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Development of epilepsy after posterior reversible encephalopathy syndrome

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ABSTRACT

Purpose: This study was intended to describe the risk of epilepsy subsequent to posterior reversible encephalopathy syndrome (PRES) and the clinical features of post-PRES epilepsy.
Method: We retrospectively identified all patients with PRES who were admitted to Severance Hospital and consulted with the Department of Neurology between 2001 and 2013 and the subgroup of these patients who subsequently developed epilepsy. We also describe clinical features of patients who were not treated with PRES as inpatients at our center but who presented later with post-PRES epilepsy during the study period. We studied clinical characteristics during the acute symptomatic phase of PRES and after the development of epilepsy.
Results: During the study period 102 patients were treated at our center during the acute phase of PRES. Four of these patients (3.9%) subsequently developed epilepsy. Two additional patients with a history of PRES presented to our hospital after the acute phase of their illness with post-PRES epilepsy. During the acute phase, five of six patients had acute symptomatic seizures and four had convulsive or nonconvulsive status epilepticus (SE). Acute phase MRI showed cytotoxic edema in five patients, and follow-up MRI showed focal atrophic changes including hippocampal sclerosis in four. Presumptive epileptogenic foci were located in the left-side temporal, parietal and occipital lobes, corresponding to the regions that showed cytotoxic edema or severe vasogenic edema as well as with the location or lateralization of EEG abnormalities during the acute phase.
Conclusion: Our findings indicate a small but not insignificant risk for the development of epilepsy after PRES. The presence of cytotoxic edema and severe, acute symptomatic seizures, such as SE suggests irreversible brain damage and may predict the development of epilepsy.

1. Introduction

Posterior reversible encephalopathy syndrome (PRES) presents with various neurological signs and symptoms, including seizures, and is characterized by a pattern of abnormalities in brain imaging studies. The prognosis in patients with PRES is favorable as most cases completely resolve without any sequelae [1] if the underlying conditions responsible for PRES are treated promptly. Recently, two studies showed that the development of epilepsy is uncommon in patients who recover from PRES [2,3]. However, cytotoxic edema (bright signals on diffusion weighted imaging, dark signals on apparent diffusion coefficient map images), hemorrhage, contrast enhancement on MRI during the acute symptomatic phase, and residual lesions on follow-up MRI are not infrequently found in PRES [4–8]. As well, pathologic evidence of partial irreversible damage has been documented in PRES in spite of radiographic resolution of abnormalities [9], suggesting the potential for irreversible brain damage. Although seizures occurring during the acute symptomatic phase, are generally well controlled by short-term antiepileptic drug (AED) treatment [10], severe seizures such as status epilepticus (SE), and delayed or non-aggressive treatment of seizures may produce irreversible injury. Herein, we attempted to investigate the risk of epilepsy subsequent to PRES, describe the clinical characteristics of patients who

Abbreviations: PRES, posterior reversible encephalopathy syndrome; AED, antiepileptic drug; SE, status epilepticus; HS, hippocampal sclerosis; GTCS, generalized tonic-clonic seizure; PLED, periodic lateralized epileptiform discharge; FLAIR, fluid-attenuated inversion recovery; DW, diffusion-weighted; HE, hypertensive encephalopathy; TLE, temporal lobe epilepsy.

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developed epilepsy after PRES, and discuss associated risk factors for this condition.

2. Methods

In order to estimate the incidence of epilepsy development stemming from PRES, we retrospectively identified all patients with PRES who were admitted to Severance Hospital and consulted with the Department of Neurology between January 2001 and December 2013 from data maintained by our department. Diagnosis of PRES was based on clinical features (predisposing conditions, headache, seizures, alterations in consciousness, and visual abnormalities); multifocal lesions on MRI, mainly suggesting vasogenic edema; clinical recovery; and when available, reversibility of MRI lesions. We identified six patients with epilepsy following PRES, who visited the epilepsy clinic of Severance Hospital between January 2001 and December 2014. Additionally, we searched the medical records of patients with PRES who were admitted to our hospital, and investigated evidence of seizure or epilepsy occurrence. Clinical information was collected for these six patients including demographics, co-morbid illnesses, medication histories, neurological manifestations, brain MRI, and EEG during the acute symptomatic phase of PRES. Clinical information on seizure semiology, EEG, brain MRI and prognosis after the development of epilepsy was investigated in detail. This study was approved by the Institutional Review Board of Severance Hospital.

3. Results

3.1. Overall incidence of epilepsy in patients with PRES

We identified 102 patients who were treated at our hospital during the acute phase of PRES. Four of these patients (3.9%) developed epilepsy subsequent to PRES. We did not find evidence of seizure or epilepsy occurrence in any other patients among the medical records of our hospital. Two additional patients (Patients 2 and 3) suffering from PRES who were admitted to other hospitals, developed intractable epilepsy and a single seizure, respectively, and visited the epilepsy clinic of our hospital.

3.2. Clinical features of patients in the acute phase of PRES

The clinical data for the patient cohort are described in Table 1. All patients except for Patient 3 had acute symptomatic seizures. Four patients (Patients 1, 2, 5 and 6) had convulsive or nonconvulsive SE. Patient 1 had recurrent episodes of deviation of the head and eyes to the right and hand automatisms without responsiveness for one day. Patient 2 showed a continuous state of the head and eyes to the right or motionless staring without responsiveness for 4 h. In Patient 5, recurrent episodes of deviation of the head and eyes to the right and clonic movements of bilateral shoulders (more prominent in the right side) with intermittent generalization were found in a state of persistent deterioration of consciousness for 2 days.

Acute phase MRI revealed cytotoxic edema in five patients (except for Patient 2). The MRI of Patient 2 showed all lobar involvement predominantly in the left hemisphere on MRI without cytotoxic edema during the acute phase although the brain MRI scans were not available due to the disposal of the old data. Patient 6 developed four generalized tonic-clonic seizures for 1 h in the initial period of PRES, followed by recurrent episodes of eye and head deviation to the right side, intermittently evolving to convulsive movements of the right face and arm in the state of persistent deterioration of consciousness for a prolonged time. He received delayed and non-aggressive AED treatment. Frequent

Table 1
Clinical features during the acute phase of PRES.

Patient number	1	2	3	4	5	6
Sex/Age (years) Medical history	F/47 Aplastic anemia, massive transfusion	F/18 Acute lymphoblastic leukemia, sepsis, granulocyte-colony stimulating factor, hypertension	F/12 IgA nephropathy, methylprednisolone (pulse), cyclophosphami-de, hypertension	F/12 Femur osteosarcoma, cisplatin, ifosphamide, adriamycin, acute renal failure, hypertension	M/64 Liver transplantation, sepsis, tacrolimus	M/42 Liver transplantation, tacrolimus
Acute symptomatic seizures	Nonconvulsive SE	Nonconvulsive SE	No seizure (headache and drowsy mental state)	Two GTCSs	Convulsive SE	Convulsive SE
MRI (Fig. 1)	Cytotoxic edema	Left parieto-occipito-temporal regions	Absent	Left hippocampus	Bilateral mesial frontal and left temporo-parietal regions	Left temporo-occipital regions
	Vasogenic edema	Right parieto-occipito-temporal regions	Multifocal involvement in bilateral cerebral hemispheres with left-sided dominance	Right parieto-occipital regions	Multifocal involvement in bilateral cerebral hemispheres	Right temporal and frontal regions	Right temporo-occipital and bilateral frontal regions, and pons
EEG		Repetitive ictal discharges and PLEDs in the left posterior region	NA	Posteriorly dominant diffuse slowing, more prominent in the left side	Diffuse background rhythm slowing with slower frequency and higher amplitude in the left side and intermittent PLEDs-like activity in the left posterior region	Recurrent ictal discharges in the left posterior quadrant region	PLEDs in the left posterior quadrant region, and continuous waxing and waning pattern of 1–1.5 Hz repetitive and periodic pattern of delta activities in the left hemisphere

Abbreviations: PRES, posterior reversible encephalopathy syndrome; F, female; M, male; SE, status epilepticus; GTCS, generalized tonic-clonic seizure; NA, not available; PLED, periodic lateralized epileptiform discharge.