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Posterior reversible encephalopathy syndrome as a complication of acute lupus activity

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ABSTRACT

Objectives: We aimed to describe the clinical and imaging characteristics; associated risk factors and neurological outcome of posterior reversible encephalopathy syndrome (PRES) in patients with systemic lupus erythematosus (SLE).
Methods: From October 2001 to January 2007, we identified patients with SLE and the criteria for PRES in our institution, which is a tertiary-care referral center for patients with SLE; the patients were evaluated at baseline and followed to determine the clinical outcome.
Results: We identified 22 episodes of PRES in 21 patients; 20 (95.2%) were women, mean age of onset was 24.9 ± 8.6 years, all patients had high systemic activity (SLEDAI scores from 12 to 39). Acute hypertension was observed in 18 episodes (81.8%), and renal failure in 16 (72.7%); only 3 patients were on cyclophosphamide at the time of the onset of PRES. Persistent neurological deficit was observed in 2 cases; one patient died during the acute episode.
Conclusions: PRES is a central nervous system syndrome that is observed in SLE patients. It was associated mainly to high systemic activity, acute hypertension, and renal failure. Although reversibility is common, residual neurological damage may be observed.

1. Introduction

Posterior reversible encephalopathy syndrome (PRES) is a clinical and radiological syndrome first described by Hinchey et al. in 1996 [1]; its main pathogenic mechanism is a disruption of the blood–brain barrier (BBB) and secondary leakage of plasma into the brain parenchyma. It is clinically characterized by headache, decreased level of alertness, seizures and visual loss of cortical type. Multiple treatments and clinical conditions have been associated to this disorder, including: immunotherapy [2], erythropoietin treatment [3], organ transplantation [4], transfusions [5], chemotherapy [6], and Guillain-Barré syndrome [7].

Reports of patients with systemic lupus erythematosus (SLE) who developed PRES, have linked it to cytotoxic treatment, fluid retention secondary to renal failure and acute hypertensive crisis [1]. Differential diagnosis of PRES in patients with SLE should include: hypertensive encephalopathy, uremic encephalopathy, ischemic stroke and central nervous system activity.

The aims of the present study are to describe the clinical manifestations, risk factors, imaging characteristics and neurological outcome of PRES in patients with SLE.

2. Materials and methods

2.1. Patients and clinical scores

The protocol was approved by our local committee of ethics. From October 2001 to January 2007, we identified those patients with clinical and imaging findings consistent with PRES in the emergency department and the inpatient section of our institution, which is a national tertiary reference center for patients with SLE and other immunological disorders. All patients had a previous diagnosis of SLE according to the American College of Rheumatology (ACR) criteria [8]; systemic activity was calculated according to the SLE Disease Activity Index (SLEDAI) [9], and chronic damage was determined according to the Systemic Lupus International Collaborating Clinics (SLICC)/ACR criteria [10] at the time of the

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PRES episode. All patients were followed-up clinically at 6 months in the neurology clinic for outside patients of our institution and evaluated by two of us (J.F.B.C. and C.C.B.).

Anticardiolipin IgG and IgM (aCL) and anti-beta2 glycoprotein 1 (anti-β2-GP 1) antibodies were determined by ELISA using cardiolipin as antigen (Sigma Chemicals, St. Louis, MO, USA) in all patients. Lupus anticoagulant was tested in 2 cases with prolonged partial tromboplastine time. Antiphospholipid syndrome (APS) was defined according to established clinical and laboratory criteria [11].

2.2. Imaging studies

A brain magnetic resonance imaging (MRI) (Signa Infinity 1.5 T, Twin Speed with Excite, G.E., Medical Systems; Milwaukee, WI, USA) employing a superconducting magnet operating at 1.5 T was performed in 20 episodes at the time of the neurological manifestations. In two episodes the evaluation was performed by a computed tomography (CT) scan (Sensation 64, Siemens, Erlangen, Germany). All studies were evaluated by an expert neuroradiologist (H.M.B.C.). Cerebral white matter edema affecting mainly posterior regions of the brain (Fig. 1A and D), not otherwise attributed to other condition (stroke, hydrocephalus, etc.) [1] was consistent with PRES.

3. Results

3.1. Clinical findings

During the study period a total of 16,600 consultations were performed at the Emergency Room (ER) of our institution, from which 1425 (8.6%) were previous or newly diagnosis cases of SLE. We identified 21 episodes of PRES in 20 patients with SLE in the ER and 1 episode in the inpatient section of our institution. PRES represented 1.5% of all SLE consultations in the ER during the study period. The clinical and laboratory characteristics for the 22 episodes are shown in Table 1. At onset all patients had high SLEDAI scores (range, 12–39) reflecting high systemic activity. Acute hypertension presented in 18 episodes (81.8%), and renal failure in 16 (72.7%); 15 patients with hypertension also had renal failure, 3 patients did not have neither hypertension nor renal failure; 3 patients were on cyclophosphamide, and 6 on azathioprine at the onset.

APS was identified in 8 episodes and positive anticardiolipin antibodies (IgG) in 12 cases, 1 patient had positive lupus anticoagulant. No patient had signs of infections at the onset of PRES.

One patient, a 29-year-old woman, developed a second episode of PRES, 7 months after the first one; SLEDAI score: 27 and 26, respectively, both episodes were treated with high dose of corticosteroids and pulses of cyclophosphamide initiated after the first one.

3.2. Imaging

The topography of the cerebral edema is shown in Table 2. Hematoma formation was documented in 2 cases (Fig. 1B). Cortical involvement was observed in 21 (95.5%) of episodes. Magnetic resonance angiography (MRA) was performed in 12 (54.5%) episodes, and evaluated carefully by 3 of us, no patient showed occlusions, focal stenosis, or beading of the cerebral arteries (Fig. 1E). Conventional angiography could not be performed in these patients because of acute renal failure, poor clinical condition or rapid clinical improvement.

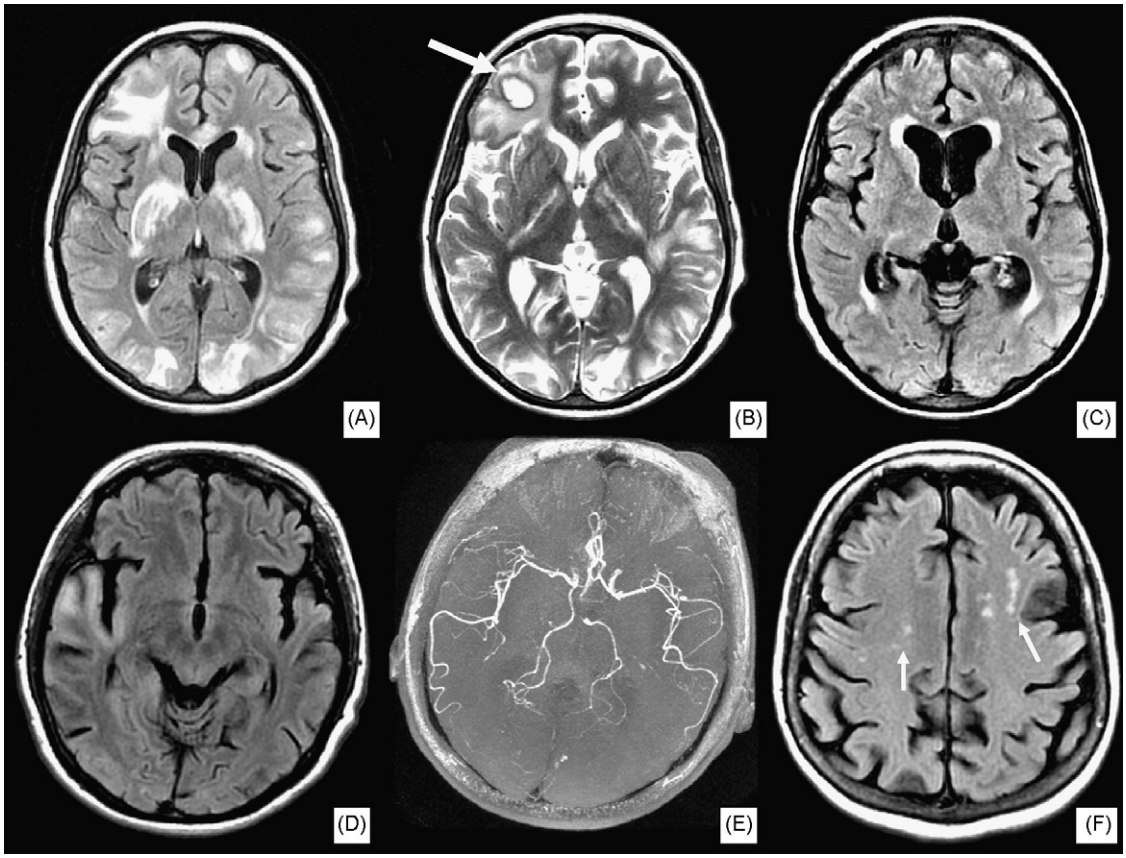

Fig. 1. In a 22-year-old woman, axial MRI showed multiple areas of edema with involvement of cortical grey and subcortical white matter (A); a right frontal lobe hematoma (arrow) was documented (B); MRI performed 3 months later shows resolution of the cerebral edema (C). The MRI of 41-year-old woman showed cortical and subcortical hyperintensities in both temporal lobes and right insula (D); the angio-MRI did not show focal or segmental narrowing of cerebral circulation (E); small confluent white-matter hyperintensities (arrows) appeared 10 days after the first MRI (F).