CHILDHOOD OCCIPITAL EPILEPSY OF GASTAUT: A LONG-TERM PROSPECTIVE STUDY

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ABSTRACT

Aim*: Childhood occipital epilepsy of Gastaut is a pure occipital epileptic syndrome that is usually accepted to have benign course. Information about the disease is mostly based on retrospective studies and its prognosis is not clearly defined. We investigated the electro-clinical course and prognostic features of the disease in this prospective study in which clinical follow-up and treatment were standardized as much as possible.*

Materials and methods*: In the study, patients (10 females, 9 males) were followed-up for an average of 9.47 ± 5.47 years (range: 2-17). The seizures were ceased in 16 (84.2%) patients, and remission was achieved in 12 (63.2%). The seizures continued in 3 patients (15.8%) despite mono- or poly-therapy. When we compared the cases with (12 patients) or without remission (7 patients), the age at disease onset was lower in cases without remission (7 ± 5.44 years) compared to those with remission (12.08 ± 2.71 years), (p=0.014). Likewise, the total number of seizures experienced before remission was higher in cases without remission (27 ± 41.04) (median: 12 range: 10-120) compared to those with (6.25 ± 7.84) (median: 4 range: 2-30) (p=0.003).*

Results: *In patients with abnormal EEG at baseline, EEG recordings were normalized in those with remission (100%) but remained to be abnormal in those couldn't achieve remission. Of 5 cases with normal EEG recording from onset to end of follow-up period, remission was achieved in 4 cases but not in one case.*

Conclusion: *Our result indicated that consistently normal EEG recordings or abnormal EEG recordings that normalized during follow-up strongly suggest good prognosis. In addition, we concluded that smaller number of seizures experienced before remission and a relative older age, given the age of onset of the disease, can be indicators of good prognosis.*

Keywords*: Occipital epilepsy, Gastaut, Prospective study.*

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Introduction

Childhood occipital epilepsy of Gastaut (COE-G) is a pure occipital epileptic syndrome that often manifests with elementary visual hallucinations and epileptic seizures readily taken under control with antiepileptic treatment in general with some patients achieving remission within a few years[(1)]. In COE-G, long-term course and prognosis haven't been fully elucidated. Although there are several studies on the clinical and EEG features, long-term course, potential risk factors for negative prognosis and prognosis of disease, these are retrospective in nature. We planned to investigate the clinical course and prognostic features of COE-G with a prospective study in which clinical follow-up and treatment were standardized as much as possible.

Materials and methods

This study was initially started by Neurology Department of xxxx University Faculty, Medicine School in 2003. In subsequent years, Pediatric Neurology Department was also involved into the study. All parents gave written informed consent. The study was approved by Ethics Committee of

xxxx University, Medicine School. In our patients, diagnosed was made based on the ILAE 1989 and 2001 classifications[2,3].

In the study, inclusion criteria were: 1- Characteristics of epileptic seizures a) elementary or complex visual hallucinations, visual illusions, blurring of vision or blindness b) and/or deviation of the eyes, eyelid fluttering or repetitive eye closure c) the symptoms in (a) and (b) may convert to hemi-convulsion or generalized tonic-clonic seizures with deterioration of consciousness. 2- EEG features: a) Spike or spike-wave paroxysms in the occipital region or regions (these may disappear with eye opening) or isolated spike or sharp waves in these regions b) or spike, sharp wave or spike-wave activity or focal bioelectrical slowdowns in the regions other than the occipital region c) or normal EEG. 3- Normal physical, neurological and mental state. In the study, no detailed cognitive examination will be performed; rather, findings of routine neurological examination and academic success according to age will be used to determine the mental state. 4- Normal brain imaging.

Exclusion criteria included presence of diseases or disorders that may lead to symptomatic epileptic seizures (especially visual seizures) and that caused brain damage.

In the study, the following clinical follow-up and treatment protocol was used in patients included: 1- The age, gender, age at onset of disease, the number of seizures experienced, seizure type(s), personal and family history (such as epilepsy, febrile seizures, migraine and mental retardation), drugs used, follow-up duration and outcome were recorded. 2- The carbamazepine at an adequate dose (10-20 mg/day) was initiated if there was no contraindication. If it was not possible to prescribe carbamazepine (due to drug side effects, drug ineffectiveness or another reason) or to maintain carbamazepine therapy, other agents such as Na valproate, phenytoin or levetiracetam was given in effective doses in the form of monotherapy or, if necessary, poly-therapy. 3- It was asked from parents to record type and number of seizures in a diary. 4- In all patients, a follow-up evaluation including complete physical examination, EEG study and blood tests was scheduled by 2 or 4 months intervals depending on the clinical state of the patient. 5- The EEG study included routine awake EEG examination (routine recording, intermittent photic stimulation, hyperventilation),and sleep EEG if indicated.

Basic bioelectric activity (background activity), the location and features of epileptic activity if it exists (meaning its morphology and topography) and its reactivity to eye opening and closure were evaluated in the EEG. 6- Two years after cessation of seizures, the dose of the medication used was tapered and the drug was withdrawn eventually (within one-year period). The patients who experienced no seizure for one year after withdrawal of drug was considered to have remission.

SPSS version 22.0 was used for statistical evaluation. The test of normality was checked by the Shapiro-Wilk test. The independent samples t-test was used to compare data with normal distribution whereas the Mann-Whitney U test was used to compare skewed data. The Chi-square test was used to compare categorical data. A p value < 0.05 was considered as statistically significant.

Results

Table 1 presents some clinical and EEG features of the patients at disease onset. There was positive family history of epilepsy in three of our patients. Of these, the same type of seizure, that is childhood occipital epilepsy, was present in the uncle of one patient. In our patients, the elementary visual hallucinations were in the form of colored rings in the visual field or colored flashes of light. Visual hallucinations usually lasted for seconds (5-6 seconds or up to 20-30 seconds).

The spike-waves were reactive to eye closure and opening in 7 of 10 patients with occipital spike-wave (bilateral or unilateral) paroxysms in EEG recordings.

In the study population, the seizures were ceased in 16 patients (16/19, 84.2%). Of these, in 12 patients (12/19, 63.2%) antiepileptic drug therapies were withdrawn according to the study protocol and no relapse was seen in seizures; thus, these patients were considered to have remission. However, in remaining 4 patients, seizures were relapsed after withdrawal of antiepileptic agents; thus, antiepileptic therapy was re-instituted in these patients who were considered to have no remission. The seizures persisted in 3 patients (15.8%) despite mono- or poly-therapy (Table 2). Of these, there was a history of epilepsy in one or two relatives in 2 patients. There was slight mental retardation in the third patient. There were rarely occurring elementary visual hallucinations in 2 cases in the study group.

Characteristics	n (%)
Sex	
Male	9 (47.4)
Female	10 (52.6)
Clinical history	
Family history	
Seizure	3
Personal history	
Febrile seizure	1
Migraine	2
Mild mental retardation	1
Age at disease onset, years, mean±SD (range)	10.21 ± 4.55 (2-17)
Seizure types, n	
Elementary visual hallucination	9
Blurring of vision or blindness	9
Deviation of eyes	4
Fluttering of eyelid	1
Complex visual hallucination	1
Impairment of consciousness and/or SGTCS	15
EEG pattern at disease onset, n (%)	
Occipital spike-wave (bilateral or unilateral)	10 (52.6)
Centroparietal spike-wave(unilateral)	1 (5.2)
Frontotemporal spike-wave(unilateral)	1 (5.2)
Focal slowing	2 (10.5)
Normal	5 (26.3)
Drugs used during treatment period as monotherapy or polytherapy, n	
Carbamazepine	8
Na valproat	7
Phenytoin	2
Levetiracetam	2
Lamotrigine	1
Topiramate	1
Clobazam	1
The total number of seizures had before remission, mean±SD (range) and median value	13.89 ± 26.55 (2-120) and 6
Outcome, n (%)	
On remission	12 (63.2)
No remission	7 (36.8)
Follow-up period, years, mean ± SD (range)	9.47 ± 5.47 (2-20)
Age at last follow-up, years, mean ± SD	19.68 ± 6.29 (11-32)

Table 1: Some clinical and electroencephalographic features of 19 cases with COE-G.

COE-G, childhood occipital epilepsy of Gastaut; SGTCS, secondary generalized tonic-clonic seizure; EEG, electroencephalography

These seizures did not show secondary generalization. The parents of these patients declined to initiate antiepileptic drug therapy; thus, we followed these patients without drug therapy. Their seizures disappeared shortly and they remitted. Temporal lobe epilepsy characterized by simple/complex partial seizures emerged in one patient 6 years after remission. Currently, the epilepsy still continues in this patient who is receiving appropriate antiepileptic drug treatment.

Clinical recovery **n %**
Patients in remission 12 (63.2%)
Patients who were seizure-free with medication but not in remission 4 (21%)
Patients who had seizures despite medication and not in remission 3 (15.8%)

Table 2: Clinical remission status in study population.

In order to determine the potential risk factors in cases without remision, we compared some predefined parameters between the cases with or without remission. The following results were found: 1- We observed no significant difference in term of gender of patients between the two groups ($p = 0.764$). 2- We found a significant difference in age of onset between groups ($p = 0.014$). Age at disease onset was higher in patients with remission (12.08 ± 2.71 years) compared to those without (7 ± 5.44 years). 3- A significant difference was determined in total numbers of seizures experienced before remission between groups ($p = 0.003$). The total number of seizures experienced before remission was lower in patients with remission (6.25 ± 7.84, median: 4, range: 2-30) than those without remission (27 ± 41.04, median: 12, range: 10-120; $p = 0.003$). 4- No difference was found in generalization of seizures between patients with or without remission ($p = 0.581$).

1-Greater age at onset of disease
2-Smaller number of seizures experienced before remission
3-Consistently normal EEG recordings from onset of disease or normalization of abnormal EEG recordings during follow-up

Table 3: Factors suggesting good prognosis.

The EEG recording was abnormal in 14 cases at disease onset. Of these, EEG recording was normalized in 8 cases (57.1%) during follow-up, all of

which achieved remission. In remaining 6 patients (42.9%), abnormal EEG recording persisted during the follow-up period, all of which failed to achieve remission. Of 5 cases with normal EEG recording from onset to end of follow-up period, remission was achieved in 4 cases but not in one case (Table 3).

Discussion

Many clinical features of our patients (disease onset age, gender, the type or types of epileptic seizures) are similar to previously published studies. The same type of seizures, namely childhood occipital epilepsy, was present in the uncle of one of our patients with positive family history for epilepsy. In our study, temporal lobe epilepsy characterized by simple/complex partial seizures emerged in one patient 6 years after remission of childhood occipital epilepsy of Gastaut.No different type of epilepsy or epileptic syndrome emerged in the follow-up in remaining patients. In some studies in the literature, it was reported that a significant portion of the cases had another type of epilepsy or epileptic syndromes concurrently[4].

The seizures were ceased in 16 patients (16/19, 84.2%) in our study group. Of these, 12 patients (12/19, 63.2%) are currently seizure-free without antiepileptic medication. These were the patients who achieved remission according to the criteria in our study protocol. In a study, it was reported that seizures were ceased in 81.9% of the patients but remission was achieved without medication in only 36.4% of the patients[5].

In another study it was reported that seizures were ceased in about 80% of the patients; however, remission was achieved in 46% without medication[4]. Again, it was reported that seizures were ceased in about 80% of patients but that only 54.5% had remission without medication[6]. The remission rate in our study group seems to be slightly higher than other studies. The rate of patients with persistent seizures despite all treatment options were found as 15.8% (3/19) in our group. This rate is given as 20.1% in one study (4), 18.2% in another study[5] and 22% in yet another[6]. While the rates are close to one another, our result is slightly lower than others.

In two of our patients there were rare elementary visual hallucinations without secondary generalization. The relatives of these patients declined to start drug treatment. The patients were taken into follow-up without medication. The seizures discontinued spontaneously in a short time. To best of our knowledge, there is no such experience in the literature. This situation raises the possibility that the disease can be end in a short time before being diagnosed in some children with rare visual seizures without secondary generalization.

When we compared some of the features of patients with or without remission, we observed that age at disease onset was significantly lower in patients without remission (7 ± 5.44 years) compared to those with remission (12.08 ± 2.71 years). The total number of seizures of patients with remission (6.25±7.84; median: 4, range: 2-30) was lower than patients without remission (27 ± 41.04; median: 12, range: 10-120) (p=0.003). We failed to find any evidence pointing in this direction in the literature.

In one study it is reported that prognosis is worse in COE-G cases combined with any other types of epilepsies compared to those with isolated COE-G[4]. In another study, a history of febrile seizure was reported to be a risk factor for worse prognosis[7].

In our study group the EEG recordings were abnormal in 14 patients at disease onset. Of these, EEG recording became normal during the follow-up period in 8 cases (57.1%), all which achieved remission during follow-up period (100%). In remaining 6 patients (42.9%), the EEG recordings continued to be abnormal during the follow-up period. These patients failed to have remission. EEG findings provide significant insight during the follow-up period of the patients as to whether or not the patient will remit. In patients with persistent abnormality in EEGs, it is inappropriate to end drug treatment within the planned period (for example 2 years), rather, it should be continued as it will prevent possible relapses. There were five patients with consistently normal EEGs from the disease onset to the end of the follow-up period. Of these, 4 patients had achieved remission at the end of the follow-up period but one patient did not. Patients with consistently normal EEG can be predicted to most likely have a good prognosis, meaning the patient will have remission. In a study in the literature it is reported that the EEGs of all patients who remitted became normal[4] and in another study[6] it is reported that EEG abnormality continued in 38.5% of patients.

In conclusion, consistently normal EEG recordings or abnormal EEG recordings normalized during follow-up strongly suggest good prognosis.

In addition, we concluded that smaller number of seizures experienced before remission and a relative older age, given the age of onset of the disease, can be indicators of good prognosis.

An important limitation of our study was the small number of patients. For this reason, we made great effort to be very cautious when interpreting the results of our study. Prospective studies with larger sample size will provide more definitive results.

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