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Electrographic patterns in patients with posterior reversible encephalopathy syndrome and seizures

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ABSTRACT

Introduction: Posterior reversible encephalopathy syndrome (PRES) is a neurotoxic encephalopathic state associated with reversible cerebral vasogenic edema. Seizures are a common clinical presentation in PRES, however its electroencephalographic and radiologic pattern correlation is limited in this subset of patients. The aim of this study is to analyze the origin of electrographic dysfunction according to the radiologic pattern in patients with PRES and seizures.

Methods: We retrospectively identified 46 cancer patients who developed PRES and seizures at The University of Texas MD Anderson Cancer Center between January 2006 and June 2012. Clinical, radiographic and electroencephalographic data were abstracted from their records and reviewed for our analysis.

Results: The average age at presentation was 49.9 ± 19.7 years. Thirty-four (73.9%) patients were women. Twenty-two (47.8%) patients had a primary hematological malignancy whereas the rest had a solid tumor. Thirty-three (71.7%) patients had received some form of chemotherapy. The mean systolic blood pressure (SBP) variation was 23.7 ± 16.4 mmHg at onset of symptoms. On brain MRI, 32 (69.6%) patients had typical pattern while 14 (30.4%) had an atypical pattern. Thirty-seven (80.4%) patients had scalp electroencephalogram (EEG) evaluation. Thirty-three (89.2%) had abnormal EEG findings: diffuse theta/delta slowing ($N = 12$, 36.4%), followed by diffuse slowing with focal dysfunction ($N = 8$, 24.2%), focal dysfunction with epileptiform discharges ($N = 4$, 12.1%), non-convulsive status epilepticus ($N = 4$, 12.1%), focal seizure activity and burst suppression ($N = 2$, 6.1% each). Lateralized Periodic Discharges (LPDs) were recorded in 1 case. Four patients had focal dysfunction localized to areas without conventional MRI signal changes. Four patients had recurrent seizures, of which 3 had an atypical PRES pattern.

Conclusion: PRES appears to be a diffuse neurotoxic encephalopathic state. Origin of seizures seen on scalp EEG may not correlate with the location of vasogenic edema/MRI signal changes raising the possibility of greater degree of dysfunction which may exist beyond those areas.

1. Introduction

Posterior reversible encephalopathy syndrome (PRES) is a neurotoxic encephalopathic state associated with reversible cerebral vasogenic edema that was first described in 1996 [1]. The clinical presentation ranges from headache to confusion or frank encephalopathy. Additionally, patients commonly have visual disturbances, and seizures [2]. Brain imaging usually demonstrates vasogenic edema preferentially in the bilateral parietal-occipital lobes, which might be related to the lower concentrations of sympathetic innervation of the posterior intracranial arteries in comparison with other cerebral regions resulting in lower autoregulatory capacity in these vessels [3,4]. There is still controversy of the pathophysiologic trigger; however the mechanism that produces vasogenic edema seems to be associated with loss of integrity of the blood-brain barrier. Recognized risk factors that are commonly found at the onset of the PRES syndrome include hypertension, preeclampsia/eclampsia, autoimmune disease, renal disease, infections and multiple drugs especially immunosuppressive agents. Moderate-to-severe hypertension is seen in approximately 75% of patients with PRES [5].

Seizures are commonly encountered in these patients and are generally responsible for severe morbidity and mortality. Although there are several single case reports or small case series documenting the association between PRES and seizures, there is still limited data eluding towards the exact pathophysiology of seizures, seizure semiology, electroencephalographic patterns and its correlation with radiologic findings. Furthermore, there has not been any study focused on the correlation between PRES and seizures in the oncologic population, although this population has a high incidence of PRES. The aim of this study is to analyze electrographic findings on routine scalp EEG in patients with PRES and seizures.

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2. Methods

We reviewed the records of all cancer patients who developed PRES manifested with seizures at The University of Texas MD Anderson Cancer Center between January 2006 and June 2012. The study was approved by the Institutional Review Board, and consent for retrospective review of patient charts was waived.

The diagnosis of PRES in all patients was confirmed by brain MRI using standard MRI sequences, which included axial T2 and FLAIR sequences; T1 axial pre and post-contrast; T1 post contrast in the coronal and sagittal planes; T2-Gradient-echo axial, DWI, and ADC map. The radiologic patterns were classified into typical and atypical according to the lesion distribution after Bartynski and Boardman 2007 [6]. The typical pattern includes the involvement of occipital, parietal, frontal and temporal lobes as well as the cerebellum. The atypical cases include the distinct involvement of basal ganglia, thalamus, corpus callosum and the periventricular white matter in addition to partial expression of the typical pattern including the lack of involvement in the parietal or occipital lobes. We collected and analyzed clinical, radiographic and electroencephalographic data from the institutional database. The diagnosis of seizures was established by a neuro-oncologist. Electroencephalograms (EEG) were recorded digitally using standard 10–20 system. EEGs (20-min routine or extended) were interpreted by one reviewer (ST). Resolution of PRES was defined as radiologic resolution of vasogenic edema. Death was confirmed by review of medical records, death certificate, and/or the Social Security Index.

3. Results

We identified 46 patients with diagnosis of PRES and seizures. All patients had diagnosis of cancer, with the average age at presentation of 49.9 ± 19.7 years. Thirty-four (73.9%) patients were women. Twenty-two (47.8%) patients had a primary hematological malignancy whereas the rest had a solid tumor. Thirty-three (71.7%) patients had received some form of chemotherapy (the most common used at the onset of PRES were cyclophosphamide ($N = 6$), vincristine ($N = 5$) and doxorubicin ($N = 4$)). Cyclophosphamide was the most frequently received in patients with atypical pattern ($N = 5$) otherwise chemotherapy agents were equally distributed in both groups. Elevated blood pressure (systolic blood pressure or diastolic blood pressure more than 140 mmHg or 90 mmHg, respectively) was observed in all the patients. The mean systolic blood pressure (SBP) variation before and at onset of symptoms was 23.7 ± 16.4 mmHg. On brain MRI, 32 (69.6%) patients had typical pattern (Fig. 2C and E) while 14 (30.4%) had an atypical pattern (Fig. 1C and 2A). There were no specific cerebrospinal fluid changes in these patients.

All patients had at least seizure episode either witnessed or detected on EEG. Twenty-nine (63%) patients had seizures and altered mental status (AMS). Thirty-seven (80.4%) patients had an EEG evaluation. Thirty-three (89.2%) of those had abnormal EEG findings. Seizures focus and seizures were identified on regular 20-min routine EEG ($N = 7$) and extended EEG ($N = 3$). As expected, seizures were mostly (50%) of occipital origin (Fig. 1B and 2B). Generalized seizures were

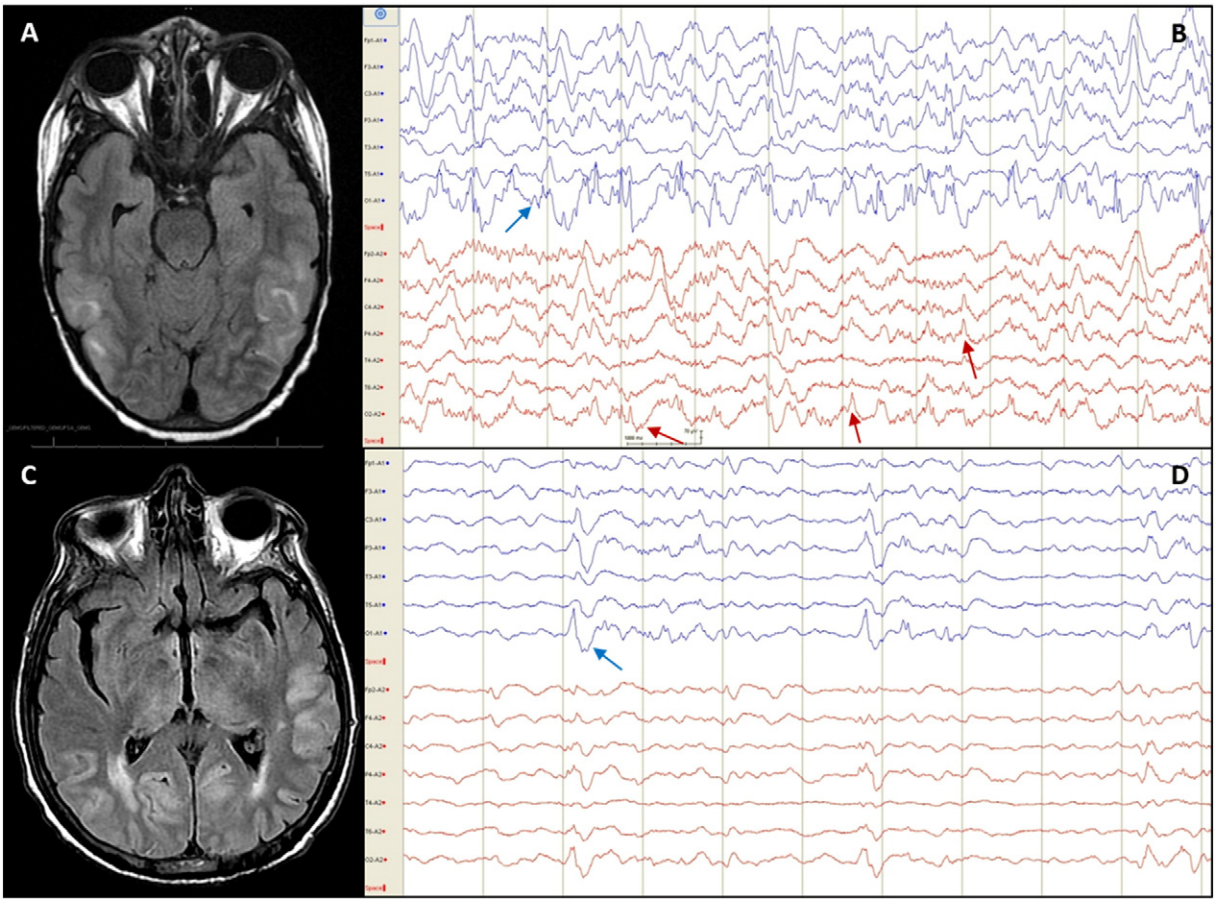

Fig. 1. Radiologic and electrographic features of typical PRES. (A) MRI-Brain shows symmetric bilateral posterior parietal and occipital area signal changes compatible with typical PRES. (B) Referential montage EEG shows focal epileptogenicity (left occipito-parietal repetitive spikes -*blue arrows*-, and independent lower amplitude right occipito-parietal region -*red arrows*-) that corresponds with areas of edema. (C) MRI-Brain in shows also symmetric signal abnormality involving predominantly posterior brain and thalamus. (D) Longitudinal bipolar EEG shows bihemispheric cortical dysfunction. Lateralized Periodic Discharges (LPDs) are occipital predominant with higher amplitude on the left -*blue arrows*- (D).