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Case Report

Prolonged Reversible Vasospasm in Cyclosporin A–Induced Encephalopathy

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Summary: The mechanisms responsible for cyclosporin-induced encephalopathy remain controversial. Herein we present a case of cyclosporin-induced encephalopathy with unusually prolonged vasospasm, which might have contributed to the slow recovery of the patient.

Vasospasm has been proposed as one of the mechanisms of cyclosporine A (CsA)–induced encephalopathy (1), although the first case of demonstrated vasospasm was reported only recently (2). T2-weighted MR images typically show hyperintense lesions involving the subcortical regions of the occipital, posterior temporal, and parietal lobes (1, 3, 4); these sometimes involve the cortical regions (2). Herein, we report a further case of CsA-induced encephalopathy with vasospasm of a protracted course.

Case Report

A 35-year-old woman receiving CsA for 1 month for myelodysplastic syndrome associated with autoimmune hemolytic anemia experienced a sudden onset of blurred vision, headache, and loss of balance. Two days later, she had left-sided limb weakness and sensory impairment; therefore, the CsA was discontinued. Upon her admission to the hospital 4 days after symptom onset, her blood pressure was 130/80 mm Hg. The neurologic examinations revealed left hemianopia, a limitation of the leftward gaze, quadriparesis (muscle power grade 2 of 5 in the left limbs and grade 4 of 5 in the right limbs), generalized hyperreflexia, and bilateral Babinski signs. The whole-blood CsA level was 189 ng/mL (range, 75–350 ng/mL). The hemoglobin level was 11.1 g/dL, and the platelet count was $23 \times 10^9/L$. Results of both direct and indirect Coombs tests were positive. The direct Coombs test revealed that the antibody was of the immunoglobulin G type. Results of the antinuclear antibody (ANA) test were negative. The complement C3 level was within the normal range. Serum biochemistry results were normal, except for low cholesterol (64 mg/dL) and magnesium (1.3 mg/dL) levels.

Brain CT scans obtained 2 days after symptom onset showed low opacities in the bilateral deep parieto-occipital regions. CsA-induced encephalopathy was then diagnosed. Her vision improved, and her right-sided limbs regained full strength 5 days after the onset of the symptoms. The next day (day 6), T2-weighted and diffusion-weighted MR imaging showed hy-

perintense lesions involving the right parieto-occipital region (both cortical and subcortical regions), the left deep parietal region, and the bilateral deep temporal regions. The MR angiogram (MRA) showed a marked narrowing of the M1 segment of the bilateral middle cerebral arteries (MCAs) and the right posterior cerebral artery (PCA). The apparent diffusion coefficients (ADCs) were low ($0.00647 \text{ mm}^2/\text{s}$), compared with 0.0090 in normal tissue, at the site of the right parieto-occipital lesions. This finding suggested ischemic cytotoxic edema (5) (Fig 1A–C). The follow-up MR image and MRA obtained on day 14 demonstrated hyperintense lesions in the right parieto-occipital areas; these were associated with gyral enhancement and a persistence of vasospasm. However, the lesions in the bilateral deep temporal and left deep parietal regions disappeared. The MRA obtained on day 27 revealed resolution of the arterial vasospasm (Fig 1D–F). The patient regained her vision but had slight residual weakness and numbness of her left limbs at follow-up on day 30. At follow-up 6 months later, only the lower-limb weakness remained.

Discussion

The underlying mechanism and pathophysiologic features of CsA-induced encephalopathy have not been well defined, and they might be multifactorial (3, 4, 6, 7). We report a patient with CsA-induced encephalopathy with both cortical and subcortical involvement. A multiple segmental arterial vasospasm was a possible underlying cause and responsible for the lesions at the bilateral parieto-occipital regions. The low intralesional ADCs were consistent with cytotoxic edema (5).

The clinical and neuroimaging findings of CsA-induced encephalopathy are similar to those of eclampsia and hypertensive encephalopathy (8). Because vasospasm is an important mechanism for eclampsia and hypertensive encephalopathy (9, 10), it is also proposed as a mechanism responsible for CsA-induced encephalopathy (1). However, the first patient with possible vasospasm was reported by Bartynski et al only recently (2). Their patient had bilateral MCAs and PCAs with a reduced caliber, as assessed by using MRA, and vasospasm or vasculitis was suggested. The patient died 5 days after imaging, and the pathologic examination showed both cortical ischemic necrosis and subcortical vasogenic edema with no disease of the involved vessels. Therefore, vasospasm rather than vasculitis was responsible for the reduced caliber of the involved arteries. Our patient was similar to that of Bartynski et al, except that ADC mapping showed only cytotoxic edema. The possibility of vasculitis was less likely in our patient because of negative ANA results and a normal complement titer. Hypertension was not found in our

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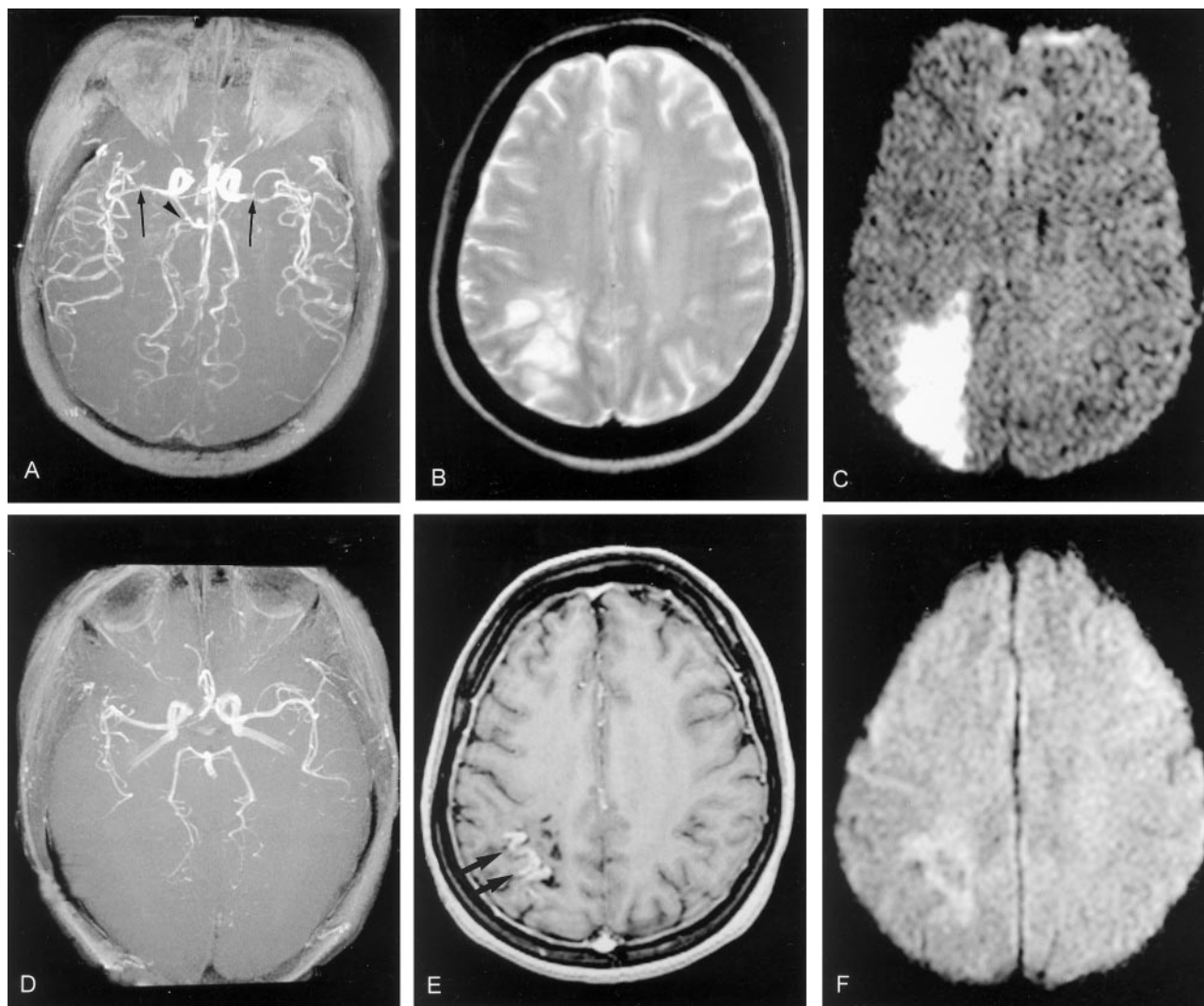


FIG 1. A–C, MR images and MRAs obtained 6 days after symptom onset. D–F, MR images and MRAs obtained 27 days after symptom onset.

A, MRA shows evidence of a marked narrowing of the M1 segment of the bilateral MCAs (arrows) and the P2 segment of the right PCA (arrowhead).

B, T2-weighted MR image (TR/TE/NEX, 3200/100/2) shows a hyperintense lesion in the right parieto-occipital region. The lesion seemed to be mainly in the subcortical white matter.

C, Diffusion-weighted MR image ($b = 1000$) shows evidence of a hyperintense lesion in the right parieto-occipital region, as compared with the T2-weighted image. Obvious involvement to the cortical region was also identified. Cytotoxic edema was indicated by measuring the ADCs.

D, MRA shows recovery of the lumen of the bilateral MCAs and right PCAs. This finding indicates that the vascular lesion seen in the previous MRA was caused by the vasospasm.

E, T1-weighted MR image (400/17/2) obtained after an intravenous injection of gadolinium-based contrast agent reveals curvilinear enhancement along the course of the gyri (arrows). This finding indicates cortical involvement.

F, The hyperintense lesion seen on the previous diffusion-weighted image became smaller and was located in the white matter. This finding indicates recovery of the diffusion activity in most of the hyperintense part seen on the previous diffusion-weighted image.

patient. Therefore, the reversible, protracted vasospasm (at least 14 days) in our patient might have been one of the possible mechanisms of CsA-induced encephalopathy, and it might have accounted for the long clinical course of recovery in our case. This observation is in contrast to what is seen in patients with CsA-induced encephalopathy and vasogenic edema; these patients usually have a reversible course and a better outcome (3). MRAs and diffusion-weighted images are helpful in understanding the pathophysiology of CsA-induced encephalopathy.

Prolonged vasospasm might be rare, but it is nevertheless an existent mechanism responsible for the cytotoxic edema of both the gray matter and the white matter in certain patients.

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