

Clinical Study of Posttraumatic Epilepsy

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Objectives: To study the manifestations of the paroxysms, the variants of the course, and to determine the significant predictive factors for post-traumatic epilepsy (PTE) in Ulaanbaatar, Mongolia. **Methods:** We obtained the histories of 109 PTE patients who came to district health associations and the Central First Clinic in Ulaanbaatar from 2011 to 2013. We conducted a questionnaire and performed clinical examination to evaluate seizures in accordance with semiologic and international classification of epileptic seizures. Clinical data was matched with the results of electroencephalography (EEG), computed tomography (CT), and magnetic resonance imaging (MRI). **Results:** Of the 109 patients, 93 (85%) presented with secondary generalized partial seizure (SGPS), 16 (15%) with partial seizure and 66 (60.5%) with motor phenomena. The seizure frequency was not correlated with the structural brain abnormalities, but there was an inverse association ($r=-0.32$, $p<0.001$) between seizure frequency and the duration of PTE. PTE was positively correlated with severe injury, contusion, early onset of seizures ($p<0.05$), and operative brain injury ($p<0.005$). **Conclusion:** Clinical features of PTE were presented as secondary generalized seizure and motor phenomena in the majority of patients. PTE was characterized commonly by long durations of high seizure frequency and significantly affected by factors such as severity of head injury and operative brain injury.

Keywords: Seizures, Epilepsy, Post-Traumatic, Partial

Introduction

Traumatic brain injury (TBI) has been recognized as a cause of epilepsy since antiquity, and it remains one of the most common and important causes of acquired epilepsy today. Post-traumatic epilepsy (PTE) may present with various clinical manifestations of seizure depending on severity, type, localization of the brain injury, loss of consciousness, and age at the time of injury [1-3]. In the USA, the overall incidence is estimated to be 1.8-2.5 per 1000 persons per year, and higher rates have been reported for Europe and South Africa [4]. PTE accounts for 30% of individuals who develop epilepsy between ages 15-34 years, 14% of

children younger than 14 years, and 8% of adults older than 65 years [4]. The risk for developing PTE is as high as 50% after a severe brain injury, 10% for children with severe brain injury, and 16-20% for similarly injured adults [3-4]. PTE is estimated to constitute 23.5% of all cases of epilepsy among the Ulaanbaatar population [5].

PTE has a number of features that make it particularly deserving of study. First, it is universally recognized as among the most common forms of acquired epilepsy: 20% of all cases of symptomatic epilepsy and patients with PTE are a regular part of the care provided by epilepsy specialists, as well as general neurologists and primary care physicians throughout the world.

Second, PTE can be particularly difficult to treat, both medically and surgically, thereby increasing the burden of the illness on patients and family members. Third, traumatic brain injury is constantly increasing with urbanization.

Therefore, we purposed to study clinical manifestations of the paroxysms, to distinguish the variants of the course, and to determine significant predictive factors for posttraumatic epilepsy. In this study we describe in detail the semiology of partial seizure paroxysms according to semiologic classification and compared it with international classification of epileptic seizures developed by the International League Against Epilepsy (1989), which is more useful in epidemiological study [6, 7]. This article is meant to provide an opportunity to distinguish types of partial epilepsy and its generalization, to control PTE, and finally to make decisions in clinical situations.

Materials and Methods

1. Study population

109 PTE patients (28 female and 81 male), aged 16-72 were involved in the study. Patients were selected by age groups of 15 to 34, 35 to 64, and over 65 years according to age classification by Annegers et al. [8]. They received health services from five district health associations in Ulaanbaatar and the Central First Clinic of Ulaanbaatar from 2011 to 2013.

2. Data collection

The severity and type of injury were defined according to the classification by Annegers et al., which uses length of post-traumatic amnesia (>24h, 0.5-24h, <0.5h) to define an injury as mild, moderate, or severe, respectively [8]. Anamnestic data and information about the principal events of the acute phase were collected from the case history taken at the district health associations and the Central First Clinic.

Inclusion criteria were: patients with a history of closed brain injury with seizure after one week of trauma; 16 to 72 years of age; negative family history of epilepsy; and no history of seizure caused by cerebrovascular disease, brain tumor, infectious diseases, inflammation and immune-mediated disorders, malformation of cortical development, toxic or metabolic disturbances. TBI victims who developed epilepsy more than 10 years following the initial injury or patients with a disability in connection with an organ system complication were excluded

from the study. The following data on these patients were taken from a pre-developed questionnaire: age, sex, cause, severity, and type of closed TBI; duration of posttraumatic amnesia; age at the time of injury; time from TBI to PTE; duration of PTE; factors precipitating seizures; complaint of patients; type of seizure; symptoms in seizure manifestation; seizure frequency; and history of operative brain injury. The patient's history and the results of EEG, CT, and MRI tests were also used.

Diagnosis of epilepsy was made in 109 patients by neurologists at the district health associations and by neurologist-researchers on the basis of clinical observation and of anamnestic data. We conducted a questionnaire, clinical examination to evaluate seizures in accordance with semiologic and international classification of epileptic seizures [6, 7].

We analyzed the seizure frequency and duration of PTE. Seizure frequency was defined as the number of seizures for a period of a year before the last recorded seizure (once a week; once in 2 weeks; once a month; once in 3 month; once in 6 month; once a year). Duration of PTE was calculated by subtracting the date of the first seizure from the date of the last seizure. Seizure types were classified as simple partial, complex partial, and secondary generalized partial (SGPS). The course of PTE was defined as favorable if remission exceeded 1 year and as unfavorable if seizure occurred twice or more in one year.

3. Statistical analyses

Data were initially analyzed using descriptive statistics. We compared groups of patients using Chi-square test for categorical data, and Student's-t-test for continuous data. Correlation analysis was performed between duration of PTE and seizure frequency. Findings were considered significant with a $p < 0.05$. Statistical analyses were performed using SPSS 17.0 program.

4. Ethical statement

Ethical approval was obtained from the Ethical Committee of the School of Medicine, Mongolian National University of Medical Sciences. Each patient signed a consent form before being involved in the study. The investigator maintained confidentiality of research data.

5. Hypothesis

First, clinical features of PTE will be presented in secondary generalized seizure and motor phenomena in majority of patients.

Second, PTE will be characterized commonly by long durations of high seizure frequency and various clinical manifestations. Third, PTE will be affected by factors such as severity of head injury and operative brain injury.

Results

Of 109 participants with PTE, 81 (74.3%) were men and 28 (25.7%) were women. The mean age of participants was 39.0±3.3 years. Of our study participants, 70 (64.2%) were from 35 to 65 years old. Males suffered from PTE 2.8 times more than females. Only 11% of participants had higher education. Among our study participants, 93 (85%) were suffering from SGPS and 16 (15%) presented with partial seizure. Of all SGPS, 26 (23.9%) had simple partial seizure, 12 (46%) had vegetative aura, 7 (27%) had sensitive, and 7 (27%) had motor symptoms. Some of the patients complained of headaches (51.1%), memory deficiency (18.8%), and neurasthenic symptoms (10.1%).

Table 1. Sensory symptom in seizure manifestation

Semiologic classification	International classification	n
Somatosensory -> SGPS	Simple partial -> SGPS	1
Visual -> SGPS	Simple partial -> SGPS	
Visual -> unusual motor -> SGPS	Simple partial ->Complex partial -> SGPS	1
Auditory -> SGPS	Simple partial -> SGPS	3
Olfactory ->Automotor -> SGPS	Simple -> Complex partial -> SGPS	1
Vegetative -> SGPS	Simple -> SGPS	3
Vegetative ->Hypermo	Simple partial -> Complex partial	1
Vegetativa ->Clonic	Simple partial -> Complex partial	1
Vegetative -> Tonic -> SGPS	Simple partial -> complex partial -> SGPS	7

Table 3. Seizure frequency and duration of PTE

Duration of PTE (year)	Seizure frequency						Total n (%)	p-value (%)
	1 week n (%)	2 week n (%)	1 month n (%)	3 month n (%)	6 month n (%)	1 year n (%)		
0-5	6 (5.5)	7(6.7)	14 (12.8)	13 (12)	10 (9)	2 (1.8)	52 (47.7)	Ref
5.1-10	7 (6.4)	6 (5.5)	4 (3.7)	2 (1.8)	-	1 (0.9)	20 (18.3)	<0.935
10.0-15	2 (1.8)	5 (4.5)	4 (3.7)	1 (0.9)	-	2 (1.8)	14 (12)	<0.001
over 15	10 (9)	6 (5.5)	4 (3.7)	2 (1.8)	-	1 (0.9)	23 (21)	<0.808
Total	25 (23)	24 (22)	26 (24)	18 (16.5)	10 (9)	6 (5.4)	109 (100)	

Table 1 shows sensory symptoms in seizure manifestation. Simple partial seizure transfer to SGPS was observed in 8 cases and simple partial seizure transfer to complex partial then to SGPS was observed in 11 cases. 7 cases of seizures with impairment of consciousness transferred to motor symptoms. Table 2 shows usual motor phenomena in seizure manifestation. In our participants, tonic seizure was mainly distributed as part of a complex partial seizure.

Table 2. Usual motor phenomena in seizure manifestation

Semiologic classification	International classification	n
Clonic	Simple partial	1
Clonic + impairment of consciousness	Complex partial	3
Clonic ->SGPS	Simple partial -> SGPS	3
Tonic + impairment of consciousness	Complex partial	6
Versive -> SGPS	Complex partial -> SGPS	4
Tonic -> SGPS	Complex partial -> SGPS	49

Sixty-seven patients (61.5%) received at least one brain CT scan after TBI. There were contraindications for MRI in 7 patients. CT and MRI investigations were performed using generally accepted methods. Interictal EEG activity was recorded on routine apparatus with 14 channels in 56 (51.4%) patients. 49 of 67 patients who received CT from 1 to 10 years after the head injury had CT abnormalities. 51.4% of them had localization of traumatic lesions in the frontal lobe, while 37.1% had lesions in the temporal lobe. MRI and EEG abnormalities were seen in 5 of 7 and in 49 of 56 patients, respectively. The EEG abnormalities included slow wave transient, sporadic spike waves, and continuous slow wave. There was no obvious correlation between the results of EEG, CT, and MRI investigations.

In our study, 50 (46%) of participants suffered from PTE for 0-5 years, and the remaining patients suffered for more 5 years. Seizure frequency was not correlated with the structural brain abnormalities, but there was inverse association ($r = -0.32$, $p < 0.001$) between seizure frequency and duration of PTE (Table

3). The mean duration of PTE was 9.6 ± 9.3 years. 11 (10%) of participants had a favorable course, with a remission of seizure exceeding one year, while 90% of participants showed a remitting course, with seizures resuming after a seizure-free period or persistent seizures (unfavorable course).

Table 4. Severity of the brain injury and onset of seizure

Time from brain injury to PTE	Severity of the brain injury			Total n (%)	p-value
	Mild n (%)	Moderate n (%)	Severe n (%)		
7 days – 1 year	5 (4.6)	23 (21.1)	28 (25.7)	56 (51.4)	Ref
1.1 – 2 years	1 (0.9)	8 (7.35)	8 (7.35)	17 (15.6)	<0.001
2.1 – 5 years	1 (0.9)	6 (5.5)	6 (5.5)	13 (12)	<0.001
Over 5 years	7 (6.4)	10 (9.2)	6 (5.5)	23 (21)	<0.619
Total	14 (12.8)	47 (43)	48 (44)	109 (100)	

According to the Table 4, 48 (44%) of all participants had severe TBI, 47 (43%) had moderate TBI, and 14 (13%) had mild TBI. While 17 (15.6%) of participants had brain concussion, 76 (69.7%) had contusion, and 6 (14.7%) had intracranial hematoma. Table 4 shows that the majority of seizures began over 7 days to 1 year after brain injury. The occurrence of PTE was positively correlated with severe injury, contusion, and early

onset of seizure ($p < 0.05$).

Factors precipitating seizures according the duration of PTE were explored. In our study, 80 (73.5%) of participants noted that tiredness precipitates seizures, while 22.9% and 20.7% of patients noted that sleep deprivation and hot, long days precipitates seizures, respectively. If a patient had over 5 years of prolonged seizure, alcohol was a trigger for seizure ($p < 0.05$).

Table 5. Operative brain injury influence on onset of seizure

Treatment type	Time from brain injury to PTE				Total n (%)
	7 days-1 year n (%)	1.1–2 years n (%)	2.1–5 years n (%)	Over 5 years n (%)	
Operated	16 (76.2)	2 (9.5)	1 (4.8)	2 (9.5)	21 (100)
Non-operated	40 (45.5)	15 (17)	12 (13.6)	21 (23.9)	88 (100)
Total	56	17	13	23	109

In our study, 21 (19.3%) of patients had operative brain injury. 76.2% of them had their first seizure from 7 days to 1 year after brain injury. In contrast, in the non-operated group,

this number is only 45.5% (Table 5). Brain surgical treatment is a factor for early onset of PTE ($p < 0.005$) and is positively correlated with early onset seizures.

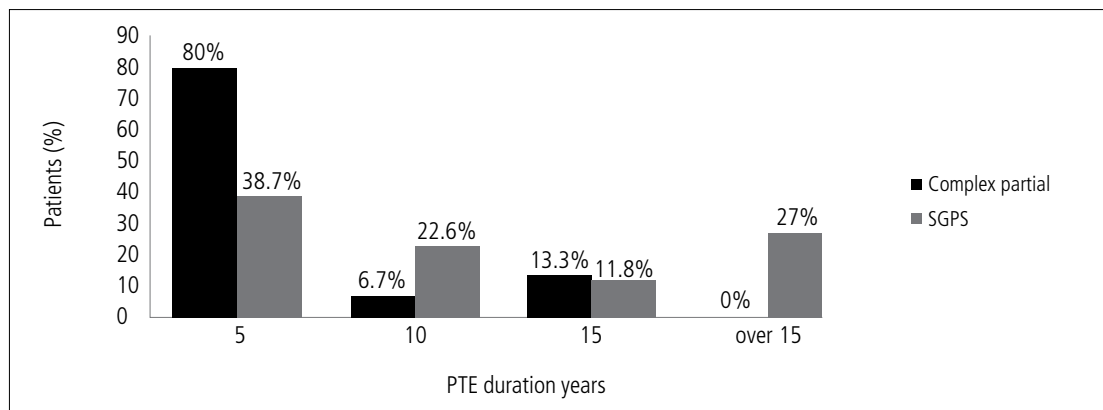


Figure 1. Type of seizures and duration of PTE.

According to Figure 1, 80% of complex partial seizures continued for less than 5 years. Also, patients who suffered from PTE for over 15 years exhibited only SGPS, which indicates rapid transformation of partial seizure in to generalized seizure.

Discussion

The mean age in this study (39) was much higher than a Russian study (26.6) and an Indian study (28) because the pediatric population was not included in this study [9, 11]. This also means that the age range of patients was narrow in comparison to the Indian and Russian study [9, 10]. The sex ratio (2.8:1 for males:females) in the current study was lower than results of Russian (4.8:1), Italian (4.7:1) and Indian studies (4.3:1) [9-11].

The findings on complex partial, SGPS, motor symptoms in the seizure, and time from brain injury to PTE partly confirms the results stated in the literature [10, 11]. Seizures following trauma were related to severity of brain injury [10, 11]. The course of PTE was unfavorable in 90% of our patients, which is higher than that reported by Grinenko and Zaitsev at 43% [9]. Many researchers including Mazzini et al. and Thapa et al. have accepted operative brain injury as a precipitating factor for early onset of seizure after TBI, which is the same result we found in this investigation [10, 11].

Our study in Mongolia showed the course of PTE might be significantly worse depending on the lack of anticonvulsant prophylaxis with phenytoin after severe and operative brain injury [12]. In the studies of Jennet and Scheid and Cramon, brain contusion was noticed as a main factor for developing PTE, which were the same results as our study [12, 13]. Gorin wrote on a few postictal symptoms in PTE, of which we found 11% of these symptoms in our results [14]. We found that the time from brain injury to PTE for the majority of patients (51%) was 1 year, which was similar to the value published by Frey (86%, 2 years) and Raymond (57.6%, 1 year) [5, 15].

In this study, the prevalence of brain abnormalities in the frontal (51.4%) and temporal (37.1%) lobe in CT scan was similar to the results of other researchers who noticed that larger extension of lesions in PTE often involve both temporal and frontal lobes [7, 11, 16]. Mazzini et al. published in their study that basal EEG recording showed a significantly higher incidence of epileptiform activity in patients who later had seizures ($p < 0.0001$), which was the same result in our study:

the main EEG sign of PTE was sharp wave complex (89.3%) [11]. We found that the average time to transfer from partial seizure to generalized seizure was 5 years, which was half of the time reported in a German study (10 years) [13].

Limitations of this study should be noted. First, we could have missed cases with subtle seizure and ictal (referring to the epileptic seizure itself) events on account of the lack of video EEG facilities. Second, as in retrospective studies, it is possible that some patients treated with medications may not be identified for their seizure type. Therefore, the use of medications in PTE patients should be studied since it may be an important issue in course of epilepsy. Another limitation, related to lack of funding, is the low number of MRI, EEG, and CT results included in the study. Further studies need video EEG, other neuroimaging investigations and genetic screening in epilepsy for every patient.

The results of our study supported our hypotheses regarding PTE in Ulaanbaatar, Mongolia. First, clinical features of PTE were presented as secondary generalized seizure (85%) and motor phenomena (60.5%) in the majority of patients. Second, PTE was characterized commonly by long durations of high seizure frequency (90%) and various clinical manifestations. Third, PTE was significantly affected by factors such as severity of head injury and operative brain injury.

Conflict of Interest

The authors state no conflict of interest.

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