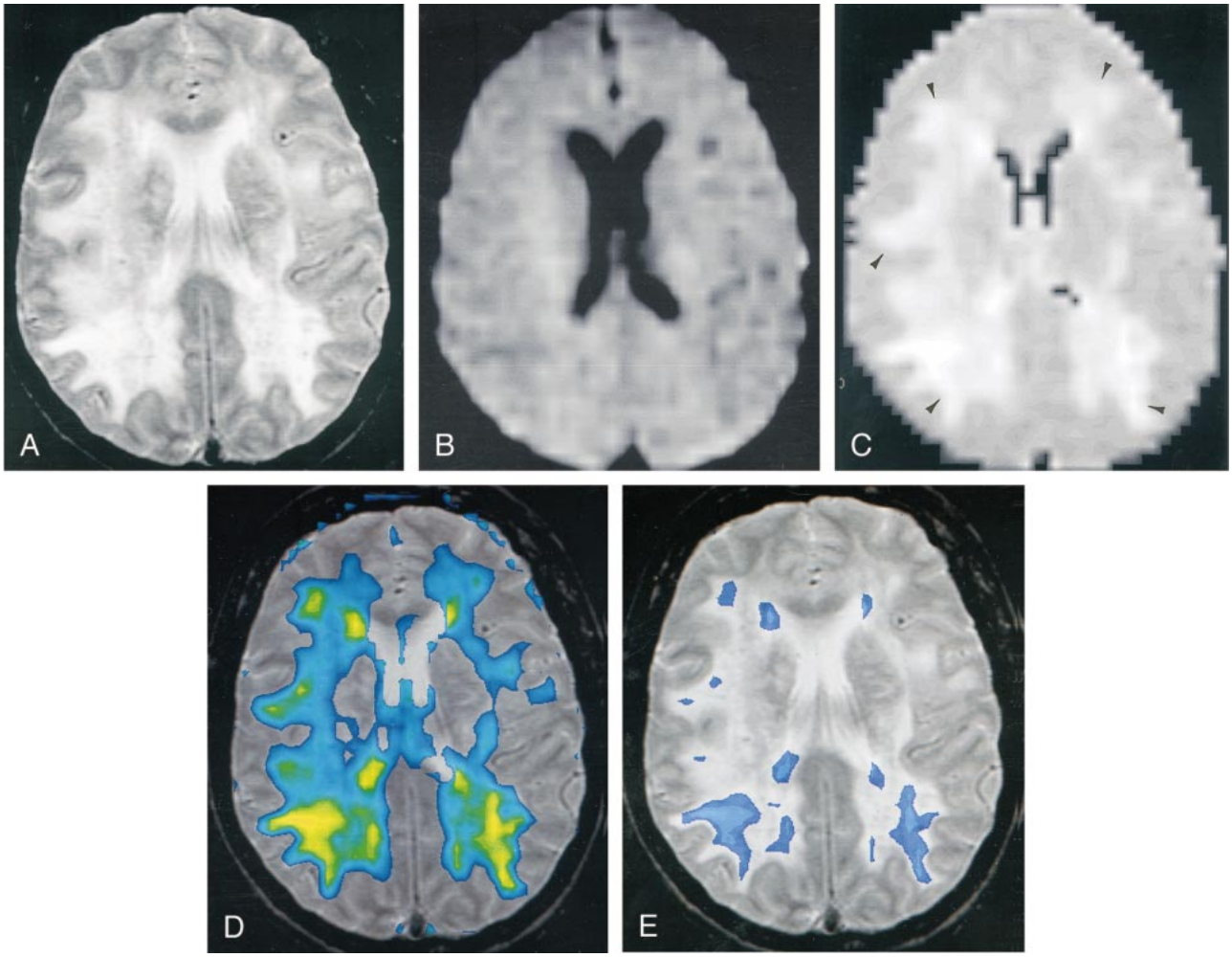

FIG 1. MR imaging of a 32-year-old woman with PRES resulting from severe hypertension. Most severe degree of elevation of ADC values is seen in posterior WM despite relatively diffuse distribution of hyperintense regions on T2-weighted images.

A, Axial T2-weighted MR image at 2800/90 (TR/TE) shows diffuse areas of hyperintense signal. Note diffuse anterior WM involvement in addition to moderately prominent posterior WM involvement.

B, Isotropic DW image at 12,000/101 (inversion recovery pulse for cerebrospinal fluid suppression, 2200 ms; b value, 1000 s/mm^2) shows very mild, diffuse increase in SI in posterior WM regions (possibly reflecting T2 prolongation effects) but no discrete abnormalities within the regions of hyperintense signal seen in *A.*

C, ADC map shows areas of hyperintense SI (*arrowheads*), consistent with vasogenic edema, within abnormal regions found in *A.* Mean ratio of ADC values within abnormal regions to values within normal WM (ADC_L/ADC_N) was 1.74. Note that the lesions having elevated ADC values are not seen as hypointense regions on the DW image shown in *A* due to balance of T2 prolongation effects and diffusibility effects (T2 washout). Because a cerebrospinal fluid suppression pulse was used for the DW imaging pulse sequence, cerebrospinal fluid appears hypointense on the ADC maps.

D, ADC map using a threshold of $\geq$ 3 SD (above mean ADC of normal WM) superimposed on axial T2-weighted image (seen in *A*) shows that nearly entire region of hyperintense signal seen in A has ADC values above this threshold. Regions of highest degree of ADC value elevation are designated by yellow or light green color.

E, ADC map with threshold of $\geq$ 10 SD (above mean ADC of normal WM) superimposed on axial T2-weighted image shows that area of ADC values above this threshold is much greater in posterior WM. This is the case even though hyperintense lesions in *A* are relatively equally distributed between anterior and posterior WM.

pointense lesions consistent with vasogenic edema by two neuroradiologists who were not blinded to diagnosis, and decisions were made by consensus. Patients were categorized as having normal-appearing DW imaging studies or abnormal-appearing studies (when hypointense lesions were present). The percentage of hypointense lesion area present on DW images (for patients with abnormal DW images) compared with the area of abnormality seen on the corresponding ADC map was assessed. Patients having hypointense lesions on DW images were compared with patients who did not have such lesions according to etiology, severity of hypertension (when present), and outcome.

Comparison of Degree of ADC Elevation in DW Imaging: Isointense and Hypointense Lesions.—To determine why lesions were conspicuous on ADC maps but were not typically seen on DW images, the increase of ADC values in hypointense lesions on DW images was compared with that of isointense lesions. For each type of lesion, ADC_L/ADC_N was calculated (Fig 2).

Comparison of Patient Characteristics and Lesion Appearance on DW Images.—In an attempt to determine whether hypointense lesion appearance on DW images had any clinical significance, characteristics of patients with hypointense lesions on DW images were compared with characteristics of

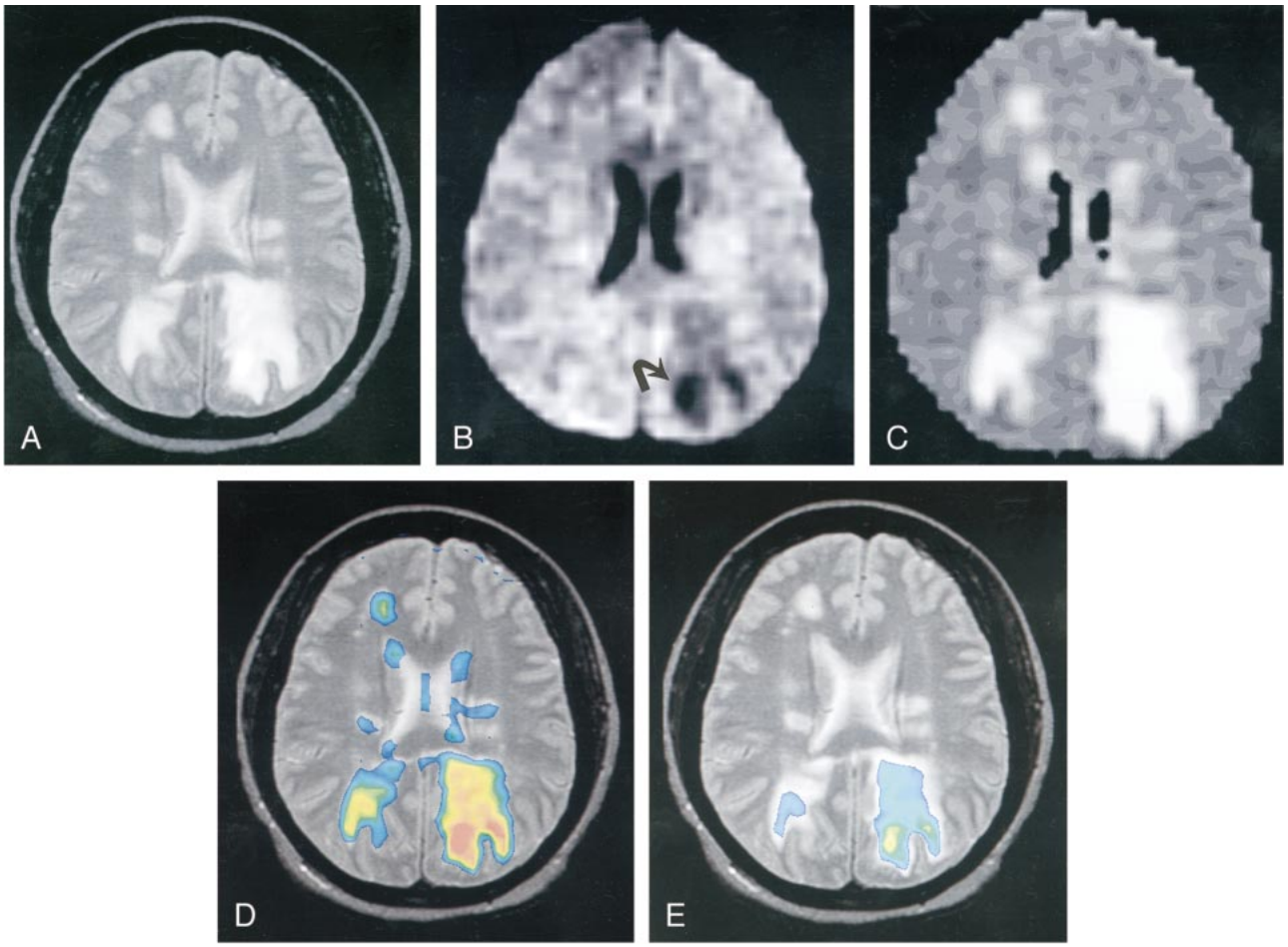

FIG 2. Region of vasogenic edema appearing much smaller on DW image than on T2-weighted images and ADC map in a 28-year-old woman with PRES resulting from severe hypertension. This case shows that lesions with decreased SI on DW images have higher ADC values than lesions that have normal SI on such images. As a result, the contribution of T2 effects in these lesions is not sufficient to cancel the decreased SI caused by elevation of ADC values, and T2 washout does not occur.

A, Axial T2-weighted MR image at 2700/90 (TR/TE) shows areas of hyperintense signal that are much more prominent within posterior WM regions.

B, Isotropic DW MR image at 12,000/101 (inversion recovery pulse for cerebrospinal fluid suppression, 2200 ms; b value, 1000 s/mm^2) shows a region of decreased SI consistent with vasogenic edema in left parietal lobe (*curved arrow*). Note that the overall extent of abnormal SI seen in *B* is much less than that seen in *A.* A small region of increased SI is seen in the right parietooccipital WM, possibly a result of T2 prolongation effects.

C, ADC map shows areas of hyperintense signal, consistent with vasogenic edema, that closely correlate with abnormal regions found in *A.* Mean ratio of ADC values within the left parietal abnormal region to values within normal WM (ADC_L/ADC_N) was 2.51, and the mean ratio in regions that were abnormal on the ADC map but appeared normal on DW image seen in *B* was 1.81. Because water diffusibility within the region of abnormal SI seen on the DW image is greater than that in other regions (as measured by the higher ADC), T2 washout does not occur.

D, ADC map with threshold of $\geq$ 3 SD (above mean ADC of normal WM) superimposed on axial T2-weighted image (shown in *A*) shows that essentially all hyperintense regions in *A* have ADC values above this threshold. Regions of highest degree of ADC value elevation are designated by red or orange color and are more severely elevated than those seen in *Figure 1D.*

E, ADC map with threshold of $\geq$ 10 SD (above mean ADC of normal WM) superimposed on axial T2-weighted image shows that only posterior WM regions have ADC values above this threshold and, therefore, severity of degree of ADC elevation is greatest in posterior WM.

patients who did not have such lesions. Patients were compared according to etiology of PRES, severity of hypertension (if present), and clinical outcome.

Results

Lesion Distribution on T2-Weighted MR Images

On T2-weighted MR images, both anterior and posterior WM involvement was seen in eight patients and solely posterior WM involvement was seen in three patients. No patients were excluded because of predominantly or solely anterior WM involvement. In the images from three patients, small areas of gray matter involvement were seen. These were seen to have resolved on a subsequent MR examination in all cases. No patients were found to have regions of restricted diffusion to suggest infarction.

Assessment of Severity of Vasogenic Edema According to Brain Region

On ADC maps with a threshold of ≥ 3 SD above mean normal WM, the size and shape of areas having elevated ADC values were essentially similar to those of hyperintense lesions on T2-weighted images. Therefore, both anterior and posterior WM were involved on ADC maps obtained from eight patients and solely posterior WM was involved on ADC maps obtained from three patients. However, in ADC maps for the eight patients with both anterior and posterior WM involvement, posterior WM involvement was more extensive than anterior WM involvement.

Six of the eight patients with both anterior and posterior WM abnormalities seen on ADC maps with a threshold ≥ 3 SD were found to have solely posterior WM abnormalities on ADC maps with a threshold of ≥ 10 SD. In the two patients with abnormal regions in both anterior and posterior WM on ADC maps with a threshold of ≥ 10 SD, posterior WM involvement was much more extensive than anterior WM involvement in one case (Fig 2) and relatively equally distributed between regions in the other case. Abnormal regions were much smaller on ADC maps using an ADC threshold of ≥ 10 SD than on those with a threshold of ≥ 3 SD (Figs 1 and 2).

Determination of Cause of Isointense Signal of Lesions on DW Images

Measurement of SI and ADC of Lesions.—On DW images, lesions appeared isointense (n = 7) or hypointense (n = 4) to normal-appearing WM. Hypointense lesions on DW images were much smaller than the corresponding individual region of hyperintense signal seen on T2-weighted images in three patients (Fig 2), and approximately equal in size to corresponding lesions on T2-weighted images in the remaining case. Nonetheless, because hypointense lesions represented a small percentage of lesions in the entire population of 11 patients, the mean SI of all lesions on DW images for each patient was essentially equal to that of normal WM. The mean SI of lesions measured 127.5 ± 47.5, the mean SI of normal WM measured 128.0 ± 37.5, and the mean SI_L/SI_N measured 0.98 ± 0.12 (range, 0.77–1.18). These values were not significantly different by Student *t* test ($P = .2$).

On ADC maps, lesions appeared brighter than normal-appearing WM in all cases. All regions of increased ADC were seen on T2-weighted images. Furthermore, all regions of hyperintense signal on T2-weighted images were found to correlate with regions of elevated ADC, indicating that all lesions seen on T2-weighted images resulted from vasogenic, rather than cytotoxic, edema. The mean ADC_L was 138 ± 18 mm^2/s, and the mean ADC_N was 76 ± 3 mm^2/s; the mean ADC_L/ADC_N was 1.81 ± 0.2 ($P < .001$; Student *t* test), consistent with vasogenic edema. Therefore, although as a group lesions were isointense on DW images (as determined by mean SI_L/SI_N), substantially increased ADC values were seen.

Comparison of Lesion Areas on DW Images and ADC Maps.—Among the four patients with regions of hypointense signal on DW images, total abnormal area on DW images was substantially smaller than the area of abnormality seen on ADC maps. In three patients, only approximately 5% of the area of regions that appeared abnormal on ADC maps were visible on DW images, and the remainder inapparent (ie, isointense to normal WM on DW images). In the fourth patient, approximately 35% of the area of regions with elevated ADC values were seen to be hypointense on DW images (Fig 2).

Comparison of Degree of ADC Elevation in DW Imaging: Isointense and Hypointense Lesions.—Among the four patients with hypointense lesions on DW images, the mean ADC of hypointense lesions was 175 mm^2/s and the mean ADC_L/ADC_N was 2.30. For areas that were isointense on DW images, the mean ADC was 133 mm^2/s and the mean ADC_L/ADC_N was 1.75 (Figs 1 and 2). These findings indicate that water diffusibility was substantially higher in regions that were hypointense on DW images compared with regions that did not have decreased SI (despite elevated ADC values compared with normal WM).

Comparison of Patient Characteristics and Lesion Appearance on DW Images.—Among the four patients with hypointense lesions on DW images, the cause of symptoms was thought to be renal hypertension for two patients, eclampsia for one patient, and treatment with both cyclosporine and tacrolimus for the remaining patient. All four patients had elevation of systemic arterial blood pressure during their clinical course. In the group of seven patients who did not have hypointense lesions, in six patients treatment with cyclosporine alone (n = 3) or in combination with tacrolimus (n = 3) was considered the cause of symptoms, and eclampsia was considered the cause in the remaining patient. Five of these seven patients had elevation of systemic arterial blood pressure. No substantial difference in degree of elevation of systemic arterial blood pressure between the two groups was seen.

One patient with hypointense lesions died, and the remaining three had good clinical recovery. No patients with solely isointense lesions died, and all these patients had good clinical recovery.

Discussion

Patients with PRES often have nonlocalizing neurologic symptoms and signs, such as confusion, headache, and seizures. However, because the posterior WM is preferentially affected, reversible cortical blindness also can be found (1, 2). Reversible WM changes associated with the symptom complex now referred to as PRES were initially described primarily in the setting of hypertension,

often related to eclampsia or cessation of antihypertensive medications (1). It subsequently was recognized that a number of medications, some of which can produce acute rises in mean arterial blood pressure, could cause this syndrome (1, 2). In addition, PRES can occur in the presence of only relatively mild increases in blood pressure (9).

On spin-echo MR images, typical findings of PRES include bilateral hyperintense foci within WM in the parietooccipital regions, often involving more than one vascular territory (1). Lesions do not generally enhance on T1-weighted images. Although WM predominantly is involved, gray matter involvement also can be seen. In a study assessing the use of fluid-attenuated inversion recovery imaging for this syndrome, approximately 95% of patients were found to have cortical lesions (10). The findings can simulate infarction but are distinguished by the fact that the findings are reversible (1). However, at times, lesions are irreversible and associated with restricted diffusion when acute infarction has occurred. Reversible regions of restricted diffusion in the setting of PRES also have been noted occasionally, when imaging is performed during or immediately after seizures (7).

The pathophysiology of reversible WM changes seen in PRES is incompletely understood. One hypothesis is that lesions are ischemic in origin and predominantly the result of vasospasm within medium-sized and large arteries supplying posterior brain regions. According to this hypothesis, vasospasm produces lesions that are characterized by (often reversible) cytotoxic edema, which can proceed to frank infarction when ischemia is not successfully treated (11). Evidence favoring this hypothesis is large artery vasospasm having been reported in some cases of preeclampsia and eclampsia (12). According to another hypothesis, lesions primarily result from vasogenic edema due to hypertension-induced failure of cerebral autoregulation, which is based on DW imaging lesions having elevated ADC values, as expected with vasogenic (but not cytotoxic) edema (4, 13). Current evidence indicates that both mechanisms could be operative in PRES. Loss of autoregulation now is considered to be the underlying common pathogenetic mechanism in a number of causes of PRES, including hypertensive encephalopathy and eclampsia (1).

In most (eight of 11) of our patients, involvement of both anterior and posterior WM regions was seen on T2-weighted images, standard ADC maps, and maps using a threshold of ≥ 3 SD above mean WM ADC values. No patients showed only anterior WM involvement. However, in six of these patients, solely posterior WM involvement was seen when particularly severe areas of vasogenic edema were depicted with a threshold of ≥ 10 SD above mean WM values. This indicates that the most severe elevations of ADC values (and most severe vasogenic edema) were seen in posterior WM. Furthermore, T2-weighted images, DW images, and standard ADC maps did not reflect severity of vasogenic edema as defined by degree of increase of water diffusibility.

The reason for preponderance of lesions in posterior WM in PRES has been attributed to the vertebrobasilar circulation (and, in particular, the posterior cerebral arteries) being relatively sparsely innervated by autonomic fibers (14). Because these fibers play a role in cerebral autoregulation, a paucity of such fibers would be expected to be associated with the highest degree of loss of autoregulation.

In our series, seven of 11 patients with markedly abnormal ADC values had normal-appearing DW images (Fig 1). In three of the remaining four patients, only a small proportion of regions having elevated ADC values were prospectively identified on evaluation of DW images as areas of decreased SI (Fig 2). Previous reports of DW imaging in patients with PRES also have shown that reversible lesions having elevated ADC values resulting from vasogenic edema are frequently isointense to normal WM (3, 5). However, to date, relatively little attention has been given to the explanation of the isointense signal that is frequently seen on DW images. One potential explanation is that ADC values are only slightly elevated and the effect of this increase in water diffusion might not be apparent on DW images. However, in our series, ADC values within lesions (138 mm^2/s) were substantially higher than those found in normal WM (76 mm^2/s). Furthermore, lesions had increased SI on ADC maps in all cases, which indicates that the ADC increase was, in fact, substantial and would have been seen if not for the presence of other factors.

On DW images, SI is known to result from a combination of diffusibility effects and contribution from T2 SI. The latter factor can be removed by calculation of ADC maps, which isolate water diffusibility contribution. In this study, we used this method to determine contribution of T2 effects to overall lesion appearance on DW images. Lesions were readily apparent on ADC maps, indicating that T2 prolongation effects are substantial in PRES lesions and contribute to isointensity of lesions on DW images, a phenomenon we term ''T2 washout.'' Diffusion-weighted images showing isointense vasogenic edema in PRES have been shown in a previously published article, but no explanation of the isointense appearance was offered (3). The typical isointense appearance of PRES lesions on DW images represents the summation of decreased SI caused by vasogenic edema and increased SI caused by T2 prolongation effects. In most of our cases, these two effects balanced one another, so that no net effect on SI was produced on DW images (Fig 1). T2 washout is analogous (but opposite in polarity) to the T2 shine-through also commonly seen on DW images. However, T2 shine-through results from summation of increased SI from T2 prolongation effects and increased SI on DW images from restricted diffusion (or normal

diffusion). On the other hand, T2 washout represents cancellation of decreased SI (caused by increased water diffusibility) by increased SI from T2 prolongation effects (Fig 1).

The mean ADC value measured within lesions that were hyperintense on T2-weighted images in our patients (138 mm^2/s) was quite similar to that reported by previous investigators (4, 13). However, wide variability of ADC values was seen among individual lesions, with ADC increases being much higher in lesions that were hypointense on DW images compared with lesions that were isointense (Fig 2). In hypointense lesions on DW images, T2 prolongation effects were insufficient to balance the decrease in SI caused by the high diffusibility of the lesions. In these cases, the net effect of the two factors was an overall decrease in SI (Fig 2). This appearance would result if such lesions had a larger increase in ADC values and/or a smaller contribution from T2 prolongation effects than isointense lesions. We tested the first possibility by comparing ADC values within hypointense lesions and isointense lesions on DW images and found that ADC values in hypointense lesions were, in fact, substantially higher (Fig 2). Because this factor was sufficient to account for the differences in appearance on DW images, we did not determine whether a smaller contribution from T2 prolongation effects was also a factor.

It is not entirely clear why some patients with PRES develop higher elevations of ADC values (and hypointense lesions on DW mages) compared with other patients. Furthermore, because our patient population is small, we were not able to determine whether presence of hypointense lesions reflects a more severe form of PRES or whether it is of prognostic value. The hypointense lesions seen on DW images are not specific for PRES but can be seen in any disease process producing substantial vasogenic edema (eg, neoplasms and abscesses). Therefore, hypointense lesions on DW images are a relatively common phenomenon. On the basis of our findings, we can reasonably predict that the presence of hypointensity (and degree of hypointensity) on DW images surrounding intracranial mass lesions producing vasogenic edema in individual cases will depend on the relative degrees of two factors: ADC elevation and T2 prolongation.

Comparison of patient groups according to whether hypointense lesions were present on DW images showed no apparent differences. Patients did not differ according to cause of PRES or severity of hypertension. One patient with hypointense lesions died, whereas no patients who had solely isointense lesions did. Therefore, no striking differences in cause or prognosis were seen, although our sample size was small.

Conclusion

Lesions were typically isointense to normal WM on DW images but were conspicuous on ADC maps. T2 washout results from a balance between contributions from T2 prolongation effects and elevated ADC values from increased water diffusibility. Abnormal regions were seen on ADC maps in both anterior and posterior WM regions on standard ADC maps and maps using a threshold of $\geq$ 3 SD above normal WM. However, solely posterior WM abnormalities were seen in the majority of patients by use of a threshold of $\geq$ 10 SD. In severe typical PRES cases, ADC maps show a tendency for more abundant accumulation of vasogenic edema within posterior WM.

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