ORIGINAL ARTICLE

Brain Tumor cases most oftenly related to Chronic Epilepsy

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ABSTRACT

Aim: There has been an increase in Neurosurgical procedures for epilepsy treatment, with some degree of benefits, specifically when it comes to epilepsies that are partial or localisation-related. Mesial temporal sclerosis (MTS) and primary brain tumour, as well as vascular abnormalities and malformations of cortical development (MCDs) are the main pathological entities in lesional epilepsies. After surgery, discussion was held on the histopathology and elimination of seizure.

Method: The patients were uncontrollable medically, and between July 1999 and April 2016 had to be admitted to the epilepsy surgery. Included among the preoperative evaluation protocol we performed are physical and neurological, as well as psychiatric, and neuropsychological examinations. We also performed scalp electroencephalogram (EEG), and not less than 0.5T magnetic resonance imaging (MRI). Intra operative electrocorticography (ECoG) was used to detectirritating lesion. Regular pathology was performed studies on resected specimens with further studies made on the hippocampus.

Results: Our surgery experiences based on partial epilepsy cases numbering more than 487 revealed that in 27 cases primary brain tumour presence was the responsible pathology linked to the chronic intractable epilepsy. Elimination of seizures revealed that Class 1was seizure free in 22 cases. Class 2, on its part, revealed that not more than 2 seizures take place every year in 3 cases, and Class 3 revealed reduction in seizure frequency of above 75% in 2 cases.

Conclusions: In long-lasting epilepsy cases, tumorous lesions presence should not be ignored, while the major purpose of surgery is seizure elimination and not just the removal of tumour.

Keywords: brain tumour, epilepsy, electroencephalography

INTRODUCTION

The manifestation of seizures brought about by brain tumours comes often in the form of focal seizures by way of or short of secondary generalization,and close to one third of patients are resistant to antiepileptic medication treatment. Several possible reasons could account for such resistance to medication[1]. Several important roles that seizures play in the general well-being of individuals, especially in the life of patients whose primary brain tumoursare slow-growing abound[2,3]. The tumour-related epilepsypathogenesis have continued to be poorly understood, in spite of the fact that this subject is very important to the scientific area of neurology and neurosurgery, as well as in the field of neurooncology. The increased application of neurosurgical procedures for the epilepsytreatment has had beneficial effects, especially epilepsies that are partial or localization-related.The launching of magnetic resonance imaging (MRI) in epilepsy has very much influenced these recent advances[4]. Mesial temporal sclerosis (MTS) and primary brain tumour, as well as vascular anomaly and malformations of cortical development (MCDs) are all part of the major pathological entities in lesional epilepsies. Patients whose epilepsy is tumour related were all given referral due to the long-lasting epilepsy and the histopathology, together with seizure elimination after discourse on surgery was undertaken.

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MATERIAL AND METHOD

Between July 1999 and April 2016, the patients were admitted to the epilepsy surgery. These epilepsy patients become surgical candidates if they are seen as medically intractable or if the seizures they had are considered to be lesion related. We utilised scalp electroencephalogram (EEG) with invasive recordings that are limited, in carrying out our evaluation. EEGs were attached to patients during their sleeping and waking moments. Physical and neurological, as well as psychiatric and neuropsychological examinations were among the preoperative evaluation protocol we conducted. Every patient has had not less than 0.5T magnetic resonance imaging (MRI) scans conducted in axial and coronal, as well as sagittal planes, slices of 5-mm at T1, T2, and fluid attenuated inversion recovery (FLAIR) classifications. the Wechsler Adult Intelligence Scale were used for the standard

neuropsychological tests for the past two years. The conducting of the Wada test or intracarotidamobarbital procedure was only on selected cases. The patients received referral for surgery if concordant data were revealed in all preoperative investigations, in the absence of which, they were either scheduled to be either re-evaluated or were recommended to undergo other alternative treatments

The removal of tumour alone is not a guarantee of good result in seizure control. This is based on the assumption that neurons surrounding the tumour make up the epileptogenic zone. Nonetheless, the same argument can also be raised in the case of irritating lesion removal. Intra operative Electro Corticography (EcoG)(picture 1) was utilised in detecting Irritating lesion. The recording of intra operative Electro Corticography (EcoG) used a series of electrodes spaced evenly andembedded in the silicone plastic's "strips" or "grids". The sizes ofgrids and strips are standard and pre-set, but it is possible to have them trimmed for the purpose of accommodating thesize and shape of the cortical surface that is exposed.Every diameter of the contact electrode is standard at 5 mm. The distance between the electrodes is also standard at 1 cm. The standard monitoring time is 5minutes and can run up to 30 minutes while having longer recordings possess increased sensitivity in the detection of uncommon happenings. Identification of abnormal signal can be made in the operating room by way of visual observations by an epileptologist. There are variations when it comes to the recordings of pre-resection and post-resection ECoG usage. The aim of performing the two is for the identification/ confirmation of seizure foci, as well as in determining the degree of resection. Monitoring and analysis of rate and location, together with the period of beginning of the observed spikes are made. Surgeons are given encouragement for minimisation of the residual tumour volume whenever it is deemed possible.

Standard pathology studies were carried out on resected specimens and further studies were also carried out on the hippocampus.

There was maintenance of AED medication, postoperatively, for a period from six months to one year in every patient, which was later reduced with the patient's consent. Re-evaluation of EEG recordings was made after a period of 6 months and every year.

RESULTS

The experiences we acquired based on more than 467 surgery cases of partial epilepsy revealed primary brain tumourpresence as the responsible pathology relative to 27 casesin long-lasting intractable epilepsy of which 11 and 16 were wuth females and males respectively (Table 1). They were made up of 10 cases and 17 cases of vascular hamartomas and Cortical DevelopmentsMalformations or Cortical Dysplasias respectively (picture 2). Their ages range from 14-41years old averaging 24.3±7.17 years. The ages at the first epilepsy seizure was from 2-30 years old, averaging 7.7±4.70 years. The time period of epilepsy was from 1-16 years, averaging 7.7±4.70 years. Electro encephalography was utilised to make evaluations in all cases intra-operatively.The studies in Histopathology revealed 9 cases to be Dysembroplastic Neuroepithelial Tumour (DNT), and 7 cases to be Ganglioglioma, while 2 cases were Pilocytic Astrocytoma and 3 cases (2 of them revealing later changes in malignancy) of Low Grade Diffuse Astrocytoma. There were also 2 cases of Tuberous Sclerosis Complex and 2 cases ofEpidermoid, as well as a case ofPleomorphic Xanthoastrocytoma (Table 2).Seizure Eliminations revealed that 22 cases in Class 1 were Seizure Free and 3 cases in Class 2 were having 2 or less seizures every year while 2 cases in Class 3 had more than75% reduction in the frequency of seizures (Table 3).

Table 1. Demografic brain tumor with epilepsy cases

Female	11
Male	6
age The average age at the first epilepsy seizure The duration of having epilepsy	 24.3±7.17 (14-41) years 14.0±7.13 (2-30) years 7.7±4.70 (1-16) years

Table 2. Patological finding

Dysembroplastic Neuroepithelial Tumor (DNT)	9
Ganglioglioma	7
Pilocytic Astrocytoma	2
Low Grade Diffuse Astrocytoma (2 of them showed malignant changes later),	3
Tuberous Sclerosis Complex	2
Epidermoid	2
Pleomorphic Xanthoastrocytoma	1

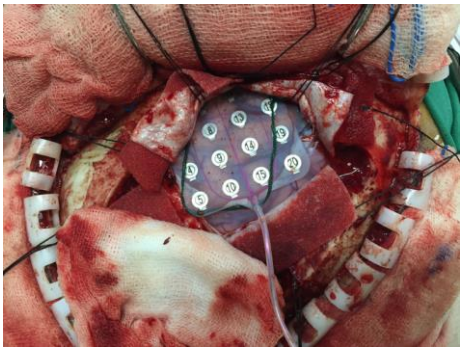
Table 3. Seizure elimination

Class 1 (Seizure Free)	22(81%)
Class 2 (not more than 2 seizures per year)	3(11%)
Class 3 (decrease of seizure frequency more than 75%)	2 (8%)

Picture 1. Intra operative EEG recording. Electode paced upon the assumed area decided by extra cranial EEG

corelated to MRI Finding. (A)Intra operative EEG recording, irritative zone marked by green line. (B) Blue line resection area.

A



B

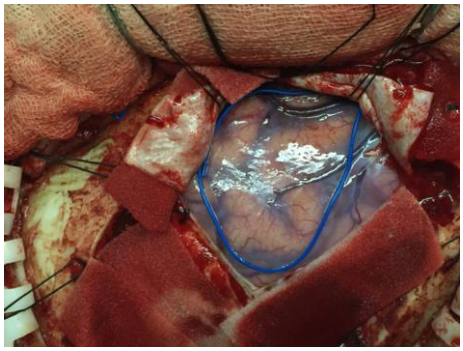
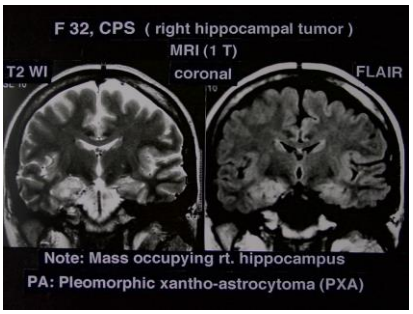
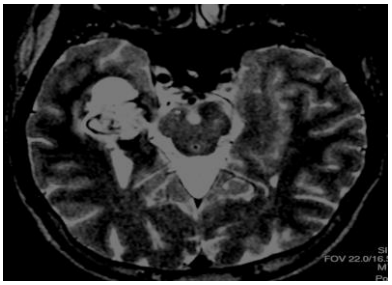
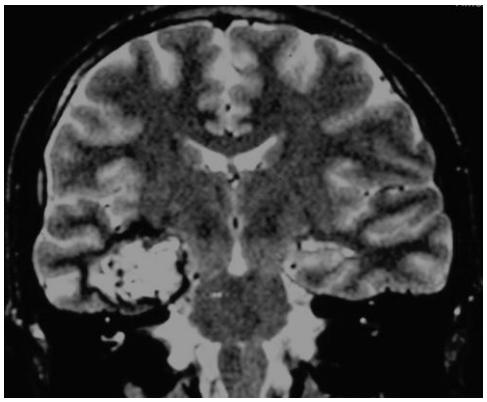


Fig.2: .A. Magnetic resonance imaging(MRI) showed mass occupyin g right hippocampus on 32 years old female present with complex partial seizure. 2.B. DNT showed at inferior temporal gyrus on 14 years old male present with compleks partial seizure.

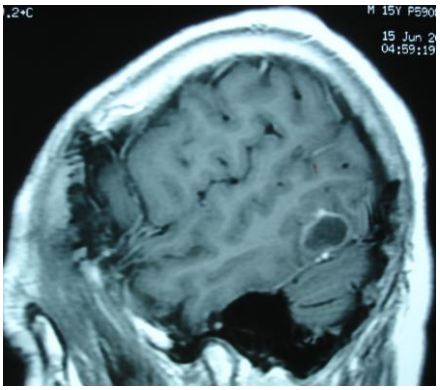
A. F 23, mass occupying right hippocampus

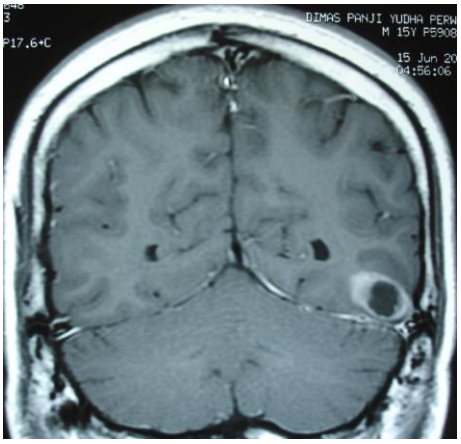






B. M 14, DNT at inferior temporal gyrus





DISCUSSION

It is common for patients suffering from low-grade tumours like dysembryoblastic neuroepithelial tumours (DNETs) and gangliogliomas (GGs), together with oligodendrogliomas (OGs) to have seizures. These are identical to the series in our cases where cortical developmentmalformation happened to be the most frequent tumour. There is lowerepilepsyincidencein high-grade brain tumours

like glioblastoma multiformes (GBMs) and metastatic tumours. There is the likelihood of seizure developmentpathogenesis being different from brain tumours having histology that is different[5,6]. Developmental tumours are made up of well-differentiated cells that have the ability of releasing neurotransmitters and other modulators involved in epileptogenesis[7]. There is the possibility of these tumours being linked to cortexstructural epileptogenic abnormalities. There is also the possibility of subcortical network vital for electrical transmission suffering damage by the fast-growing high-grade brain tumours' highly infiltrative growth [8] while there has been suggestion of slow-growing tumours, inducing cortical regions' partial differentiation, resulting in the hypersensitivity of denervation[7, 9] and the production of an epileptogenic milieu. Furthermore, there is the possibility of changes taking place in gliosis, and chronic inflammatory within the peri-tumoral regions leasing to epileptic seizures. It is possible for Brain tumours that have identical grade but differ in histology to have seizure incidences that are different.[10] In addition, not all patients having identical localization and histology suffer from seizures[5]. Such is a strong suggestion of the possibility of genetic factors playing a part in thedevelopment of tumour and tumour-related epilepsy.

The endothelial cells and astrocytes are all part of the cellular components of the blood–brain barrier (BBB). Others include pericytes and neurons, together with junctional complexes. These junctional complexes are made up of the transmembrane junctional proteins that include occlude in and claudins, together with junctional adhesion molecules which are formed as part of thecellular components of the BBB.[11] Studies of humans and animals have given suggestion of perturbations in neurovascular integrity and BBB breakdown resulting in neuronal hyper-synchronisation and epileptiform activity. Reduction in transmembrane junctional proteinsexpression[12] and heightened vascular endothelial growth factor (VEGF)release[13] are all relevant molecular changes in brain tumours affecting the structure and function of BBB.VEGF diffusion into the peri-tumoral brain has the possibility of aggravating the edema which surrounds the lesion. There were endothelial tight cell junctions'structural defectssurrounding human gliomas which were reported by Stewart et al.[14] There is suggestion by a more current study on the possibility of this being arbitrated through the transformation of the growth factor β (TGF-β) receptor. This leads to its stimulation thereby resulting in extracellular potassiumactivity which depends on accumulation and N-methyl-D-aspartate (NMDA) receptor-arbitrated neuronal hyper-excitabilityfacilitation. It is also dependent on ultimate epileptiform activity. One other study demonstrated[16] the likelihood of epileptogenesis becoming reduced by TGF-β receptors blockade taking place in a living organism.

Summing up these results suggests the possibility of BBB pathological disruptioni n brain tumour patients contributing to seizure activity. Defining the possibility of the degree to which BBB disturbances result in seizure induction is difficult. Nonetheless, there is a general consideration that the likely causes of seizures are tumours like LGGs that lead to BBB disturbances, although they do not succeed in the destruction of the subcortical network.

On the basis of the assumption that the tumour constituting the epileptogenic zone is surrounded by neurons, removal of the tumour alone is never a guarantee that the results of seizure control will come out well.Nonetheless, it is possible to argue on the ability of microenvironment returning to normal and the surrounding neurons ceasing to discharge abnormally if there is removal of irritating lesion. Lesionectomy alone produced very good results for majority of surgical series where paediatric patients were involved.[17, 18] Nonetheless, studies on adult patients revealed the possibility of gross total resection or even extended lesionectomy greatly improving seizure prognosis.[10, 19] This is in line with the findings we made of extended lesionectomy having the ability of improving seizure free after surgery. Shorterseizure history and lesspermanent secondary changes opportunity like hippocampal sclerosis can be attributed as a possible reason for the better lesionectomy results in children. Surgeons are, in general, given encouragement in seeing to it that the residual tutor volume is minimised whenever possible.

The traditional AEDs efficacy like valproic acid (VPA) and carbamazepine (CBZ) have not undergone anyrandomized clinical trials evaluation in patients suffering from brain tumours. Also not undergonerandomized clinical trials arephenytoin (PHT) and phenobarbital (PB). Drawing any firm conclusions based on available studies is difficult.Therefore, the basis for the decision regarding AEDs to be administered to patients suffering from brain tumours is mainly on the preference of the individual rather than on clinical evidence.Nonetheless, a quantitative and formal epidemiological study design of 12 informative studies made by Glantz and et al.[20] on the investigation conducted on prophylactic anticonvulsants use such as PHT or PB or VPA in patients who have primary and metastatic brain tumours revealed the absence of efficacy in the prevention of the first seizure or in the reduction of

the initial seizures'frequency. The report of Temkin also revealed that no evidence exists on the possibility of long-term treatment with PHT and CBZ providing protection against late seizures.[20] There are questions that still beg for answers on whether or not a traditional AED choice should be based entirely on their side effect profile.

There is a belief of VPA inhibition of epileptic discharges through the stabilisation of neuronal membranes and improvement of GABA transmission. It has the ability of inducing apoptosis and growth arrest, as well as cell diversity of tumour cells through histone deacetylaseinhibition.[22] A current study revealed thatautophagy in glioma cells is induced by VPA with such action being independent of apoptosis.[23] There is indication regarding the study of Weller et al. on the VPA potential anti-tumour activity in patients suffering from GBM who required an AED at the time of temozolomide-based chemoradiotherapy.[24] The fact of tumoral and peri-tumoral factors contributing to the tumour-related epilepsypathogenesis suggesting of VPA being taken into consideration as a first line therapy in the treatment of tumour-related epilepsy.

CONCLUSIONS

The use of neurological surgery in the treatment of epilepsy has gone up, and such treatment does come with lots of benefits, precisely when it comes to partial or localisation- related epilepsies. Tumorous lesions presence must never be ignored when it comes to long-lasting cases of epilepsy. Developmental tumours are made up of well-differentiated cells that have the ability of releasing neurotransmitters and other modulators involved in epileptogenesis. There is the possibility of these tumours being linked to cortex structural epileptogenic abnormalities. Seizures are common among patients with low-grade tumours like dysembryoblastic neuroepithelial tumours (DNETs) and gangliogliomas (GGs), together with oligodendrogliomas (OGs).Well-differentiated cells that have the ability of releasing neurotransmitters and other modulators involved in epileptogenesis make up the developmental tumours. There is the possibility of these tumours being linked to cortex structural epileptogenic abnormalities. There is the possibility for Brain tumours having identical grade but different in histology to have seizure incidences that are different.Tumour removal alone is not a guarantee of good result will be obtained in seizure control. The removal of tumours, therefore, must never be the major purpose for patients to undergo surgery but for the elimination of seizures.

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