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TEMPORAL LOBE EPILEPSY

(PAST, PRESENT, AND THE FUTURE)

By

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ABSTRACT

Background: The temporal lobe is the most epileptogenic region of the human brain. There are two types of temporal lobe epilepsy (TLE), the medial involves the medial or internal structures, and neocortical involves the outer portion of the temporal lobe. It can be associated with a magnetic resonance imaging (MRI) lesion or be non-lesional. The main causes of lesional TLE are Herpes simplex, benign tumors, vascular malformations, cortical development malformations, and post-traumatic or post-infectious gliosis.

Objective: To discuss temporal lobe epilepsy with all its different causes, evaluating different modalities of treatment, obstacles in applying all modalities in developing countries, and ways to overcome these obstacles with future scope of epilepsy treatment especially temporal lobe epilepsy.

Patients and methods: The study performed on twenty patients admitted to Al-Hussein and Sayed Galal University hospitals, and Al-Ahrar teaching hospital. There were pre-surgical evaluations by a multidisciplinary team of neurologists, clinical neurophysiologists, neuroradiologist, epileptologists, psychologists, psychiatrists, and neurosurgeons. Most of cases were temporal lobe lesional epilepsy. Surgical management was carried out for the included patients according to present pathology.

Results: Our patients' ages ranged from 7 to 55 years old with the mean age of 21.2 ± 13.79 years. 60% were in 2nd decade. 70% of patients were males and 30% were females, 90% were right handed and 10% left handed. The range of duration of the disease was 2-8 years with the mean 4.1 ± 2.125 years. As regard MRI pathological findings; 10% normal, 10% left temporal sclerosis, 10% right insular dysplasia, 5% right temporal encephalomalacia, 10% temporal covernoma, 10% temporal arachnoid cyst, 5% right temporal epidermoid cyst and 40% temporal neoplastic lesions of MRI findings. 55% Left temporal epileptic discharge, 25% right temporal epileptic discharge, 10% bilateral temporal epileptogenic activity with tendency to generalization and 10% normal of EEG. 65% lesional excision, 10% excision and fenestration of cyst to subarachnoid space, 15% amygdalohippocampectomy, and 15% temporal lobectomy. Among the patients surgically operated, 4 patients (20%) had temporarily complications.

Conclusion: Temporal lobe epilepsy surgeries provided a good chance for seizure control when the clinical and radiological data were concordant with seizure semiology, in particular with tumor-related epilepsy. TLE surgery can be safe when performed by experienced surgeons.

Keywords: Temporal lobe epilepsy, Epilepsy, EEG.

INTRODUCTION

Epilepsy is a chronic medical disorder or condition of the central nervous system defined by any of the following conditions: At least two unprovoked or reflex seizures occurring >24 h apart. One unprovoked or reflex seizure with probability of further seizures (two

unprovoked seizures, occurring over the next 10 years). Epilepsy is considered to be resolved when patients have remained seizure-free for the last 10 years, with no seizure medicines for the last 5 years, or past the applicable age of an age-dependent epilepsy syndrome *(Fisher et al., 2014)*.

The most common form of focal (partial) or location related epilepsy is temporal lobe epilepsy, it has a lot of different older names, including, "psychomotor seizures," "limbic seizures," "temporal lobe seizures," "complex partial," and "simple partial." The modern name is "focal onset," which is then characterized by awareness. The seizures beginning in the temporal lobe can be extremely varied; there may be a mixture of different feelings, thoughts, emotions, and experiences, which may be familiar or completely foreign. Some cases a series of old memories resurfaces. Others may feel as if everything appears strange including home and family. Hallucinations of voices, music, smells, people, or tastes may occur. These features are called “auras” or “warnings.” They may last for just a few seconds, a minute, or two. The sensations and experiences that accompany these seizures are often difficult to be described, even for the most eloquent adult. There are two types of TLE. The medial involves the medial or internal structures, and neocortical involves the outer portion of the temporal lobe. The medial temporal lobe epilepsy is the most common; it is also frequently resistant to medications if there is hippocampal sclerosis. It is usually begins at the end of a first or second decade, following either a seizure with fever or an early injury to the brain *(Gregory et al., 2013)*.

Diagnostic modalities of TLE are a good history and physical examination, Computed tomography (CT), Magnetic resonance imaging (MRI); the neuroimaging modality of choice for temporal lobe epilepsy, especially coronal cuts, Positron emission tomography (PET); useful for interictal seizure localization in surgical candidates when MRI is normal, Single-photon emission CT (SPECT); adjunctive imaging modality useful for surgical candidates, when done as ictal study, Magnetic resonance spectroscopy(MRS); of some use in trying to evaluate lesion for neoplastic signal, Electroencephalography (EEG); indicated in all patients with suspected temporal lobe epilepsy, Magneto encephalography (MEG); mainly used for co-registration with MRI to give magnetic source imaging in 3-dimensional space. There are many anti-epileptic drugs (AEDs) used for seizure control in temporal lobe epilepsy. Neurostimulation is a treatment option if the patient is refractory and is not a good surgical resective candidate. Vagus nerve stimulation (VNS) was approved by the US Food and Drug Administration (FDA) in 1997 for the treatment of intractable partial epilepsy in patients aged 4 years and older. Responsive neurostimulation (RNS) is another option when the seizure focus is known and it could treat multifocal epilepsy. Deep brain stimulation (DBS) is awaiting FDA approval but has been available in other countries. Temporal lobectomy is the definitive treatment for medically intractable temporal lobe epilepsy, as it has a high seizure-free rate. For patients

who had mesial temporal lobe epilepsy and disabling seizures for no more than 2 consecutive years following adequate trials of 2 brand-name AEDs, Respective surgery plus AED treatment result in a lower probability of seizures for at least 2 years post treatment, as well as improved health-related quality of life, than continued AED treatment alone *(Fisher et al., 2017).*

In our study, the main goals were to discuss temporal lobe epilepsy with all its different causes, evaluating different modalities of treatment, obstacles in applying all modalities in developing countries, and ways to overcome these obstacles with future scope of epilepsy treatment especially temporal lobe epilepsy.

PATIENTS AND METHODS

This prospective and retrospective study was conducted on 20 cases with drug resistant epilepsy at to Al-Hussein and Sayed Galal University hospitals, and Al-Ahrar teaching hospital, with 1 year follow up.

Inclusion criteria: All cases of TLE that were not controlled on 2 antiepileptic drugs (drug resistant), and cases of TLE that cannot tolerate side effects of antiepileptics.

Exclusion criteria: All cases that were controlled on two or less antiepileptic drugs without intolerable side effects, and patients with any epileptic focus other than temporal lobe.

Pre-surgical evaluation was detected by a multidisciplinary team of neurologists, clinical neurophysiologists, neuroradiologist, epileptologists, psychologists, psychiatrists, and neurosurgeons. The patients, who are diagnosed as refractory to medical treatment, underwent a highly sophisticated process called presurgical evaluation of epilepsy surgery.

Pre-operative work up:

History:

Patients were assessed pre-operatively for detailed history taking for (personal, present, past, and family history) with detailed seizure history for:

- Presenting seizure semiology.
- Associated symptoms.
- The presence of aura.
- Nature of the attack.
- Duration.
- Frequency.
- Post ictal status.
- All the pre-operative AED were accurately documented.

Clinical Examination:

Detailed examination was done in the form of general, neurological, psychological and psychiatric examination.

- General examination included (vital sings, general appearance, body built, the respiratory system, cardiovascular system, GIT system, endocrine manifestations, skin abnormality, and scars of previous trauma or surgery) was done.
- Detailed neurological and psychological examinations include:

- Assessment of the detailed intellectual functions (IQ, Memory), speech and cerebral dominance.
- Motor system examination for muscle bulk, tone and power, co-ordination, gait, reflexes and pathological reflexes.
- Sensory examination for both superficial and deep sensations.
- Sphincteric function.
- Cranial nerve examination.
- Local examination for the cranium, spine and abnormalities.

Investigations:

- CT and MRI brain with contrast (epilepsy protocol) to ensure concordance of clinical semiology and lesional lateralization.
- EEG and Video EEG.
- PET (positron emission tomography) as an adjunct test in surgical planning it depends on cortical glucose metabolism.
- FMRI to determine hemispheric dominance for language instead of Wada test (blood oxygenation level dependent response).
- Upon preparation for surgery, routine laboratory investigations were done.
- Reassessment of the patients and insurance about any new events.
- Reassessment of all investigations done.
- Assessment for fitness for anesthesia by the anesthesia team preparing for surgery and any required additional investigations were done upon their request.
- Consent is taken from all for surgery.

Operative work up:

For all of the patients:

- Under general anesthesia.
- The patient was positioned supine with a foam wedge or shoulder roll ipsilateral to the side of surgery. The use of three point rigid fixation was not a rule.
- Intraoperative functional mapping and electrophysiological monitoring were used in the most of cases.
- Surgical management was carried out for the included patients and the surgical procedures were categorized into:

  1. Lesionectomy.
  2. Selective Amygdalohippocampectomy.
  3. Temporal lobectomy.

Post-operative care:

- The patients were assessed for vital stability and their conscious level.
- Post-operative CT brain was done to exclude post-surgical complications.
- ICU admitted until their conditions were stabilized and then discharged to the ward.
- Patients were re-assessed for post-operative complications if present.
- Histopathological examination of the excised lesional specimens.
- Late MRI was done after 3 months of surgery to assess the extent of excised specimens.

Statistical analysis:

Recorded data were analyzed using the statistical package for the social sciences, version 20.0 (SPSS Inc., Chicago, Illinois, USA). Quantitative data were expressed as mean± standard deviation (SD), range and median. Qualitative data were expressed as frequency and percentage.

RESULTS

The results of our study were collected along 1 years of follow up of 20 cases which were undergone surgical intervention at Al-Hussein and Sayed Galal University hospitals and Al-Ahrar teaching hospital.

The patients' age ranged from 7 to 55 years with the mean age of 21.2 ± 13.79 years, the 2nd decade (60.0%). The males (70.0%) and female (30.0%). The duration of patients complained epilepsy ranged 2-8 y with the mean 4.1±2.125 y and the median 3 y. were right handed and (10.0%) were left handed. From history of risk factors we found (10.0%) positive family history, (30.0%) head trauma, (60.0%) febrile convulsions, (25.0%) CNS infection and (25.0%) no history of risk factors. Ten patients (50.0%) of patients presented without aura and (40.0%) with epigastric pain or gastritis. The most common seizure was complex partial seizures (50.0%), then Partial with 2nd generalization (30.0%) and Simple partial (20.0%). The automatism that observed Oroalimentary (30.0%), verbal (10.0%) and no automatism (60.0%). (70.0%) of lateralization were on lt. side and (30.0%) on Rt. Site **(Table 1)**.

Table (1): Distribution of the studied patients according to age, sex, handedness, types of aura, types of seizures, types of automatism and lateralization site (n=20)

Parameters \ Distributions		No.	%
Age (years)	1 st decade	2	10.0%
	2 nd decade	12	60.0%
	3 rd decade	2	10.0%
	4 th decade	1	5.0%
	5 th decade	2	10.0%
	6 th decade	1	5.0%
	Min. – Max.	7 - 55	
	Mean ± SD.	21.2 ± 13.79	
	Median	16	
Sex	Male	14	70.0%
	Female	6	30.0%
Handedness	Rt	18	90.0%
	Lt	2	10.0%
Risk factor	Febrile convulsions	10	50.0%
	Head trauma	6	30.0%
	Positive family history	2	10.0%
	CNS Infection	5	25.0%
	No risk factors	5	25.0%
Types of aura	Epigastric pain	8	40.0%
	Fear + gastritis	2	10.0%
	Without aura	10	50.0%
Types of seizures	Simple partial	4	20.0%
	Complex partial	10	50.0%
	Partial with 2nd generalization	6	30.0%
Types of automatism	Oroalimentary	6	30.0%
	Verbal	2	10.0%
	No automatism	12	60.%
Lateralization	Lt	14	70.0%
	Rt	6	30.0%

MRI findings were Normal in (10.0%), Left temporal sclerosis in (10.0%), Right insular dysplasia in (10.0%), Right temporal encephalomalacia in (5.0%), Temporal covernoma in (10.0%), Temporal arachnoid cyst in (10.0%), Right temporal epidermoid cyst in (5.0%) and Temporal neoplastic lesions in (40.0%). EEG finding were Left temporal epileptic discharge (55.0%), Right temporal epileptic discharge (25.0%), Bilateral temporal epileptogenic activity with tendency to generalization (10.0%) and Normal (10.0%). The surgical interventions were Excision (65.0%), Excision & fenestration of cyst to subarachnoid space (10.0%) and Amygdalohippocampectomy (15.0%) and temporal lobectomy (15.0%) **(Table 2)**.

Table (2): Distribution of the study group according to MRI findings, EEG, types of decision of operation (n=20)

Parameters \ Distributions		No.	%
MRI findings	Normal	2	10.0%
	Left temporal sclerosis	2	10.0%
	Right insular dysplasia	2	10.0%
	Right temporal encephalomalacia	1	5.0%
	Temporal covernoma (Left, Right)	2	10.0%
	Temporal arachnoid cyst (Left, Right)	2	10.0%
	Right temporal epidermoid cyst	1	5.0%
	Left temporal low grade glioma	2	10.0%
	Left temporal Ganglioglioma grade I	2	10.0%
	Left temporal Oligodendroglioma grade II	2	10.0%
	Left temporal Xanthoastrocytoma grade II	2	10.0%
EEG	Left temporal epileptic discharge	11	55.0%
	Right temporal epileptic discharge	5	25.0%
	Bilateral temporal epileptogenic activity with tendency to generalization	2	10.0%
	Normal	2	10.0%
Decision of operation	Excision	13	65.0 %
	Excision & fenestration of cyst to subarachnoid space	2	10.0%
	Amygdalohippocampectomy	3	15.0%
	Temporal lobectomy	2	10.0%

Post-operative (15.0%) of patients had surgical complications which managed conservatively, (5.0%) neurological complication as transient hemiparesis and (80.0%) without any complication **(Table 3)**.

Table (3): Distribution of the studied patients according to presence of complications (n=20)

Parameters \ Distributions	No.	%
Surgical	3 (20)	15.0%
EDH	1	5.0%
SDH	1	5.0%
Subgaleal CSF collection	1	5.0%
Neurological	1 (20)	5.0%
Transient hemiparesis	1	5.0%
Non complicated	16 (20)	80.0%

DISCUSSION

Epilepsy surgery outcome assessment is mainly based on seizure-freedom or reduction, neurocognitive functioning, and change in overall quality of life. Of particular concern, are language, verbal and memory function *(Shin et al., 2011)*.

Our study performed on selected twenty patients admitted to Al-Hussein & Sayed Galal University hospitals, and Al-

Ahrar teaching hospital. We depended in our pre-operative evaluation on the cumulative data gathered through proper history taking, seizure semiology, clinical examination, lesional location on cerebral imagining and electrophysiological studies.

Our patients' ages ranged from 7 to 55 years old with the mean age of 21.2 ± 13.79 years. 60% were in 2nd decade. 70% of patients were male and 30% were female, 90% were right handed and 10% left handed. The range of duration of the disease was 2-8 years with the mean 4.1 ± 2.125 years.

A study by *Tubi et al. (2019)* found that post traumatic epilepsy were 81% males and 19% females, with a mean age of 37.72 ± 17.83, *Morshed et al. (2019)* found that the mean age of the patients on their study on gliomas of mesial temporal lobe was 46.8 years, and most of the patients were males (82%), and left-sided tumors comprised 64% of lesions. also *Ormond et al. (2018)* found that 66 % of lesions were on the left side.

Among predicted risk factors, we found 10% positive family history, 30% head trauma, 60% febrile convulsions, 25% CNS infection and 25% no history of risk factors.

Cendes (2011) found that the main causes of lesional TLE are HS, benign tumors, vascular malformations, cortical development malformations, and post-traumatic or post- infectious gliosis.

Auras are usually subjective symptoms without objective signs that can be documented by an observer. These usually occur at the beginning of a seizure (warning symptoms) for seconds up to minutes. We found 40% of patients complaining of epigastric pain or gastritis as aura and 50% not associated with aura, the typical aura is an indescribable rising epigastric sensation, often described as butterflies *(Thompson et al., 2010)*. The most common seizure occurred was complex partial seizures 50%, then Partial with 2nd generalization 30% and Simple partial 20% (Table 11). Automatisms are repetitive, involuntary, purposeless movements that are usually inappropriate, but occasionally may simulate relatively normal events 30% of patients showed Oroalimentary, 10% verbal and 60% no automatism. 70% of lateralization was on lt. side and 30% on right side.

Kennedy and Schuele (2012) left found that of neocortical TLE more than 80% of patients report an aura, such as auditory phenomena, psychic experiences or d_ej_a vu and jamais vu, visual distortions, and vertiginous symptoms. *Pascual (2007)* said that the abdominal sensation or epigastric rising sensation is the most characteristic of the somatosensory auras, and probably the most frequent due to its high incidence in TLE. *Morshed et al. (2019)* found that the main presenting symptom is seizures (82%), syncope of unknown origin (4%) and headache 4%, Ormond et al. (2018) found complex partial (91%), simple partial (30%) and generalized seizures (20%).

As regard MRI pathological finding, 10% were normal, 10% left temporal sclerosis, 10% right insular dysplasia, 5% right temporal encephalomalacia, 10% temporal covernoma, 10% temporal arachnoid cyst (Left, Right), 5% right temporal epidermoid cyst and 40%

temporal neoplastic lesions of MRI findings.

Due to the presence of an obvious lesion on brain MRI that was concordant with seizure semiology, surgery was done even if the EEG was non-contributory. The convergence of evidence pointing to the lesion encouraged proceeding to surgery without the need for more invasive investigations such as cortical grids or depth electrodes. The patients associated with lesional CT and or MRI lesions were operated by surgical excision.

As regard to EEG and video EEG, 55% Left temporal epileptic discharge, 25% Right temporal epileptic discharge, 10% Bilateral temporal epileptogenic activity with tendency to generalization and 10% Normal of EEG.

Despite the variability of the lesions included in our study regarding their exact their relation to the cerebral parenchyma or even their histopathological nature, lesionectomy was successful to guarantee a satisfactory outcome, 65% lesional excision, 10% excision and fenestration of cyst to subarachnoid space, 15% amygdalohippocampectomy, and 15% temporal lobectomy.

The results of one randomized controlled study conclusively show that patients with medial temporal lobe epilepsy benefit from antromedial temporal resection with regard to seizure outcome *(Dwivedi et al., 2017)*.

Tandon and Esquenazi (2013) found that resection strategies in patients with tumor related epilepsy vary from lesionectomy to larger epilepsy operations with no consensus on optimal approaches.

Although surgical modalities have been improved in the modern era, there are still unpreventable complications related to the surgical process itself. While most of the authors reported no mortality, it may reach up to 3.5% very rarely *(Lee et al., 2012)*. The neurological and surgical complications excluding visual field defects and neuropsychological disorders after ATL ranged between 0% and 16% *(Georgiadis et al., 2013)*.

Among twenty patients surgically operated, 4 patients (20%) had temporarily complications. 3 surgical complications EDH, SDH and subgaleal CSF collection which managed conservatively, 1 neurological complication as transient hemiparesis and 80% without any complication post-operative.

The outcome of seizures after epilepsy surgery is classified according to international league against epilepsy *(ILAE outcome scale 2001)*, 65% class 1, 10% class 2, 15% class 3, 5% class 4 and 5% class 5. The longer a patient was seizure free, the less likely the chance of relapse *(De Tisi et al., 2011)*.

It is difficult to determine whether the absence of postoperative seizures is a consequence of the resection of the focus or the destruction of the network topology *(Palmigiano et al., 2012)*. Outcome at one year postoperatively is highly predictive of long term outcome after temporal lobe epilepsy surgery *(Unnwongse et al., 2002)*.

The large meta-analysis of long term seizure outcome by *Tellez-Zenteno et al.* showed the long-term outcome in TLE to be similar to the outcome in short-term

controlled studies *(Téllez-Zenteno et al., 2010)*.

CONCLUSION

Temporal lobe epilepsy surgeries provided a good chance for seizure control when the clinical and radiological data are concordant with seizure semiology, in particular with tumor-related epilepsy. TLE surgery can be safe when performed by experienced surgeons.

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صرع الفص الصدغي
(الماضي والحاضر والمستقبل)

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خلفية البحث: الفص الصدغي هو المنطقة الأكثر صرعًا في الدماغ البشري. هناك نوعان من صرع الفص الصدغي: أولهما الإنسي وهو ينطوي على الهياكل الإنسية أو الداخلية وثانيهما القشرة المخية الحديثة وهي تتضمن الجزء الخارجي من الفص الصدغي, ويمكن أن تترافق مع آفة في التصوير بالرنين المغناطيسي أو تكون غير آفاتية. ومن الأسباب الرئيسية لمرض صرع الفص الصدغي الآفاتي التصلب الحصين، الأورام الحميدة، التشوهات الوعائية، تشوهات نمو القشرة المخية وتليّف ما بعد الصدمة أو ما بعد العدوى. وتتضمن الصورة السريرية الشائعة لمرضى صرع الفص الصدغي أثناء نوبة الصرع التحديق وعدم الاستجابة. وغالبًا ما يكون مصحوبًا بآليات الفم أو اليد.

الهدف من البحث: مناقشة صرع الفص الصدغي بكل أسبابه المختلفة، تقييم الطرق المختلفة للعلاج، العقبات في تطبيق جميع الطرق في البلدان النامية وطرق التغلب على هذه العقبات بالنطاق المستقبلي لعلاج الصرع وخاصة صرع الفص الصدغي.

المرضى وطرق البحث: أجريت الدراسة علي عشرين مريض تم قبولهم في قسم جراحة المخ والأعصاب مستشفيات جامعة الأزهر ومستشفى الأحرار التعليمي، بين سبتمبر 2018 ومايو 2019، يعانون من الصرع أو نوبة صرعية ناتجة من الفص الصدغي. تم أخذ التاريخ المرضي كاملا بالتفصيل وتم عمل الفحوصات المتاحة . وكانت معظم الحالات صرع الفص الصدغي آفاتية وأجريت الجراحة للمرضى وفقا للآفة الموجودة.

نتائج البحث: تراوح عمر المرضى الذين شملتهم الدراسة والذين كانوا يعانون من نوبات صرع الفص الصدغي والذين لم يستجيبوا للعلاج الدوائي في فترة تتراوح من 2 – 8 اعوام بين 7 - 55 عامًا, وكان 60 % في العقد الثاني. ومن بين

مسببات المرض 60 % التشنجات الحرارية, 30% اصابات الراس, 25% عدوي الجهاز العصبي, 10% وراثي, 25 % بدون مسببات. ووجد ان نصف الحالات لا يسبقها اعراض تحذيرية و 40% احساس بالام بالمعدة. ثم يتبعها نوبة تشنجية وكانت النوبات الأكثر شيوعًا هي النوبات الجزئية المعقدة 50% ثم قد يتبعها حركات أوتوماتيكية بنسبة 40%. تم عمل الفحوصات اللازمة وكان 90% نتيجة أفات بالفص الصدغي منها 40% اورام, 10% تصلب بالفص الصدغي, 10% ورم دموي و 10% سليم. خضع جميع المرضى للجراحة على حسب كل حالة 15٪ فقط قاموا باستئصال الفص الصدغي, 15% استئصال جزء من الفص الصدغي و70٪ قاموا باستئصال الآفة بطرق مختلفة حسب نوع الآفة. تمت السيطرة على النوبات الصرعية 65% درجة الاولى, 10% الدرجة الثانية, 15% الدرجة الثالثة. ومن بين المرضى العشرون تعرض أربعة مرضى لمضاعفات بنسبة 15٪ جراحية, 5% وظيفية وتم علاجهم في جميع الحالات بشكل تحفظي.

الاستنتاج: يوفر استئصال الآفة الكامل فرصة جيدة للسيطرة على النوبات عندما تتوافق البيانات السريرية والإشعاعية مع نوبة الصرع وخاصةً مع الصرع المرتبط بالورم. وتؤكد هذه الدراسة على أهمية وجود فريق متعدد التخصصات في التقييم المعقد قبل الجراحة لمرشحي إجراء الجراحة.

الكلمات الدالة: صرع الفص الصدغى، نوبات الصرع، رسم المخ الكهربى.