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Case Report

Posttraumatic epilepsy: A single institution case series in Indonesia

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ABSTRACT

Background: Posttraumatic epilepsy (PTE) is a debilitating sequelae following traumatic brain injury (TBI). Risk of developing PTE is higher in the first 6 months following head trauma and remains increased for 10 years. Many cases of PTE developed into drug-resistant epilepsy in which need surgical treatment.

Case Description: Fourteen patients were identified from 1998 until 2021. Mean age at onset was 21.00 ± 6.13 years, mean age of surgery was 29.50 ± 6.83 years. All patients had partial complex seizure with more than half of cases (n = 10, 71.4%) reported with focal impaired awareness seizure and focal to bilateral tonic–clonic type of seizure which were observed in the remained cases (n = 4, 28.6%). Abnormal magnetic resonance imaging findings were observed in 12 patients: mesial temporal sclerosis (n = 7), encephalomalacia (n = 4), brain atrophy (n = 4), and focal cortical dysplasia (n = 2). More than half of cases presented with mesial temporal lobe epilepsy despite site and type of brain injury. Most patients who undergone epileptogenic focus resection were free of seizure, but two patients remained to have seizure with worthwhile improvement.

Conclusion: This study emphasizes the clinical characteristic of PTE cases in our center in Indonesia. While encephalomalacia is a typical finding following TBI and often responsible for epilepsy, electroencephalogram recording remains critical in determining epileptic focus. Most of PTE patients presented with temporal lobe epilepsy had excellent outcomes after surgical resection of epileptogenic focus.

Keywords: Epilepsy, Posttraumatic epilepsy, Seizure, Temporal lobe epilepsy, Traumatic brain injury

INTRODUCTION

Approximately 69 million people worldwide each year are affected by traumatic brain injury (TBI). The highest incidences have been reported from the United States and Europe with 1299 cases/100,000 people and 1012 cases/100,000 people, respectively.[3] TBI defined as injury to the brain resulted from external mechanical force, such as a blow to the head, concussion, acceleration-deceleration forces, blast injury, or a penetrating head injury. Survivor of TBI still carries a burden as a result of their injury such as seizures and epilepsy.[9]

Posttraumatic epilepsy (PTE) is disabling sequelae of TBI that accounts for 20% of all acquired epilepsy and is frequently drug resistant. The risk to developing PTE is higher in patients who have suffered severe brain injury with structural damage.[15] Individuals with PTE face significant disadvantages in terms of physical, cognitive, and affective difficulties, all of which impair functional outcome following TBI.[9]

Reports of PTE are scarce in low- and middle-income countries, including Indonesia. Herein, we present a case series of medically intractable PTE patients who were eligible for surgical treatment from 1998 to 2021.

METHODS

This is a retrospective and Institutional Review Board approved study. We use our admission database to identified posttraumatic epilepsy patients from 1998 to 2021. Patients who admitted for epileptic surgery with documented history of TBI (skull fracture; intracerebral or intracranial hemorrhage; or traumatic encephalomalacia on neuroimaging obtained nonacutely during their epilepsy) were selected in this study. Records were reviewed for demographic information, magnetic resonance imaging (MRI) findings, ictal electroencephalogram (EEG) recording, and type of surgery. Engel class classification was used to assess patient outcomes at least 1 year following epileptic focus surgical procedure. Informed consent was obtained from the patients.

ILLUSTRATIVE CASE

Case 1

A 24-year-old male who suffered from drug-resistant epilepsy was admitted to our hospital. His medical history was consistent with bilateral frontal contusion resulted from vehicle collision. Three years after the accident, a focal impaired awareness seizure was observed. The seizure begins with sudden uncomfortable sensation in the head, followed by uncontrolled movement of the eyes to the right, dystonia of the right arm, and loss of consciousness. He had received two antiepileptic drugs: carbamazepine and lamotrigine but free seizure state was not accomplished. MRI revealed bilateral frontal encephalomalacia and left mesial temporal sclerosis (MTS) (Figure 1). Ictal left temporal epileptic discharges were observed on EEG recording. The patient was considered as eligible for surgical intervention and underwent left selective amygdalohippocampectomy. Seizure-free status was achieved at 1-year follow-up.

CASE DESCRIPTION

Fourteen posttraumatic epilepsy patients were enrolled in this study. Eleven (78.6%) patients were male, mean age of surgery was 29.50 ± 6.83 years, mean age at epilepsy onset 21.00 ± 6.13 years, and mean latency from head injury to epilepsy onset 2.83 ± 2.12 years [Table 1]. All patients were reported with focal onset seizure, with 10 cases (71.4%) had focal impaired awareness type of seizure, whereas focal to bilateral tonic–clonic type of seizure was observed in 4 remained cases (28.6%). Auras were reported in 8 patients (57.2%): experiential (n = 2), a feeling of nausea or gastrointestinal uprising (n = 2), general somatosensory

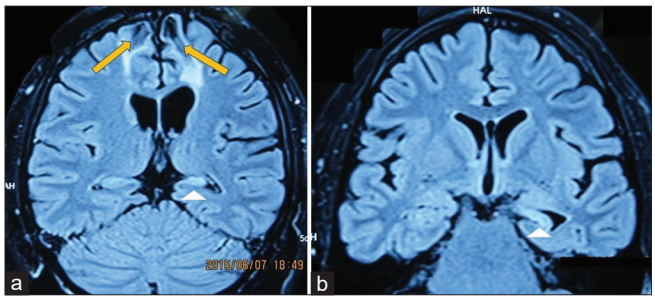

Figure 1: Case 1: (a) and (b) coronal fluid attenuated inversion recovery (FLAIR) revealed bilateral frontal encephalomalacia (yellow arrow) and left mesial temporal sclerosis (white arrowhead).

Table 1: Patient demographic.

	Patients n (n=14)	Percentage %
Sex		
Female	3	21.4%
Male	11	78.6%
Mean Age of HI Occurrence (years)	18.83 ± 7.05	
Mean Age of Surgery (years)	29.50 ± 6.83	
Mean Age of Epilepsy Onset (years)	21.00 ± 6.13	
Mean Latency of HI to Epilepsy (years)	2.83 ± 2.12	
Mean Duration from Epilepsy Onset to Surgery (years)	8.64 ± 5.41	
MRI		
Atrophy	4	35.7%
Cortical Dysplasia	2	14.3%
Encephalomalacia	4	35.7%
MTS	7	50%
Normal	2	14.3%
Type of Attack		
FIAS	10	71.4%
FBTCS	4	28.6%
Aura		
Absent	6	42.9%
Experiential	2	14.3%
GI	2	14.3%
General Somatosensory	2	14.3%
Palpitation	2	14.3%
Seizure Frequencies		
< 3x/month	6	42.9 %
≥ 3x/month	8	57.1 %
Surgery Type		
ATL	12	85.7%
SAH	2	14.3%
Outcome		
Free Seizure	12	85.7%
Seizure	2	14.3%

MTS: Mesial temporal sclerosis, ATL: Anterior temporal lobectomy, SAH: Selective amygdalohippocampectomy, FIAS: Focal with impaired awareness seizure, FBTCS: Focal to bilateral tonic–clonic seizure

(*n* = 2), and palpitation (*n* = 2). Eight patients reported with more than 3 seizures frequencies in a month (57.1%). Abnormal MRI findings during epileptic surgery admission were identified in the majority of patients (*n* = 12, 85.7%). Pathological findings recognized were MTS (seven patients); encephalomalacia (four patients); focal cortical dysplasia (two patients), and brain atrophy (four patients). Epileptic focus was identified using ictal EEG examination and more than half of cases presented with temporal lobe seizure (*n* =9, 64.3%). Most patients who undergone epileptic focus resection had favorable Engel Class I outcome (85.7%).

We present four cases of encephalomalacia following TBI who presented with temporal lobe epilepsy in Table 2. Four patients demonstrated MTS regardless of encephalomalacia location. Epileptiform discharges were consistent with temporal lobe epilepsy and considered eligible for resection. One of which was observed with Engel Class III outcome.

DISCUSSION

PTE accounts for 20% of acquired epilepsy, with severe brain injuries increasing the incidence to 16% over a 30-year period.[1] The risk of developing PTE is increased up to 30% in those with nonpenetrating head injuries such as focal contusions and intracranial hematoma.[4] In the case of intracranial bleeding, the toxic effects of hemoglobin breakdown products on neuronal cells may contribute in the epileptogenic mechanism.[14]

Seizure after TBI is classified into immediate (occurring within 24 h), early (within the first 7 days), and late (occurring after 7 days).[4] According to the International League Against Epilepsy, an isolated late unprovoked seizure associated with a known TBI now fulfills the criteria for epilepsy.[11] Initial seizure following TBI is often the generalized tonic–clonic type, whereas late seizures are more likely to have focal onset.[5]

A study by Xu *et al*. identifies PTE-related risk factors: sex, history of alcohol abuse, focal neurological sign, posttraumatic amnesia, and loss of consciousness following TBI. Abnormal imaging findings in TBI such as skull fracture, midline shifting, contusions, intracranial hemorrhage, and subdural hemorrhage also pose a higher risk for the occurrence of PTE.[15]

Encephalomalacia is a common lesion resulting from TBI and often responsible for epilepsy. Recent study by Wang *et al*. revealed that FLAIR hyperintense part surrounding encephalomalacia contains more dendrites. Higher neural density was thought to be correlated with the production of repetitive excitatory circuit which leads to epilepsy. Larger encephalomalacia and larger hyperintense lesion were also common findings in epilepsy group.[13] However, not all encephalomalacia and FLAIR hyperintense area were consistent with epilepsy. Therefore, adequate localization of epilepsy is crucial.

Following a TBI, the brain initiates acute neuronal and glial responses that often result in considerable cell loss in lesional and perilesional areas and long-term changes in the architecture of neural networks, most notably in the hippocampus and neocortex. Within minutes to hours following injury, shearing of white matter tracts, contusions, hematomas, and edema result in neurotransmitter release, free radical generation, calcium-mediated damage, angiogenesis, mitochondrial dysfunction, and inflammatory responses, all of which have been linked to epileptogenesis.[9] Neuronal cell death, most notably of c-aminobutyric acidergic (GABAergic) interneurons, reactive synaptogenesis, and axonal sprouting,

Table 2: Clinical characteristics.

S. No.	Sex	Age (years)			Site of injury	Type of injury	EEG findings	MRI findings	Type of attack	Aura	Surgery	Engel class
		TBI	Onset	Adm								
1.	M	16	19	24	Bilateral frontal	Contusion	Lt. temporal	Bilateral frontal encephalomalacia and Lt. MTS	FIAS	GS	SAH	I
2.	M	18	23	33	Rt. frontal	Contusion	Rt. temporal	Rt. temporal encephalomalacia, Rt. hippocampal atrophy, Rt. frontal traumatic contusion.	FIAS	None	ATL	I
3.	M	24	26	32	Rt. frontal	Contusion	Rt. temporal	Rt. frontal cortical dysplasia, bilateral MTS	FIAS	None	ATL	III
4.	M	22	25	34	Rt. frontal	Contusion	Rt. temporal	Rt. frontotemporal encephalomalacia. Rt. hippocampal atrophy	FBTCS	GS	ATL	I

Adm: Admission, ATL: Anterior temporal lobectomy, SAH: Selective amygdalohippocampectomy, FIAS: Focal with impaired awareness seizure, FBTCS: Focal to bilateral tonic–clonic seizure, GS: General somatosensory, Exp: Experiential, MTS: Mesial temporal sclerosis

most notably from glutamatergic neurons, and molecular reorganization of glutamate and GABA receptor subunits are frequently observed in both humans and animal epilepsy models. These characteristics are also present in models of TBI.[8] Reactive oxygen species promote the production of neurotoxic guanidino compounds that are known to be endogenous convulsant. Impact on endogenous seizure regulation includes release of excitatory amino acids such as aspartic acid, with decreased release of inhibitory amino acid such as GABA. The resulting imbalance of excitatory and inhibitory neurotransmitters is thought to increase the likelihood of spontaneous seizures by establishing an excessive number of recurrent excitatory synapses.[14]

Direct injury to cortical drivers after TBI triggers pathogenesis in hippocampus and is associated with both limbic seizures and thalamocortical like seizures that present different clinical correlates depending on the ictal sites.[8] The most common forms of human PTE are frontal and temporal lobe epilepsies, whereas parietal/occipital seizures were uncommon. Human frontal and temporal cortices may be especially susceptible to contusion due to the shape of the bony vault which may explain why posttraumatic contusion is greater in frontal than in occipital cortex, even with caudal injuries. Frontal neocortical seizures may kindle the hippocampus since about 56% of frontal neocortical seizures spread to the hippocampus.[2]

Temporal lobe epilepsy is the most commonly reported subtype in series of PTE. Histopathologic studies in PTE patients have demonstrated that diffuse temporal neocortical and hippocampal cell loss are present in most cases undergoing surgery.[12] This predilection for temporal lobe epileptogenesis is consistently observed in prior published surgical PTE series. Two studies revealed that 73% and 82.6% of PTE patients presented with temporal lobe epilepsy and most of the cases were consistent to MTS.[7] Seizure freedom rates in individuals with mesial temporal lobe epilepsy (MTLE) who have temporal lobe resection can range from 80% to 90%, suggesting that patients with posttraumatic MTLE may be especially good candidates for epilepsy surgery. Patients with extratemporal lesion can also achieve excellent outcomes with epilepsy surgery, especially those with a region of encephalomalacia on imaging can benefit from electrocorticography-guided resections.[6] Meanwhile, patients with neocortical PTE are less likely to be surgical candidates. Although unifocal localization is the most common findings, it is important to note that TBI can result in multifocal pathology. In the setting of multifocal structural abnormalities, adequate localization of epileptogenic focus is mandatory. In such cases, invasive monitoring may provide critical information regarding seizure focus localization, although this modality presents unique challenges given that significant adhesions and scarring may preclude safe and effective placement of strips and grids.[10]

This study has several limitations including small sample size and the retrospective nature. Due to its small sample size, determining the statistical significance was challenging. In addition, retrospective study is subject to bias of unmeasured factors. Our study may not accurately reflect the true number of PTE cases as we omitted drug-sensitive epilepsy in this study. Therefore, multicenter study that incorporates both drug-resistant and drug-sensitive PTE is needed to reflect the true number of PTE in Indonesia, which we believe to be quite high.

CONCLUSION

This study emphasizes the clinical characteristic of PTE cases in our center in Indonesia. While encephalomalacia is a typical finding following TBI and often responsible for epilepsy, electroencephalogram recording remains critical in determining epileptic focus. Most of PTE patients presented with temporal lobe epilepsy had excellent outcomes after surgical resection of epileptogenic focus. Clinician should be careful to determine the region of interest in the setting of multiple structural abnormalities. Therefore, comprehensive and throughout examinations are mandatory in epilepsy cases.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of interest

There are no conflicts of interest.

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