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Original Research

Evaluation of Magnetic Resonance (MR) Findings in Patients with Refractory Epilepsy

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Abstract

Objectives: Epilepsy is characterized as a tendency towards recurrent seizures and it is a significant health problem in the world and one of the most common severe neurologic disorders among children. This study aims to evaluate the outcome of magnetic resonance imaging in determining the etiology in patients with refractory epilepsy and to reveal pathologies that may have the potential to be treated with methods, such as epileptic surgery.

Methods: Data were obtained from the patient files of the patients diagnosed with epilepsy and monitored for at least two years between 01.01.2009-12.31.2012 in the Uludag Faculty of Medicine, the Division of the Pediatric Neurology. File records of the patients, age, sex and MRI findings of the patients were recorded.

Results: One hundred twenty were girls (49%) and 125 were male (51%) of the cases. The age range ranged from 1 to 18 years and the median value was 8.3 (1-18) years. One hundred twenty of the 245 patients who met the diagnostic criteria for resistant epilepsy was found as well controlled. In patients with resistant epilepsy, the findings of these two groups of patients were compared concerning MR findings. Among all patients, 154 (62.8%) patients were found to have MR pathology. Of these patients, 83 (53.9%) were in the resistant group and 71 (46.1%) were in the well-controlled group. There was no significant difference in the presence of MR findings between the two groups (p=0.354). The highest incidence (24.8%) of the encephalomalacia in patients in the resistant group may explain the association of perinatal hypoxia with resistance development.

Conclusion: If patients with epilepsy can be predicted early in the disease, which group of the patients will not respond well to medical treatment; unlike other patients, different treatment modalities, such as antiepileptic use, vagal nerve stimulation, ketogenic diet and epilepsy surgery, can be applied to this group of the patients. We think that clinicians can guide the planning of treatment of the MR findings.

Keywords: Child; epilepsy; magnetic resonance; resistant epilepsy.

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Epilepsy is a significant health problem common in the world, characterized by recurrent seizure tendency, and is also one of the most common severe neurological disorders in children.[1] There is no consensus on the definition of treatment-refractory epilepsy in the literature.

Patients whose seizures cannot be controlled although multiple antiepileptics constitute the refractory epilepsy group. There are wide differences between treatment methods, number and duration of drug therapies, frequency of seizures and observation times in different studies.[2–4]

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Given that there are many factors that may cause the development of resistance in epilepsy, many studies have been conducted to evaluate their effects.

Among these factors:

- Gender
- Age at onset
- Seizure type
- Frequency of seizures before diagnosis and in the first six months after diagnosis
- History of febrile seizure
- Neonatal seizures
- Family history
- Motor retardation
- Mental retardation
- Neuroimaging abnormality
- History of status epilepticus
- Presence of the specific epileptic syndrome
- Coexistence of more than one seizure type
- EEG abnormality
- Behavior problem can be enumerated.[5–7]

The present study aims to evaluate the results of magnetic resonance imaging in determining etiology in patients with refractory epilepsy and to reveal pathologies that may have a chance of treatment with methods, such as epileptic surgery.

Methods

Medical files of the patients who were diagnosed with epilepsy in the Pediatric Neurology Department of the Faculty of Medicine, and were under follow-up for at least two years between 01.01.2009 and 31.12.2012 were examined. From the patient's file records, age and gender of the patients, pathological findings in MR in refractory epilepsy patients, if any, were recorded. After this study was planned, ethical approval was obtained from the Ethics Committee of the Uludag Faculty of Medicine with the decision dated 09/30/2014 and numbered 2014-18/3.

Statistical Analysis

Relationships between variables were analyzed using the SPSS 21.0 statistics program. The differences between frequencies of categorical variables were examined with chi-square test and Fisher's exact test. The suitability of the data to normal distribution was investigated using the Shapiro-Wilk test. Mann-Whitney test was used for the comparisons between two independent groups for the data that did not conform to normal distribution. Descriptive statistics of the data that with nonnormal distribution were given as median (min-max). Significance level was taken as $\alpha=0.05$ ($p<0.05$).

Results

The files of the 1500 patients diagnosed with epilepsy by applying to the Child Neurology outpatient clinic between January 2009 and December 2012 due to convulsions were examined. Patients who were followed up for at least two years with a diagnosis of epilepsy, who took three or more antiepileptic drugs individually or in combinations and those without a seizure-free period of three months despite effective serum levels of the drugs were achieved, and patients who had a seizure every month on an average were considered as cases with refractory epilepsy. Drugs that were used in emergency situations due to convulsions, and during status epilepticus, medications discontinued before effective serum drug level could be established or after their side effects occurred were not included in the three study drugs. Among these patients, 245 patients who were followed-up for at least two years and who met the criteria for refractory epilepsy were included in this study.

Among the patients with refractory epilepsy, the patients who received at least three antiepileptic drugs in the first two years and did not respond to classic antiepileptic drugs, patients whose seizures were completely or partially controlled after use of the classic antiepileptic drugs alone or in combination with a new generation antiepileptic drug (felbamate, gabapentin, lamotrigine, levetiracetam, oxcarbazepine, pregabalin, topiramate) in the follow-up period were included in the well-controlled group. Then, 120 of the 245 patients who met the criteria of refractory epilepsy were included in the well-controlled group due to their partial or complete response to treatment. These two groups were compared concerning MR findings in refractory epilepsy patients.

One hundred and twenty cases were female (49%) and 125 were male (51%). Ages of epilepsy patients evaluated ranged between 1 and 18 years (median: 8.3 years). The mean age of the refractory group was 7.8±4.7 years, and the mean age of the well-controlled group was 9 years ± 4.8 years. Mean duration of the follow-up period of the patients ranged between 3.5-14.8 years (mean 7.4±2.1 years).

Given the cranial MR results of the patients, among all patients, 154 (62.8%) patients had pathologic findings in MR. Of these patients, 83 (53.9%) were in the refractory, and 71 (46.1%) in the well-controlled group. There was no significant difference in the presence of MR findings between the two groups ($p=0.354$). When the results of the patients with positive MR findings were evaluated

separately, encephalomalacia ranked on top with a total of the 50 (20.4%) patients in both groups. Thirty-one (62%) patients in this group were among treatment-resistant patients and 19 (38%) patients were among well-controlled patients. Among 154 (62.8%) patients with positive MR findings, 46 (29.8%) patients and the group with signs of cerebral atrophy took the second place. Of all the patients with positive MR findings, 21 (51.2%) of the 41 (26.6%) patients with developmental cerebral anomalies were in the treatment-resistant group and 20 (48.8%) patients in the well-controlled group. None of the patients had mesengial temporal sclerosis. MR findings of the patients are seen in Table 1 and Figure 1.

Discussion

Epilepsy is a crucial health problem common in the world, characterized by recurrent seizure tendencies, and is also one of the most common severe neurological disorders in children.[1] Given that there are many factors that may cause the development of resistance in epilepsy, many studies have been conducted to evaluate their effects. Despite appropriate and effective medical treatment in the literature, an average of 10-30% of cases cannot achieve seizure control, and these cases fall into the treatment –refractory group.[8, 9–14] It is difficult to control the seizure unless the underlying pathology is removed in the development of resistance.

In some studies performed, it was observed that there was a significant relationship between the detection of pathology in admission MR findings and the development of resistance.[15, 16] In the study of Gruraj et al.,[17] pathology was found in the MR findings of the 78% of the patients in the resistant group and 8% of the cases in the control group. In our study, 154 (62.8%) patients were found to have pathology among MRI among all patients. Of these patients, 83 (53.9%) were in the treatment-refractory group, and 71 (46.1%) were in the well-controlled group. Any significant difference was not found between the two groups concerning the presence of MR findings (p=0.354).

Hypoxic-ischemic encephalopathy (HIE) develops as a result of maternal, placental and/or intrauterine or perinatal hypoxia related to the fetus.[18] Perinatal asphyxia-low oxygen saturation at birth[19] -leads to a chain of neurotoxic events, including insufficient energy and accumulation of reactive oxygen radicals.[20, 21] Brain damage caused by the lack of defense capacity against free oxygen radicals in the immature brain and especially low glutathione peroxidase activity may cause chronic neurological pathologies, such as epilepsy and cerebral palsy.[19, 22–24] While Casetta et al.[25] defined perinatal brain injury as the most important risk factor for resistant epilepsy, Othuska et al.[26] found the leading risk factors for resistant epilepsy as cranial nerve infection and perinatal hypoxic-ischemic injury. Similarly, in our study, the highest rate of encephalomalacia in patients in the treatment-resistant group (24.8%) may explain the relationship between perinatal hypoxia and the development of resistance.

If the patient group that will not respond well to medical treatment in the early period can be predicted, then unlike other patients' different treatment methods, such as ear-

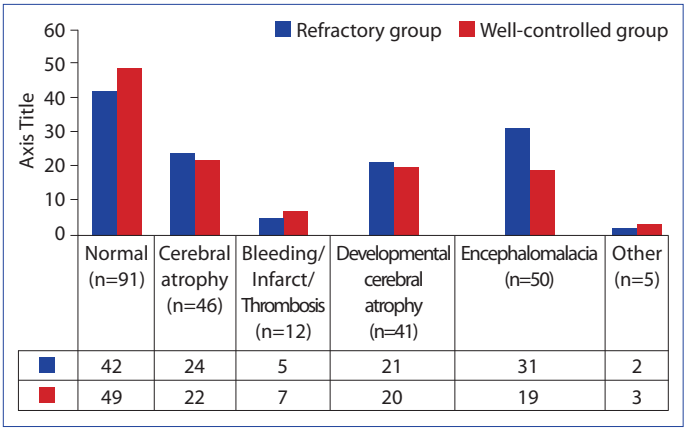

Figure 1. MR findings of the patients.

Table 1. MR findings of the patients

MR findings	Patient a		Refractory group		Well-controlled group	
	n	%	n	%	n	%
Normal	91	37.2	42	33.6	49	40.9
Pathologic	154	62.8	83	66.4	71	59.1
Cerebral atrophy	46	18.8	24	19.2	22	18.3
Bleeding /infarct /thrombosis	12	4.9	5	4	7	5.8
Developmental cerebral anomaly	41	16.7	21	16.8	20	16.7
Encephalomalacia	50	20.4	31	24.8	19	15.8
Other	5	2	2	1.6	3	2.5
Total n	245	100	125	100	120	100

lier use of new generation antiepileptic drugs, vagal nerve stimulation, ketogenic diet, and epilepsy surgery, can be applied to this patient group. We think that MR findings may guide clinicians in treatment planning.

Disclosures

Ethics Committee Approval: Ethics Committee of the Uludag Faculty of Medicine with the decision dated 09/30/2014 and numbered 2014-18/3.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

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