Periodic epileptiform discharges in hypoxic encephalopathy: BiPLEDs and GPEDs as a poor prognosis for survival


Neurophysiology Department, Massachusetts General Hospital, MA, USA

1. Introduction

Hypoxic–ischemic injury to the brain is a major cause of morbidity and mortality in infants and adults. Hypoxic encephalopathy (HE), after cardiac arrest and traumatic brain injury represent the most common etiologies.1 In current practice, prognostic decisions rest principally on clinical observations, neuroimaging studies, neurochemical tests and neurophysiologic evaluation. Clinical assessment of the unresponsive patient is limited to examination of brainstem reflexes and simple motor responses to stimulation. Neurochemical tests have not been validated and have significant limitations. However, electrophysiologic investigations provide a window into cerebral function and are clinically safe, available, and inexpensive.2 Electrophysiologic tests in HE consist of EEG and evoked/event-related potential studies. In most studies the generalized periodic epileptiform complexes have been reported combined with other EEG patterns and were indicators of a poor outcome in different etiologies of hypoxic encephalopathy (HE), but these have rarely been examined independently.

Methodology: We analyzed from 2000 to 2007 the outcome of patients with HE and generalized periodic epileptiform complexes. We abstracted and tabulated clinical information, imaging findings, and outcome from the medical records.

Results: We found 52 patients in our database. Fourteen patients (eight BiPLEDs and six GPEDs) were associated with HE. Patients with BiPLEDs were 68 ± 19.4 years old, 5 female (62%) and 3 (38%) men. GPEDs patients were 52.5 ± 19.1 years old, 2 women (20%) and 4 (80%) men. Myocardial infarction and ventricular tachycardia were responsible of 57% of the HE cases. Neuroimaging studies in both groups showed cortical structural lesions in 84%. All patients were comatose and died. Two GPEDs patients developed status epilepticus.

Conclusion: GPEDs and BiPLEDs after an anoxic insult carried a poor prognosis for survival. Aggressive treatment of patients may not be warranted when these EEG patterns are seen after anoxic brain injury.

© 2009 British Epilepsy Association. Published by Elsevier Ltd. All rights reserved.
cardiopulmonary resuscitation. We abstracted and tabulated clinical information (etiology, age, gender, physical findings, clinical seizures at onset, AED therapy), imaging findings (cortical and subcortical injuries or both), and outcome from the medical records. Acute seizures occurred at onset or within 24 h after hypoxic event. All patients had digital EEG recordings with 24 scalp electrodes positioned according to the standard 10–20 system of electrode placement, reformatted to both bipolar and off-head referential montages. The filter setting was 0.3 s (0.53 Hz) and 70 Hz. GPEDs were defined as the occurrence of periodic complexes occupying at least 50% of a standard 20 min EEG, over both hemispheres in a symmetric, diffuse and synchronized manner. BiPLEDs were defined as bilateral independent periodic lateralized epileptiform discharges. All EEGs were recording without sedative drugs and within 24–48 h after cardiopulmonary resuscitation. All patients, but one underwent imaging studies including CT and MRI scans; when both studies were available we considered only the MRI findings. Relevant cortical imaging abnormalities (on CT and MRI) included increased signal intensity within the cortical ribbon, border-zone infarctions, and laminar necrosis. Notable subcortical imaging findings included increased signal intensity in the deep gray matter nuclei and white matter abnormalities.

3. Results

We found 52 patients in our EEG database including 33 with BiPLEDs and 19 with GPEDs with different etiologies. Fourteen patients (eight BiPLEDs and six GPEDs) were associated with HE. Organized electrographic seizure activity was not seen in any of these EEG recordings. Nine (64%) patients had at least one EEG in their follow up after their diagnostic EEG. The age and gender distribution of patients with BiPLEDs associated with HE were from 23 to 85 (68 ± 19.4) years old, 5 female (62%) and 3 (38%) men, respectively. The age and gender distribution of patients with GPEDs associated with HE were from 26 to 76 (52.5 ± 19.1) years old, 2 women (20%) and 4 (80%) men, respectively (Fig. 1) (Table 1).

Myocardial infarction and ventricular tachycardia were responsible of 57% of the HE patients. Neuroimaging studies were abnormal in 11/13 (85%), normal 2/13 (15%) and 1 was not performed in the patients. Both normal studies were CT head scans. All studies showed cortical injury and only 3/13 (23%) cases showed a mixed subcortical injury as well (Fig. 2). In reference to the clinical findings all the patients were in a coma and only two (14%) patients also showed motor focal neurological findings. Acute seizures were seen in four (28%) cases with the same frequency distribution between BiPLEDs and GPEDs patients. The tonic clonic generalized seizure type was the only kind reported in both groups. Only one patient had a history of epilepsy.

After electrophysiological diagnosis, two GPEDs patients developed status epilepticus. All patients received multidisciplinary management including ventilatory support with propofol or phenobarbital and treatment with multiples antiepileptic drugs (Table 1). All patients died within 4 week of the original incident.

4. Discussion

Electroencephalography provides data that influences clinical decision-making in the setting of epilepsy related situations, hypoxic encephalopathy and brain death examination. Previous studies have showed that different EEG patterns which are related to HE include suppression, burst-suppression, alpha and theta pattern coma, and generalized periodic complexes in combination with burst-suppression. These EEG patterns had a poor correlation with the outcome, but they have rarely been examined separately, specifically GPEDs. Our study is the first report that specifically makes a correlation between generalized periodic complexes and the outcome including a higher number of patients with HE.

BiPLEDs are usually caused by anoxic encephalopathy or central nervous system infections (thus the high incidence of coma), and are typically associated with a poorer prognosis than PLEDs. A recent study that included 21 patients with BiPLEDs with a variety of etiologies found a poor prognosis for survival.
of etiologies showed a mortality of 52%, twice of that of PLEDs patients. However, they only included two BiPLEDs patients with HE. De la Paz and Brenner,9 included 5 patients with BiPLEDs and HE in their clinical report of 18 patients with BiPLEDs, and all patients died. A similar mortality rate was seen in our patients, independently of the etiology or management.

GPDs are very rare patterns and may be classified as periodic short-interval diffuse discharges (PSIDDs), periodic long-interval diffuse discharges (PLIDDs) and suppression burst patterns according to the interval between the discharges. They occur in hypoxic or hepatic encephalopathy, drug toxicity and degenerative disorders such as Creutzfeld–Jakob disease. PSIDDs due to anoxia were reported to be associated with a fatal outcome or severe neurological sequelae especially if associated with repetitive myoclonic jerks. Yemisci et al.15 reported 37 GPDs patients with different etiologies, of these, 7 (18%) GPDs patients were associated with HE. However, the authors did not describe the clinical findings of this specific population and neuroimaging studies were performed only in three patients with cortical and subcortical lesions. The EEGs features were classified as three

Table 1 Clinical findings, neuroimaging studies and outcome of the 14 patients with BiPLEDs and GPDs and HE.

<table>
<thead>
<tr>
<th>Pt</th>
<th>Age (year)</th>
<th>Sex</th>
<th>Type of PED</th>
<th>Diagnosis</th>
<th>MR/CT (abnormal)</th>
<th>Localization: Cortical</th>
<th>Mental status: Coma</th>
<th>Clinical seizures at onset</th>
<th>SE</th>
<th>AED therapy</th>
<th>Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>23</td>
<td>M</td>
<td>BiPLED</td>
<td>Laceration myocardial</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td>PRO, PHT</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>67</td>
<td>F</td>
<td>BiPLED</td>
<td>Heroine overdose</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td>PRO</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>72</td>
<td>F</td>
<td>BiPLED</td>
<td>Myocardial infarction</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td>PRO, PHT</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>74</td>
<td>F</td>
<td>BiPLED</td>
<td>Myocardial infarction</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td>PRO, PHT, DZP</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>83</td>
<td>F</td>
<td>BiPLED</td>
<td>Cardiogenic shock</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td>PRO, CNZ, PHT</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>85</td>
<td>M</td>
<td>BiPLED</td>
<td>Ventricular tachycardia</td>
<td>Nl</td>
<td></td>
<td></td>
<td></td>
<td>PRO, PHT, VPA, CNZ</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>71</td>
<td>M</td>
<td>BiPLED</td>
<td>Myocardial infarction</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td>PRO, GBP</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>75</td>
<td>F</td>
<td>BiPLED</td>
<td>Laceration myocardial</td>
<td>?</td>
<td></td>
<td></td>
<td></td>
<td>PB, PHT</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>26</td>
<td>M</td>
<td>GPED</td>
<td>Carbon monoxide poisoning</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td>PRO, CNZ</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>51</td>
<td>M</td>
<td>GPED</td>
<td>Myocardial infarction</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td>PRO</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>76</td>
<td>F</td>
<td>GPED</td>
<td>Bithalamic stroke</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td>PRO</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>71</td>
<td>M</td>
<td>GPED</td>
<td>Respiratory failure</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td>PRO</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>37</td>
<td>M</td>
<td>GPED</td>
<td>Ventricular tachycardia</td>
<td>Nl</td>
<td></td>
<td></td>
<td></td>
<td>PRO</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>54</td>
<td>F</td>
<td>GPED</td>
<td>Ventricular tachycardia</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td>PRO</td>
<td>+</td>
<td></td>
</tr>
</tbody>
</table>

(a) Not performed; SE, status epilepticus; PRO, propofol; PHT, phenytoin; DZP, diazepam; CNZ, clonazepam; LEV, levetiracetam; VPA, valproate; PB, phenobarbital; GBP, gabapentin.

Fig. 2. Patient 9; 71 years old M. MRI FLAIR sequence shows multifocal areas of hyperintensity involving cerebral cortex.
However, the pathophysiological mechanism responsible for periodicity in the EEG is unknown. As in prior studies, GPEDs and BiPLEDs after an anoxic insult carried a poor prognosis for survival. Thus aggressive treatment of patients may not be warranted when these EEG patterns are seen after anoxic brain injury.

5. Conclusion

GPEDs and BiPLEDs after anoxic insult carried a poor prognosis for survival.

Conflict of interest

The authors report no disclosures or any conflict of interests.

Acknowledgements

The study was funded by grant from the Foundation Mexico (FMH) in Harvard. San-juan OD is supported by FMH Fellowship.

References