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Original Article

Outcome of Epilepsy Surgery for Extratemporal Focal Cortical Dysplasia

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ABSTRACT

Background: Focal cortical dysplasia, a malformation of cortical development, is the most prevalent cause of drug-resistant epilepsy in children and the second or third most common cause in adults. Our study aimed to analyze the outcome of resective surgery in the treatment of extra-temporal focal cortical dysplasia.

Methods: This study took place at the department of neurosurgery at Zagazig University Hospitals and included thirty patients with extra temporal focal cortical dysplasia treated by resective surgery using intra operative electro coticography.

Results: Our study showed that 60% of patients had right sided lesions. About 46.6% had frontal lobe lesion, 6.7%, 10% and 36.6% had occipital lobe lesion, parietal lobe lesion, and multi-lobar lesion respectively. In our study histopathological analysis showed that FCD type I was in 9 patients (30%) and FCD type II in 21 patients (70%). In our study we found that 83.4% of patients passed uncomplicated.10% with general complications (UTI, chest infection, Electrolyte disturbance) which managed conservatively and 6.6% with regional complications (small hematoma and superficial infection) which managed conservatively. As regard outcome evaluated by Engel classification about 83.4% had class I, 10%, 3.3%, 3.3% had class II, III and Class IV respectively.

Conclusions: Surgery achieves seizure freedom in about 65% of cases of FCD. Complete resection of the FCD is the most important prognostic factor of seizure freedom. Subtotal resection, longer duration of seizures before surgery, occurrence of secondarily generalized seizures and multilobar FCD are negative predictors.

Keywords: Epilepsy; Extratemporal; Focal Cortical Dysplasia

INTRODUCTION

Chronic brain disease epilepsy is characterized by episodic, recurring, and temporary central nervous system dysfunction and can be brought on by many factors stemming from an overabundance of neuronal firing from the brain **[1].**

The most common serious neurologic disorder is epilepsy. A total of 222 papers were considered, 48 of which focused on incidence and 197 on prevalence. The point prevalence of epilepsy was 6.38 per 1,000 people [95% confidence interval [95% CI] 5.57-7.30], while the lifetime prevalence was 7.60 per 1,000 people [95% CI 6.17-9.38]. The yearly cumulative incidence of epilepsy was 67.77 per 100,000 persons [95% CI 56.69-81.03], despite the incidence rate being 61.44 per 100,000 person-years [95% CI 50.75-74.38]. The prevalence of epilepsy did not vary according to age, gender, or study quality **[2].**

Despite the ongoing advancements in antiepileptic medication over the past few decades, over 30% of epileptic patients continue to progress to drug-resistant epilepsy, which is defined as the inability to achieve sustained seizure freedom through adequate trials of two well-tolerated anti-epileptic drug (AED) schedules, either alone or in combination. **[3].**

One kind of abnormalities of cortical development [MCD] is focal cortical dysplasia. An "umbrella" term, MCD is used to refer to a variety of developmental disorders. Histopathologic examination is used to define the cortical dysplasia grading after surgery. Cortical dysplasia

is at least defined by aberrant neuronal grouping in the subcortical white matter, frequently accompanied by lack of normal organization and architecture of the cortical laminar layer. If there are no further symptoms, this constellation is classified as mild type I cortical dysplasia; if cortical abnormalities, dysmorphic neurons [FCD IIA], and balloon cells [FCD IIB] are present, it is classified as severe type II cortical dysplasia **[4].** In addition to type I and type II cortical dysplasia, the International League Against Epilepsy [ILAE] has devised a new consensus classification system that includes a third tier, called FCD III. Patients with FCD type III have cortical dysplasia in addition to other epileptogenic lesions, such as hippocampal sclerosis (FCD type 3a), epilepsy-associated tumors (FCD type 3b), adjacent vascular malformations (FCD type 3c), and other acquired epileptogenic lesions (FCD Type 3d) **[5].** It is still difficult to treat Extratemporal Epilepsy [ExTLE] surgically because of difficulties establishing the epileptogenic zone [EZ]. However, recent developments in noninvasive methods like functional neuroimaging (PET and SPECT) and epilepsy-specific magnetic resonance imaging (MRI) have enhanced the diagnostic capabilities of ExTLE and made surgical treatment easier. The term "ExTLE" refers to a range of seizures that may originate from sources elsewhere than the temporal lobe in the cerebral cortex **[6].**

Likewise, electrographic activity can be modified by intraoperative electrocorticography [ECoG], which can yield important information on resection extension. [**7].**

Examining the results of resective surgery for the treatment of extra-temporal focal cortical dysplasia was the goal of this study. It offers a thorough overview of the rapidly developing fields of epilepsy surgery and functional brain mapping.

METHODS

The prospective study was carried out in the Neurosurgery Department at Zagazig University Hospitals on 30 cases with extra temporal focal cortical dysplasia with the availability of getting repeated follow-up visits during the period from first of August 2022 to the end of June 2023.

Content validity of the tools: Two specialists from the Department of Neurosurgery at the Faculty of Medicine examined the tools for content validity. The clarity, relevance, comprehensiveness, applicability, and understanding of the instruments were evaluated by these experts. Every suggested adjustment to the instruments was made.

Inclusion criteria included patients of all age groups, drug resistant focal epilepsy**,** patients who have been proved to have extra-temporal focal cortical dysplasia diagnosed by preoperative planning [clinical, neurophysiological and radiological] and so were applicable for resective surgery and proved by post-operative histopathology. Identified FCD was concordant with clinical semiology, Neurophysiological and Radiological studies. Acceptance of patient and family of surgery. General fitness for surgery was considered.

Exclusion criteria included patients who didn't meet criteria of DRE, patients who had been proved by preoperative planning to had multifocal epilepsy or generalized Epilepsy, lesion that was not concordant with clinical semiology, neurophysiological and radiological criteria of FCD, patients were not fit for surgery.

The study was carried out in a ten-month period; from the first of August 2022 to the end of June 2023. According to the pre-planned time schedule, the researcher visited the study location and got to know the study patients after receiving approval to carry out the investigation. The purpose of the study was explained to each subject fulfilling the inclusion and exclusion criteria individually, and then each subject was invited to participate in the study. Upon agreement to participate, the researcher started the interview with each subject using the data collection tools. The study work was done three days per week, over three stages [preoperative, intraoperative and postoperative stages].

Each patient included in this study, was subjected to the following: -

Pre-operative stage:

1- Full history taking in the form of:

Personal background [name, age, sex, place of residence, marital status, type of work, unique habits], cerebral dominance]. Complaint: Headache, nausea and vomiting, seizures, visual disorders, motor or sensory deficits, language disorders and cognitive or affection disorders. History of present illness : onset ,course and duration of epilepsy, the new ILAE classification was used to categories seizure semiology **[8]**. A reliable witness or a home camera clip of the seizures or seizures recorded in the epilepsy unit described it. Past medical history, co-occurring conditions, or risk factors [DM, HTN, hepatic, immunosuppression, chronic lung disease, steroid therapy]. History and Medication used by patients [types, doses, times and if used regularly by patients]. Family history of same disease or any other diseases.

2- Full clinical examination:
Vital indicators such as blood pressure, heart rate, oxygen saturation via pulse oximeter, and respiratory rate are recorded along with a general examination. Full Neurological examination.

3- Routine hematologic investigations:
Complete blood picture [CBC]. testing for liver function. testing for renal function. Partial thromboplastin time and prothrombin time and concentration.

4- Interictal EEG monitoring [usual and long trace] It is necessary to match the electrical anomalies that cause the clinically incapacitating seizure with relevant ones to potentially pinpoint the seizure focus.

5- Video EEG: All recruited patients had their ictal video EEG recordings performed by an experienced EEG technician. The withdrawal of ASMs prior to based on the kind, frequency, and dosage of ASMs used in seizures, ictal recording was scheduled. To shorten the period until the first seizure, quickly remove up to 30% of the daily dosage while sleep-deprived before recording the EEG **[9]**. The electrodes were placed includes additional electrodes at the T1/T2 sites and for ECG recording, in accordance with the global 10-20 system. **[10,11]** Seizures occurred throughout the recording and were recorded for extensive semiology examination. All recordings were examined by a skilled clinical neurophysiologist for evidence of lateralization during ictal recording, seizure onset location, and interictal epileptiform discharge (Figure 1).

6- Neuropsychological assessment:
A qualified and competent psychologist used patients' levels of anxiety and sadness using the Wechsler Adult Intelligence Scale-Version IV (WAIS-IV). The Beck depression and anxiety inventory questionnaires were administered to the patients in Arabic. In accordance with the recommendations of the ILAE 2015, a battery of assessments measuring verbal and visual memory, executive function, language, attention, and social cognition was given in Arabic **[12]**.

Surgical procedures:
All our patients had intraoperative ECoG conducted utilizing a portable 64-channel intraoperative neurophysiological monitoring devices [NIM Eclipse, Medtronic, Minneapolis, Minnesota] or [ISIS, IOM system, INOMED, Inc. To cover the probable epileptogenic area, several strip and grid electrodes were employed. To appropriately define EZ and confirm good resection, both before and after the resection One skilled neurophysiologist, who was blind to the electrode's location during surgery, conducted ECOG recordings. Using SSEP, VEP, and motor evoked potentials as modalities, direct cortical and subcortical stimulation techniques were utilized to determine the eloquent area of interest and design the customized resection based on any proximity to eloquent areas, such as visual and motor domains. Standard microsurgical resection procedures were used in both awake and GA instances. Resective surgery was conducted according to clinical and radiological data and fitness of the patient for surgery. The idea behind a successful epilepsy surgery is that seizure independence can only be attained by removing the lesional area and the surrounding epileptogenic area **[11]**.

The following are the clear benefits of intraoperative ECoGs: They permit the insertion of electrodes for stimulation and recording; To evaluate the extent of the surgery, recordings can be made both prior to and following every resection step. This method enables the brain to be directly stimulated electrically potentially sparing the parts of the brain responsible for certain activities (such as the eloquent cortex). There are no long-term placement hazards, such as infection problems.

Surgical outcomes:
Postoperative follow up was conducted for immediate postoperative clinical and neurological evaluations, as well as CT/MR follow-up to make sure there are no new surgical issues. It was customary to leave the hospital on the third day following surgery. 2 weeks for removal of stitches and 3 months: with the epileptologist to examine the outcome and ASM adjustments and withdrawal and evaluation of frequency of seizures, adjustment of doses of drugs and cognitive and neurological examination.

The standard approach for assessing our patients' surgical outcomes for epilepsy was the Engel classification at their most recent clinical visit with at least a six-month follow-up.

2- Engel classification for postoperative frequency of seizures [13].

3- Postoperative complications assessment and management:
Three main categories of postoperative problems were identified: neurological, regional, and systemic issues.

4- Postoperative Neurological follow up:
Postoperative assessments of neurological results were carried out and documented three times: first, following surgery, when patients could be thoroughly assessed, and second, at the one- and three-month follow-up exams.

Ethical consideration:
The study protocol was authorized by the Faculty of Medicine Zagazig University's ethical

committee and the institutional review board (IRB # 10242). Every participant in this study gave their informed consent. They were briefed on the purpose and methodology of the investigation. They received assurances that all information they provided would be kept strictly confidential and that the study's findings would only be used for further research. Every participant was free to withdraw from the study without fear of reprisal or retaliation. Both the service offered, and the study procedures had no negative effects on the participants.

STATISTICAL ANALYSIS

The following is how the Statistical Package for Social Science [SPSS] software 22.0 for Windows [SPSS Inc., Chicago, IL, USA] was used to record, present, and statistically analyze the data: The Kolmogorov-Smirnov test was utilized to assess the normality of distribution for the variables under analysis. For quantitative symmetrical data, the collected data were summarized as mean ± standard deviation [SD], for quantitative non-symmetrical data, as median and interquartile range [IQR], and for qualitative data, as number and percentage. In the case of categorical data, Fisher's Exact Test [FET] and Chi-square [$\chi 2$] were used to compare the various research groups. When suitable, the MC Nemar test was utilized to identify differences in the same group both before and after the intervention. When it was suitable given the normal distribution of the data, the student t-test [t] was employed to assess differences in the mean value between two groups for quantitative variables. The F test and one-way analysis of variance (ANOVA) were employed to compare mean value differences across more than two groups. The Kruskal-Wallis test and the Z Mann Whitney U-test were used to assess non-parametric variables. A paired t-test was used to compare the pre-intervention and post-intervention groups for the numerical variables when appropriate according to normal distribution, while nonparametric variables were analyzed by Wilcoxon Signed Ranks Test. For normally distributed variables, Pearson's correlation test [r] was used to examine the relationship between the two variables; for ordinal and skewed variables, Spearman's correlation test [rs] was employed. Every test had two sides. In this work, the recognized level of significance was [$p < 0.05$]. A p-value of less than 0.01 was deemed highly statistically significant (HS), whereas a p-value greater than 0.05 was deemed non-significant (NS).

RESULTS

This table shows that 60% of patients had right sided lesions. About 46.6% had frontal lobe lesion, 6.7%, 10%. and 36.6% had occipital lobe lesion, parietal lobe lesion, and multi-lobar lesion respectively **[Table 1].** This table shows that 30% of patients were FCD type I while 70% of patients was FCD type II **[Table 2].** As regard neurologic deficit, 80% of patients had no deficit pre and postoperatively [**Table 3].** This table shows that 83.4% of patients passed uncomplicated.10% with general complications (UTI, chest infection, electrolyte disturbance) which managed conservatively and 6.6% with regional complications (small hematoma and superficial infection) which managed conservatively **[Table 4].** As regard outcome evaluated by Engel classification, 83.4% had class I, 10%, 3.3%, 3.3% had class II, III and Class IV respectively [**Table 5].**

Case Presentation

A 3-years-old male patient with focal drug-resistant epilepsy. Patient was enrolled in our proposed presurgical evaluation protocol. Seizure Semiology focal motor to bilateral tonic ended by nose wiping rt, with an ictal EEG onset in right frontocentral derivation. This was concordant with neuroimaging which revealed right frontal focal Cortical dysplasia. Patients underwent resective surgery using intraoperative mapping techniques and electrocorticography (ECoG), with Engel Class I outcome. (**figure 2**) (A, -C): Axial, coronal, and sagittal magnetic resonance (MR) neuroimaging shows right frontal focal cortical dysplasia in the form of cortical thickening and blurring of grey-white matter junction with transmantle sign (highlighted by circle). (D, -F) Axial, coronal and sagittal Positron emission tomography (PET -MRI coregistration) image shows the interictal right frontal hypometabolism area (circle) corresponding to the location of the focal cortical dysplasia. (G) Preoperative 3-dimentional illustration planning model shows the lesion (circle). (H and I) Intraoperative photograph shows pre and postresection with ECoG strip around the surgical target. (J) screenshot shows preresection ECoG recording rhythmic sharp waves. (k)screenshot shows postresection ECoG recording shows normal electroencephalography findings. (L)Intraoperative motor mapping through direct cortical and subcortical stimulation. **[Figure 1].**

Table (1): Distribution of studied patients according to MRI.

	N=30	%
MRI side		
Left	**12**	**40%**
Right	**18**	**60%**
MRI site		
A -Lobar	**19**	**63.3%**
Frontal	**14**	**46.6%**
Occipital	**2**	**6.7%**
Parietal	**3**	**10%**
B-multi-lobar	**11**	**36.7%**
Fronto-insular	**3**	**10%**
Parieto-occipital	**2**	**6.7%**
Parieto-temporal	**2**	**6.7%**
Parieto-tempo-occipital	**1**	**3.3%**
Temporo-occipital	**3**	**10%**

Table (2): Distribution of studied patients according to Histopathology of the FCD

Histopathology	N=30	%
Type (I)	**9**	**30%**
Type (II)	**21**	**70%**

Table (3): Distribution of studied patients according to neurological deficit pre and postoperatively.

	N=30	%
Preoperative neurological deficit		
No	**24**	**80%**
Spastic weakness	**2**	**6.7%**
Weakness, foot drop	**1**	**3.3%**
Mental delay	**1**	**3.3%**
Speech delay	**2**	**6.7%**
Low IQ	**2**	**6.7%**
ADHD	**1**	**3.3%**
Postop		
No	**24**	**80%**
Increased weakness	**1**	**3.3%**
Permanent dysphasia	**1**	**3.3%**
Transient supplementary motor syndrome	**2**	**6.7%**
Temporary SMA syndrome	**1**	**3.3%**
Temporary visual field defect	**1**	**3.3%**

Table (4): Distribution of studied patients according to complications.

	N=30	%
Complications:		
Worsened/new deficit **Immediate(temporary)** **After 3months follow up**	**29** **1**	**96.6%** **3.3%**
Absent	**25**	**83.4%**
General **UTI** **Chest infection** **Electrolyte disturbance**	**3** **1** **1** **1**	**10%** **3.3%** **3.3%** **3.3%**
Regional **Small hematoma** **Superficial infection**	**2** **1** **1**	**6.6%** **3.3%** **3.3%**

Table (5): Distribution of studied patients according to Engel classification.

	N=30	%
Engel classification:		
Engel class (I)	**25**	**83.4%**
Engel class (II)	**3**	**10%**
Engel class (III)	**1**	**3.3%**
Engel class (IV)	**1**	**3.3%**

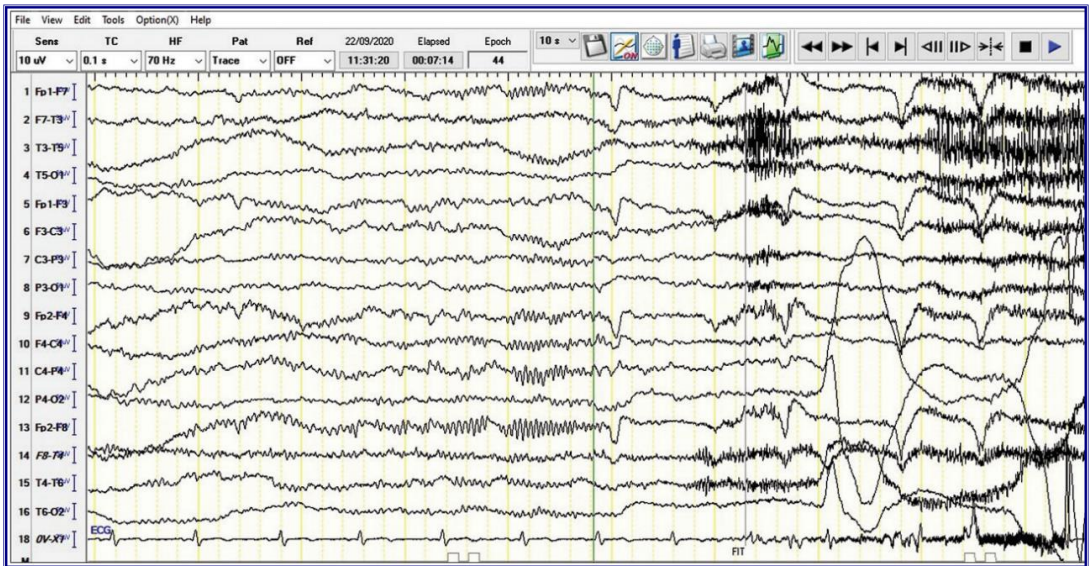
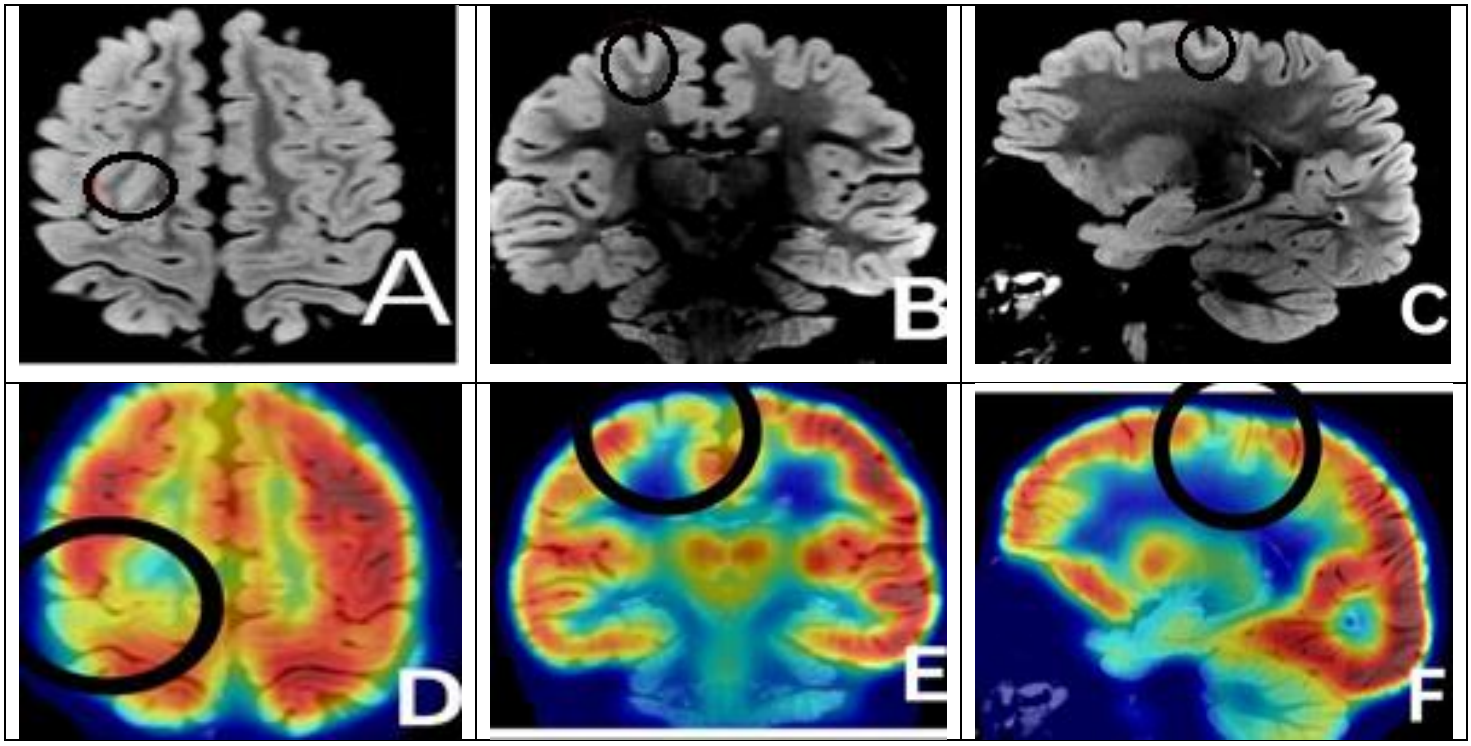


Figure [1]: EEG trace of the patient showing an ictal EEG onset in the right frontal**.**



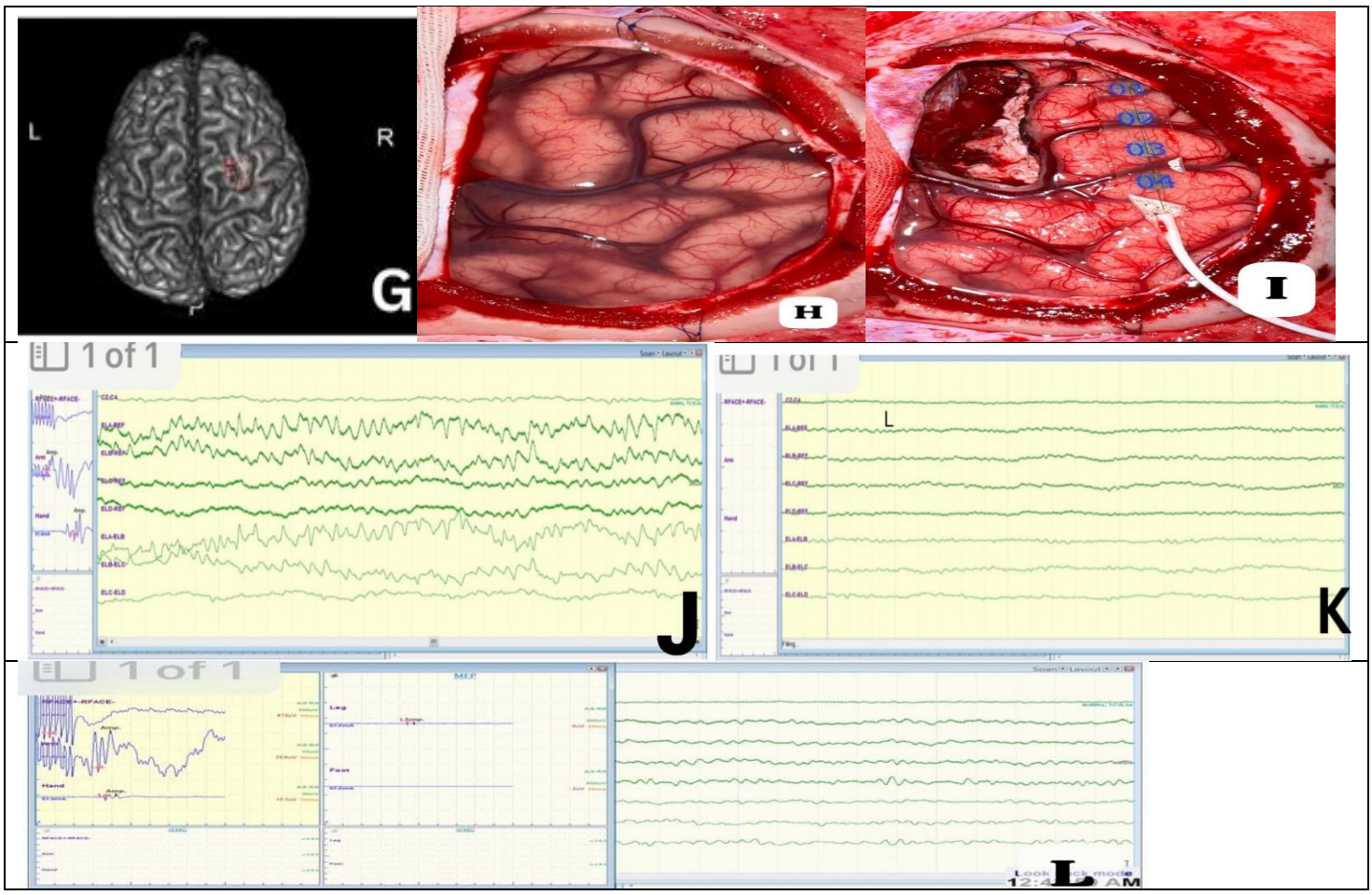


Figure (2): A 3-years-old male patient with focal drug-resistant epilepsy.

DISCUSSION

In our study, 60% of patients had right sided lesions. About 46.6% had frontal lobe lesion, 6.7%, 10%. and 36.6% had occipital lobe lesion, parietal lobe lesion, and multi-lobar lesion respectively.

Sun et al., [14] discovered that all the patients had MRIs, and that 64 of the patients' lesions were on the left side and 46 on the right. Three patients (2.7%) had epilepsy in the parietal lobe, fifteen patients (13.6%) in the frontal lobe, and seventy-eight patients (70.9%) in the temporal lobe.

Delev et al., [15] found that among 178 cases. About 47.7% had frontal lobe lesion, 5.6%, 6.7%, 2.3% and 37.7% had occipital lobe lesion, parietal lobe lesion, insular and multilobar lesion respectively.

Chaturvedi et al., [16] found that among 52 patients, the lesion was left hemispherical in 25 [48.1%] patients, right hemispherical in 22 [42.3%] patients, and bilateral in 5 [9.6%] patients. The most common lobar involvement was temporal [n = 23; 44.2%] followed by frontal [n = 15; 28.8%], parietal [n = 3; 5.8%] and occipital [n = 2; 3.8%]. Multi-lobar dysplasia was found in the rest of the nine [17.3%] patients.

In our study histopathological analysis showed that Nine patients (30%) had FCD type I, while twenty-one patients had FCD type II [70%].

Jyalakshmi et al., [17] conducted a study on 188 patients, histopathological analysis showed FCD type I in 102 patients [54.3%], and FCD type II in 79 patients [42%] and mixed Type I and Type II in 7 patients [3.7%].

Chen et al., [18] reviewed the data of 92 patients with FCD who underwent resective surgery. Specimens of 34 patients [37%] showed FCD type I on histopathological examination,20 patients [21.7%] had FCD type II, while 38 patients [41.3%] had FCD type III.

In our study, as regards neurologic deficit, 80% of patients had no deficit pre and postoperatively.

In our study 83.4% of patients passed uncomplicated.10% with general complications [UTI, chest infection, electrolyte disturbance] which managed conservatively and 6.6% with regional complications [small hematoma and superficial infection] which managed conservatively.

Delev et al., [15] found that in 76 patients (20%), postoperative neurological abnormalities such as hemiparesis and aphasia were noted. In 38

patients (9%), surgical complications such as deep vein thrombosis, wound infections, and meningitis were noted. Nonetheless, during the subsequent postoperative course, most of these problems were fully cured. As a result, 41 patients [10.8%] experienced persistent neurological morbidity, which was primarily related to mild dysphasia, hemiparesis, or visual field loss. 16 [4%] of the 41 individuals with persistent neurological morbidity developed hemiparesis, an unforeseen defect [n = 6], dysphasia [n = 6], hemianopia [n = 3], and dysphasia and hemiparesis [n = 1]. Permanent surgical morbidity was seen in 5 patients [1.0%]: 4 Due to postoperative hydrocephalus, patients required VP-shunts, and one patient had a second surgery to address subdural empyema.

Morales et al., [19] discovered that there was no mortality in our population regarding surgical complications. Three patients experienced postoperative neurological abnormalities, such as paresis, while the remaining three cases displayed surgical problems, such as vision impairment, wound infection, and deep vein thrombosis. During the postoperative period, most of these disorders were resolved. Just three patients (about 13%) had permanent neurological morbidity, which included paresis and blindness.

In our study, the outcome evaluated by Engel classification about 83.4 % had class I, 10%, 3.3%, 3.3% had class II, III and Class IV respectively.

Sun et al., [14] discovered that the surgical results for the 110 individuals following a year of follow-up following epilepsy surgery, 72 patients [65.4%] attained Engel class I, 20 [18.2%] achieved Engel class II, 11 [10%] achieved Engel class III, and 7 [6.4%] obtained Engel class IV.

Delev et al., [2019] found that among 363 patients complaining of extratemporal epilepsy operated with resective surgery, 60 patients [58.8%] achieved engel class I, 13 [12.6%] Engel class II, 9 [8.7%] Engel class III, and 21 [19.7%] Engel class IV.

Morales et al., [19] found that 52.6% of the samples were classified as Engel class I and 47.3% as class II–IV after a year of follow-up; at 24 months, 41.1% of the Class I occurrences were registered, and class II–IV cases made up 58.8% of the total cases.

CONCLUSIONS

In over 65% of FCD sufferers, surgery results in seizure independence. The most crucial predictor of seizure independence is total excision of the FCD. Subtotal resection, longer duration of seizures before surgery, occurrence of secondarily generalized seizures and multilobar FCD are negative predictors. Positive results are shown by a multidisciplinary and multimodal approach that uses sequential intraoperative electroencephalography (ECoG) to guide surgical operations for extratemporal drug-resistant epilepsy and presurgical epilepsy workups. The methods used demonstrate a workable, safe process with negligible morbidity and no fatality.

Declaration of interest

The authors report no conflicts of interest. The authors along are responsible for the content and writing of the paper.

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