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Surgical Treatment of a Seven-Year-Old Boy with Refractory Epilepsy Due to Focal Cortical Dysplasia, Case Report

Filip Hristo Duma, Aspazija Sofijanova, Ana Stamatova, Vesna Sabolic-Avramovska, Sonja Bojadzieva, Natalija Angelkova

University Pediatrics Clinic, Medical Faculty, Skopje
University Children's Hospital, Neurology ward, Medical Faculty Skopje, Macedonia,

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Abstract

The most common developmental malformation encountered in patients with refractory epilepsy is Focal Cortical Dysplasia (FCD). Malformations of cortical development, in particular FCDs are identified in 20–25% of patients with focal epilepsy, and approximately 76% of these patients are supposed to suffer from drug-resistant epilepsy. A promising therapy option for these patients could be surgical treatment. We present a seven-year-old child with drug-resistant epilepsy, who underwent surgical treatment that had an excellent outcome. Throughout the period of five years, the index patient was admitted several times to the Department of Neurology at the University Pediatrics Clinic-Skopje. He was initially admitted at the age of two years, because of his first episode of febrile seizures accompanied by diarrhea. In the following period, during the hospitalization, febrile seizures also developed. CT findings showed a slight degree of front parietal cortical reduction, while the first MRI showed a slight dysmorphia at the frontal gyri, yet no focal abnormalities. The initial EEG revealed a bihemispheric epileptogenic focus. The reason for constant treatment alterations was drug-resistance. Although some encephalographic stabilization had been achieved, a full clinical response had never been obtained for a prolonged period. At the age of seven years, a pediatric epilepsy surgical team at the University School of Medicine–ACIBADEM, Turkey, evaluated the patient. The conclusion of the team was that the child is a candidate for surgical treatment of epilepsy. The child underwent surgery at the age of eight years and has been seizure free since.

Keywords: Focal Cortical Dysplasia, Epilepsy, Surgery.

Introduction

The most common developmental malformation encountered in patients with refractory epilepsy is Focal Cortical Dysplasia (FCD). Developmental aberrations of normal processes that take place mostly during the first two trimesters of pregnancy and involve cells participating in the formation of the normal cerebral cortex have been pointed out as the cause of FCD (1). Malformations of cortical development, in particular FCD, are increasingly recognized in epilepsy patients, because of improved MRI techniques, including post-processing of 3D data sets (2, 3, 4, 5, 6, 7, and 8). Nowadays, FCD is identified in 20–25% of the patients with Focal Epilepsy (9, 10) and approximately 76% of these patients are supposed to suffer from drug-resistant epilepsy (11).

A promising therapy option for these patients could be surgical treatment. (12 and 13). We present a seven-year-old child with drug-resistant epilepsy, who underwent surgical treatment that had an excellent outcome.

Materials and Methods

Patient

Throughout the course of five years, the index patient has been hospitalized several times at the Department of Neurology at the University Pediatrics Clinic-Skopje. He was initially admitted at the age of two years, because of his first episode of febrile seizures accompanied by diarrhea. In the following period, during the hospitalization, afebrile seizures also developed. He was the firstborn child from a first normal pregnancy, during which the mother had regular check-ups and was healthy. He was born in term and during the natural birth there were no complications. His postpartum and early childhood period showed a delay in the cognitive development. At the age of six years, the child was scarcely speaking; his speech was incomprehensible, consisting of only simple words. There was also evident hyperactivity with repetitive stereotyped motions. Motor skills were satisfactory. The neurological, as well as the surgical examination, were normal. Laboratory tests, abdominal and brain ultrasounds, as well as a lumbar puncture were performed and showed normal findings. CT findings showed a slight degree of front parietal cortical reduction, and at that time Phenobarbital was introduced; he was stable for a period of five months under the initial therapy with Phenobarbital, after which long-lasting generalized seizures occurred, both in febrile and afebrile state, when asleep and while awake. The therapy was altered, thus valproic acid was introduced, and the patient was stable for a period of six months. The neurological status of the patient was normal. Extensive analyses were performed, including imaging studies and MRI of the brain (Fig.1), which showed slight dysmorphia of the frontal gyri, but no focal abnormalities. The EEG revealed a bihemispheral epileptogenic focus (Fig.2).

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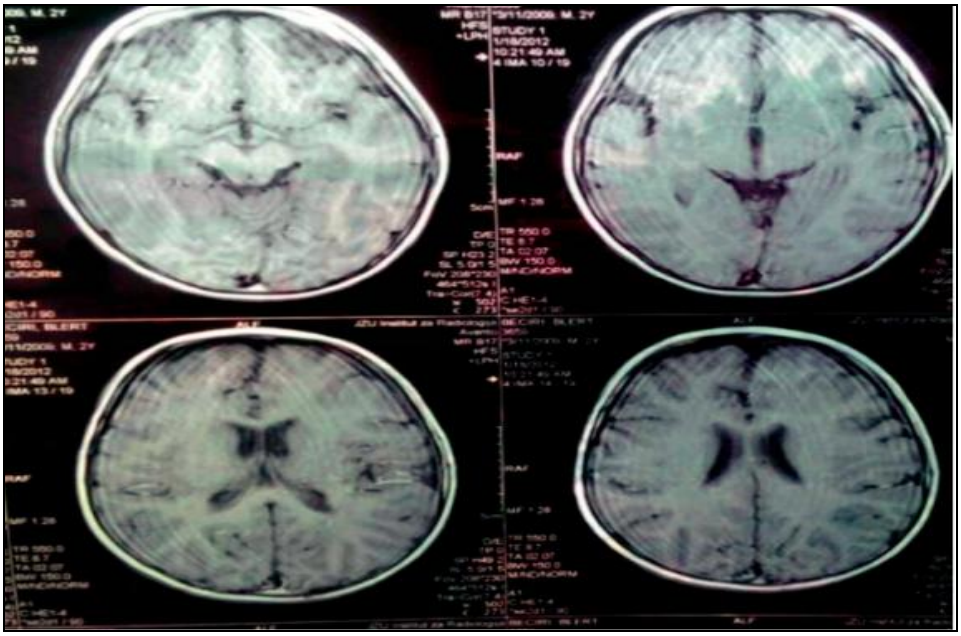

Fig.1 MRI of the brain with slight dysmorphia of the frontal gyri

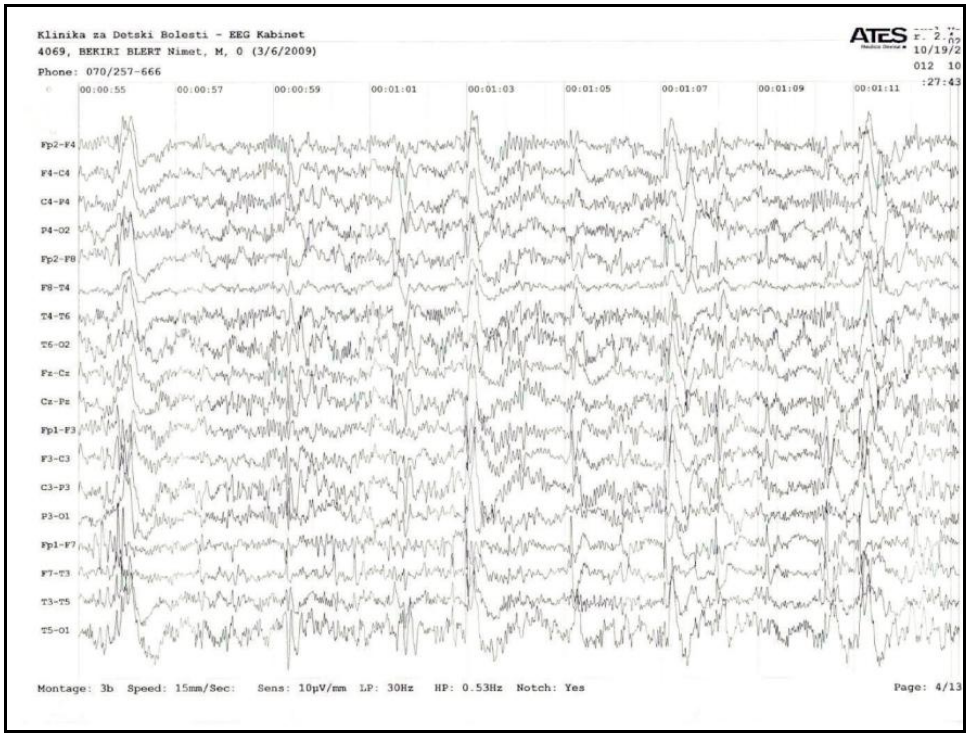

Fig.2 EEG recording which shows bihemispheral epileptogenic focus

The reason for constant treatment alterations was drug-resistance. At the age of two years, Clonazepam was added, because the seizures were not controlled and the child was observed as LGS. At the age of three and a half years, the patient was receiving valproic acid, Levetiracetam and Clobazam, and the response to therapy was not

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satisfactory. Thereafter, instead of valproic acid, Topiramate was introduced and a relative reduction of seizure frequency was achieved, that is to say the patient had only a few seizures while asleep, and this lasted only 6 months. At the age of five years, 1.5T MRI was repeated and no abnormalities were detected. Several antiepileptic drug combinations were tried in sufficiently high doses. He is currently receiving Lacosamide and Levetiracetam, after a six-week treatment with hydrocortisone and consecutive trial to reduce the Levetiracetam for monotherapy with Lacosamide. Several imaging studies (1.5T MRI, Angio-MRI and MRI Spectroscopy) were performed, all of them had normal findings. The EEG showed diffuse changes with left-sided spike waves. After receiving the hydrocortisone therapy, the EEG revealed stabilization. After seven months, the EEG revealed short periods of preserved main activity with spike-wave paroxysms from frontal to central on the right side, and a generalized spike-wave activity (Fig.3).

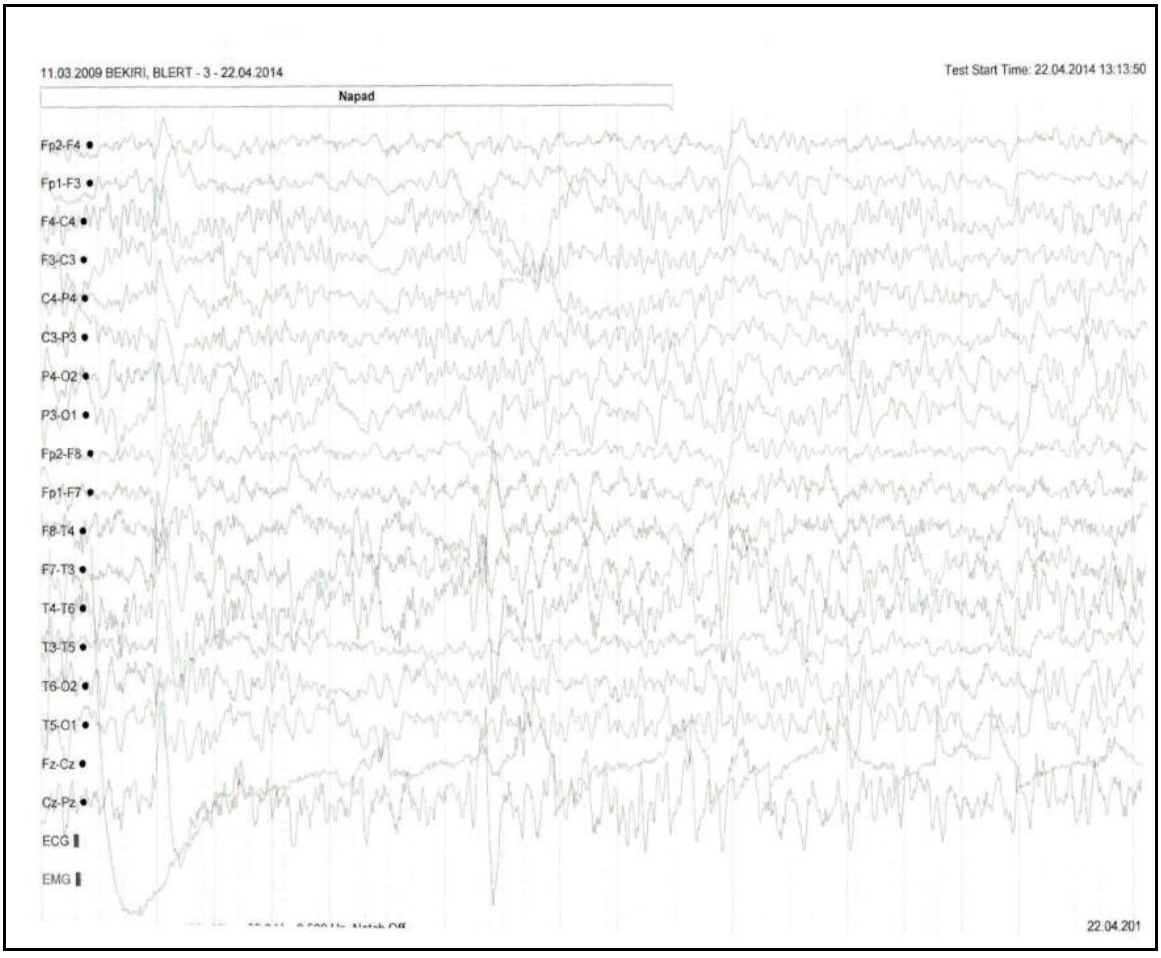

Fig.3 EEG recording which shows spike-wave paroxysms from frontal to central mostly on the right side and generalized spike-wave activity

The EEG in the awaken state showed alpha rhythm, spikes and a 10 seconds 2-3 c/s seizure activity. Stiripentol and Lamotrigine were added, on the account that the first-year febrile seizures followed with refractory epilepsy and unsatisfactory development could be due to the Dravet Syndrome. Genetic tests were not done and this protocol was without a satisfactory clinical response.

The longest seizure-free period was achieved when Sultiam was introduced; unfortunately it had to be discontinued after six months due to an allergic reaction to the drug. During the last hospital admission, the child again presented with frequent complex partial seizures. The therapy was altered to Lacosamide and a six-week treatment with hydrocortisone. The child was seizure-free for a few months, but when the seizures reoccurred there were only a few of them during the awaken state. The treatment with Lacosamide resulted in progress of the social activities and the attention span. The last EEG revealed low voltage polymorphic and spike wave alpha rhythm in the frontotemporal region.

Results

For five years the patient has been under careful monitoring by our team, a series of EEG recordings, a CT scan of the brain and three MRI's of the brain were performed. Only the first MRI and the CT scan of the brain have shown some structural abnormalities, the EEG recordings showed negative progression of the condition, which correlated with the worsening of the clinical picture.

Although some encephalographic stabilization was achieved, a full clinical response has never been obtained for a prolonged period. The patient was never seizure-free, but with each adjustment of the therapy he was receiving, the frequency of the seizures was slightly reduced, but only for a short period of time.

A pediatric epilepsy surgical team at the University School of Medicine–ACIBADEM, Turkey evaluated the patient. The preoperative evaluation consisted of 3T MRI (Fig.4), with left frontal cortical dysplasia and a three-day video EEG, and multiple seizures were recorded. The conclusion of the team was that the child is a candidate for invasive EEG recording and may be a candidate for surgical epilepsy treatment. The child underwent surgery at the age of eight years and has been seizure free for a whole year since the operation.

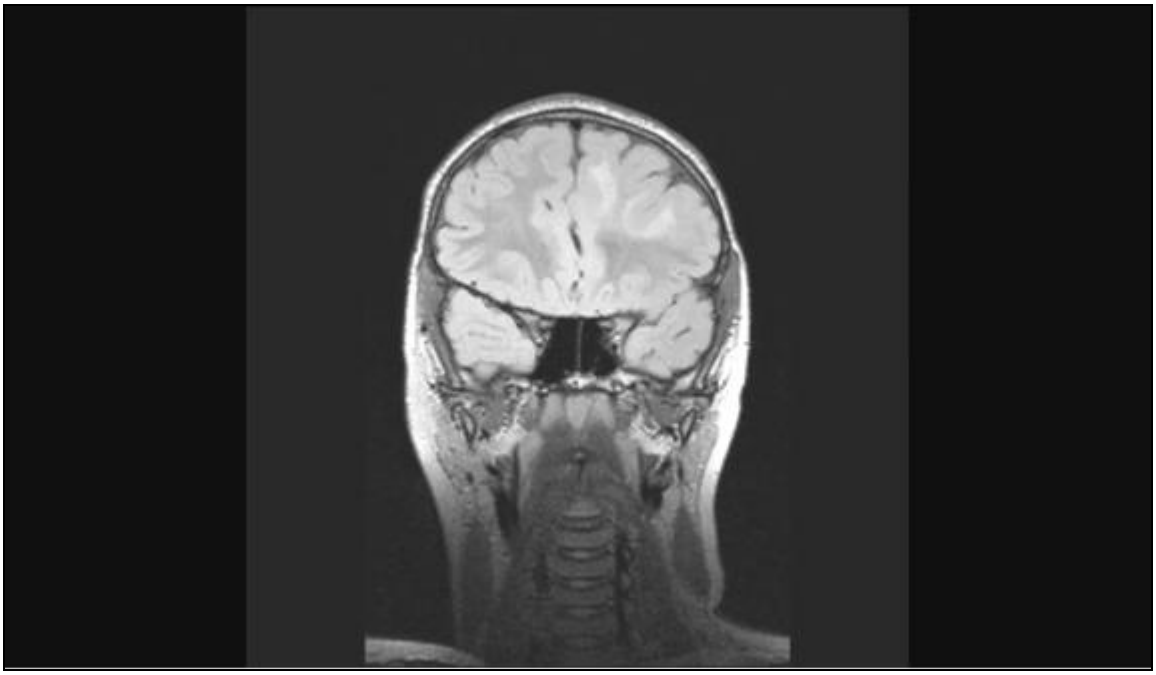

Fig.4 3T-MRI of the brain with left frontal cortical dysplasia.

Discussion

The most common presentation of FCD is epilepsy (14). The number of patients with epilepsy who have some form of FCD is very high. The main reason for surgical intervention in patients with FCD is refractory epilepsy. Preoperative neuro imaging, which usually includes high-resolution MRI imaging, can reveal approximately 60 to 90% of the cortical abnormalities in these patients (14, 15, and 16). Increased cortical thickness and subcortical signal intensity, an abnormal gyral pattern and poor gray-white matter differentiation were the characteristic findings shown on the CT2-weighted and fluid-attenuated inversion-recovery MRI images (14, 15, and 17). Additional diagnostic procedures are performed very often, especially in patients with normal MRI imaging findings. One of the more important modalities during early surgical series was scalp EEG, which was frequently used. Approximately one half to two thirds of patients with abnormal EEG findings have a regional ictal abnormality (14, 15).

The first published description of the surgical outcome in patients with FCD was by Taylor et al.(18) in 1971. The study included 10 patients, eight of whom had FCD that was confirmed histologically. Six patients out of ten were seizure-free after surgical treatment.

Conclusion

Since 3-T MRI and longtime EEG recording are unavailable in our country, we are presenting this patient as the first patient that was evaluated using these methods, approved by the Health Fund and operated for refractory epilepsy. With this patient, all the possible epilepsy medications were introduced in effort to treat the seizures with more or less success. The outcome of the surgical treatment of this patient is a prolonged seizure free period, with furtherance in cognitive, learning and speaking capabilities, as well as improved functioning in everyday activities. Reduction of therapy or its complete removal is the end-point treatment in this patient.

Surgical treatment in selected patients with refractory epilepsy proves to be a superior treatment method compared to the other therapeutic methods, such as: medicaments, ketogenic diet, vagal nerve stimulation, and etc.

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