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Original article

Recurrent status epilepticus in posterior reversible encephalopathy syndrome as initial feature of pediatric lupus: A newly diagnosed case and literature review

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Abstract

Introduction: Posterior reversible encephalopathy syndrome (PRES) is a recently described clinico-neuroradiological syndrome with several predisposing conditions. Systemic lupus erythematosus (SLE), beginning in 15–20% in childhood, is considered as a potential underlying etiology of PRES. In children, status epilepticus (SE) rarely complicates PRES, and exceptionally occurs in SLE.

Methods: We report on an illustrative case of PRES complicating pediatric lupus revealed by recurrent SE, and we further review through a Pubmed search the previously reported cases of pediatric SLE, PRES and SE.

Results: We describe the case of a 12-year old girl who presented with recurrent status epilepticus associated to high blood pressure and renal involvement. Brain imaging showed classical aspects of PRES. Immunological tests including antinuclear, anti-DNA, and anticardiolipin antibodies were positive. The diagnosis of SLE was established. The Pubmed search identified a total number of 9 children with SE in SLE, and 26 with PRES, including our patient.

Conclusions: We discussed the clinical and paraclinical features of PRES in SLE with epilepsy, their underlying pathophysiological aspects, and their management challenges. PRES should be considered in initial recurrent SE in children, justifying a battery of tests comprising immunological testing. Anticardiolipin antibodies seem to play a crucial role in epilepsy, PRES and renal involvement in pediatric SLE. Further studies are needed to clarify whether PRES should be considered one of the neuropsychiatric manifestations of SLE or a consequence of active disease in other organ systems or its treatment.

Keywords: Status epilepticus; PRES; Lupus; Glomerulonephritis; Child

1. Introduction

Posterior reversible encephalopathy syndrome (PRES) is a cliniconeuroradiological syndrome, recently described by Hinchey and coworkers in 1996 [1–2]. Systemic lupus erythematosus (SLE), beginning in 15–20% in childhood [3–4], has been described as a potential underlying etiology of PRES [2]. Seizures are one of the most frequent manifestations of PRES [1]. However, status epilepticus (SE), a potential life-threatening event, has been described more frequently in adults than in children with PRES [1–6].

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2. Materials and methods

We report on an illustrative case of PRES complicating pediatric lupus revealed by recurrent SE, and we further review the key clinical and paraclinical features of PRES in SLE with epilepsy. We performed a Pubmed search using the terms "Lupus", "SLE", "child", "childhood", "pediatric", "girl", "boy", "PRES", "posterior reversible encephalopathy", "epilepsy", "seizure" and "status epilepticus". We identified all the previously reported cases of status epilepticus and the cases of PRES in children with SLE. Each case was reviewed for clinical features, laboratory and imaging findings, management and outcome. This mini review will help with the understanding of the underlying pathophysiological aspects and the management challenges of these associations.

3. Results

3.1. Illustrative case

A 12-year-old girl presented with diarrhea, incoercible vomiting and fever, 2 weeks before her admission to our department of neurology. A week later, she had a SE with generalized hypotonic and tonic seizures and loss of consciousness persisting for 45 min. She was admitted in intensive care unit (ICU). She received intravenous (IV) infusion of phenobarbital and clonazepam with cessation of seizures and post-ictal confusion. Her blood pressure (BP) reached 180/100 mmHg (>95th percentile for age and sex), and she presented generalized edema with periorbital, abdominal and limb swelling. The blood cell count showed normochromic normocytic anemia and hyperleukocytosis (38,000 elements/mm^3) predominantly neutrophilic. The C-reactive protein (42 mg/l) and blood urea nitrogen levels (13 mmol/l) were elevated. Serum protein electrophoresis including serum albumin was normal with a total protein at 65 g/l and albumin at 36 g/l. Urinalysis demonstrated microcytic hematuria, proteinuria and elevated polymorphonuclear leukocytes, with proteinuria of 1 g on a 24-h urine collection. Chest and abdominal X-rays, abdominal ultrasound and doppler ultrasound of the kidneys were all normal. The cerebrospinal fluid (CSF) analysis showed isolated hyperproteinorachia (680 mg/dl). Brain CT scan showed multiple bilateral asymmetric cortico-subcortical parieto-occipital hypodensities. Antibiotherapy was initiated (cefotaxime, gentamicin and vancomycin). Apyrexia was obtained with resolution of edema, vomiting and diarrhea in two days, but hypertension persisted. Four days after the first SE, she presented headache and vomiting followed by loss of consciousness and left-side myoclonic seizures with secondary generalization persisting for more than 30 min. IV diazepam was initially administered unsuccessfully. SE was stopped by the association of IV infusion of phenobarbital, then, she was transferred to our department. Her examination was normal except for mild hypertension (130/90 mmHg). The interictal electro-encephalogram (EEG) was normal. Initial brain MRI showed extended asymmetrical bilateral cortico-subcortical fronto-parieto-occipital signal abnormalities with hyposignal T1, hypersignal T2, FLAIR and diffusion with elevated ADC (Fig. 1A). A control brain MRI two weeks later showed a partial regression of lesions (Fig. 1B). Activated partial thromboplastin time, prothrombin time and international normalized ratio were normal. Syphilitic, C and B hepatitis, Lyme disease and HIV serologies were normal. Thyroid function tests showed elevated TSH with normal FT4. Anti-nuclear antibodies were positive at 1/640 with speckled pattern. Anti-native DNA, anti-cardiolipin (IgM: 45U/ml ($N < 12$ U/ml) and IgG:12 U/ml ($N < 12$ U/ml)), anti-gliadine, anti-transglutaminase antibodies and direct antiglobulin test (DAT) were positive. Anti-thyroperoxydase, anti-thyroglobulin, anti-endomysium, anti-phospholipid, anti-b2 glycoprotein, anti-SSA, anti-SSB, anti-Sm, and anti-SCL70 antibodies were negative. The complement blood test showed low C3 complement component levels (0.58 g/l for a normal value of 0.97–1.57 g/l); normal C4 (1.161 g/l; normal: 0.162–0.445 g/l) and CH50 (90%; normal: $100 \pm 30\%$). Lactate and pyruvate ratio in blood was normal. The diagnosis of pediatric lupus was established according to the Systemic Lupus International Collaborating Clinics classification criteria for systemic lupus erythematosus with two clinical criteria (proteinuria and hemolytic anemia) and four immunological criteria (positive ANA, anti-DNA; anticardiolipin with medium to high title and low C3 level). She received valproic acid at the dose of 20 mg/kg/day, and remained free of seizures. HTA was controlled with fluid and salt restriction. Hydroxychloroquine was initiated at the dose of 5 mg/kg/day in association with oral corticosteroids at the dose of 1 mg/kg/day during one month then progressively tapered by 5 mg/week, with good outcome. Brain MRI performed 2 months after the initial episode showed a quasi total regression of lesions.

3.2. Review of cases

In addition to the above reported illustrative case, we identified 8 previously published cases of SE (Table 1) and 25 of PRES (Table 2) in children with SLE. A detailed summary of these published cases in the literature is also provides as Supplementary Material (see Supplementary Material 1 and 2).

3.2.1. Status epilepticus in pediatric lupus

Among the 9 identified children in this group including our patient (sex-ratio: 0.5; age at onset: 7–17 years),