Atypical Posterior Reversible Encephalopathy Syndrome: A Flare of Systemic Lupus Erythematosus

To the Editor:

Posterior reversible encephalopathy syndrome (PRES) is typically characterized by headache, altered alertness and behavior, seizures, nausea, vomiting, and abnormalities of visual perception¹. PRES has been described as an uncommon neurological manifestation in systemic lupus erythematosus (SLE), mainly associated with hypertension, renal insufficiency, and use of immunosuppressive drugs². Cases without hypertension and/or renal dysfunction are very rare^{3,4}. Endothelium dysfunction caused by systemic inflammation in SLE has been proposed as an alternative mechanism to the hypertension-induced cerebral autoregulatory dysfunction⁵. Use of hydroxychloroquine (HCQ) therapy has recently been described as possibly associated with PRES⁴.

A 45-year-old woman, a smoker who had had a diagnosis of cutaneous lupus for 2 years, was seen at our hospital for new-onset neurological symptoms. She had normal stature, no previous neurological symptoms such as migraine, and no family history of neurological disease. A diagnosis of lupus was based on discoid rash, photosensitivity, abnormal titer of antinuclear antibody (ANA: 1/320), and chilblain lupus upon skin biopsy; it was controlled with HCQ 400 mg/day and prednisone 5 mg/day. She

developed insidious fever, temporal headache, weight loss, thrombocytopenia (107,000/ μ l), lymphopenia (690/ μ l), and small pericardial effusion. A diagnosis of lupus exacerbation was made and the dose of prednisone increased to 15 mg, with partial relief of symptoms. Three weeks later she experienced acute aphasia, right homonymous hemianopsia, and on the next day, intense headache. Decreased consciousness, seizures, or other visual disturbances were not reported. Blood pressure and renal function were always normal. Computed tomography of the head showed a cortico-subcortical left fronto-insular hypodensity, suggestive of ischemic lesion. Transthoracic echocardiography ruled out a cardioembolic cause and cerebrospinal fluid examination was normal. Magnetic resonance imaging (MRI) was performed on the next day; it showed multiple T2 and fluid-attenuated inversion recovery hyperintense lesions in left cortical temporal and frontal areas, head of caudate nucleus, left thalamus, and the brain stem (Figure 1A, 1B); none of these lesions showed restriction in diffusion-weighted imaging, or decreased apparent diffusion coefficient signal or gadolinium enhancement. Spectroscopy showed a mildly decreased N-acetylaspartate peak and increased lactate peak. MR-angiography excluded major intracranial arterial irregularities. Immunological studies revealed ANA positivity (1/1280), without other antibodies, including antiphospholipid. Anti-aquaporin-4 specific, anti-N-methyl-D-aspartate, and anti-voltage-gated potassium channel antibodies were all negative as

Figure 1. Fluid-attenuated inversion recovery magnetic resonance imaging at the onset of the clinical investigation (A, B) and 2 months later (C, D). The first images show hyperintense lesions in the brain stem (A), left cortical temporal area, head of caudate nucleus, and left thalamus (B). Two months later, there was a complete resolution on MRI (C, D).

well. HCQ was suspended and prednisone was increased to 60 mg/day. She improved gradually and 1 week later had only a mild motor aphasia. There was a progressive improvement in the brain MRI, with reduction of size of the lesions (1 month after the onset) and almost complete resolution of the lesions 2 months later (Figure 1C, 1D).

Radiological characteristics, especially the diffusion-weighted images, pointed mainly to lesions of a metabolic etiology such as PRES or MELAS (mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episodes)^{6,7}. Clinical characteristics, although atypical, pointed in the direction of PRES. The second hypothesis was clinically unlikely: no previous personal or family history, absence of mitochondrial disease phenotype and systemic characteristics, and a late onset for a first episode. The basal ganglia and brain stem MRI signal changes, although possible, are not typically seen in MELAS. Good response to corticotherapy and a probable association with SLE flare made the MELAS hypothesis even less probable. From a therapeutic viewpoint it was essential to distinguish PRES from stroke. Considering the absence of other factors (high blood pressure, use of other immunosuppressive agents, or renal dysfunction) it was considered that PRES occurred in the context of an SLE flare and it was treated with high-dose steroids. Subsequent rapid progression to clinical and radiological improvement strongly supports the diagnosis.

There are some descriptions of the association of PRES with neuromyelitis optica spectrum disorders (NMOSD)⁸, and also linking NMOSD and SLE. Therefore we tested our patient for the aquaporin-4 specific antibodies, which were negative. Use of HCQ was proposed as a possible etiological factor in a recent report by Bag, *et al*⁴, which made us suspend this therapy in our patient. Lupus exacerbation and consequently immunological damage of endothelium has been proposed by different authors. We believe that the pathogenesis of this clinical case was related to exacerbation of lupus or use of HCQ therapy, or a combination of the two. More descriptions of similar cases may contribute to a better understanding of PRES.

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