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Original article

Seizure Burden and Antiepileptic Drug Utilization in Brain Tumor Patients

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Abstract
Seizures are a common neurological complication of pediatric brain tumors and contribute significantly to morbidity and impaired quality of life. The burden of tumor-associated seizures and patterns of antiepileptic drug (AED) utilization in children remains variable and incompletely characterized, particularly in low-resource settings. This study was conducted to evaluate seizure prevalence, AED utilization patterns, and changes in AED requirements before and after surgical treatment in pediatric patients with brain tumors. This retrospective cohort study included 53 pediatric patients (≤16 years) with brain tumors who underwent neurosurgical intervention at a specialized pediatric neurology center in Tripoli, Libya. Clinical data were extracted from medical records, including demographic characteristics, tumor location, histopathology, WHO tumor grade, seizure presence and type, and AED use before and after surgery. Seizure types were classified according to International League Against Epilepsy criteria. Early postoperative AED response was defined as seizure freedom during the first postoperative week without escalation of therapy. Descriptive statistics were used, and paired comparisons of AED requirements before and after surgery were analyzed using the McNemar test. The mean age at diagnosis was 9.23 ± 4.9 years, and 77.4% of patients were male. Tumors were predominantly supratentorial in 65.4% of cases. Seizures were present at presentation in 15.1% of patients. AED therapy was prescribed in 84.9% of patients, most commonly phenytoin. Seizure prevalence was higher among patients with supratentorial tumors and low-grade gliomas compared with infratentorial and high-grade tumors (p = 0.028). Surgical intervention was associated with improved early postoperative seizure control and reduced need for AED escalation. No seizures were documented among patients who received radiotherapy or chemotherapy at presentation. Seizure prevalence in this pediatric brain tumor cohort was relatively low; however, AED utilization was high, reflecting common prophylactic prescribing practices. Seizure burden and AED response varied according to tumor location and grade. These findings highlight the importance of individualized seizure management strategies and the need for prospective studies to optimize AED use in pediatric neuro-oncology.
Keywords: Pediatric Brain Tumors, Tumor-Associated Epilepsy, Antiepileptic Drugs.

Introduction

Seizures are common and serious complications of brain tumors, especially among pediatric patients, causing significant long-term morbidities and lower quality of life [1]. The pediatric brain is more vulnerable to epilepsy, as it is still involved in the growth and development process [2]. Brain neoplasms can cause epilepsy in multiple ways (e.g., peri-lesional edema, cortical irritation, or hemorrhage) [3,4]. The prevalence of seizures among children with brain tumors, as reported in the literature, is extensively variable, ranging from 15% to 34% [5–7].

Tumor-induced seizures in children differ from adult brain tumor-associated seizures in multiple ways, including the biochemical basis [8], clinical course [5,9], and response to drugs (AEDs) [10,11]. Several factors have been linked with seizures in brain tumors, including the histopathology, location, and size of the tumor[12–14]. Multiple studies have linked Low-grade gliomas and dysembryoplastic neuroepithelial tumors with a higher frequency of seizures among patients as the presenting symptoms[15]. Furthermore, supratentorial lesions are more commonly associated with higher seizure prevalence[7]. Anti-epileptic drugs (AEDs) are the first line of treatment for tumor-associated epileptic seizures [16]. However, administering the correct AED in the right dose requires careful consideration of the complex interplay of the patient-specific factors, tumor characteristics, and type of seizures with which the patient presents [17]. This complexity is further compounded in pediatric patients by the potential impact of the AED on the neurodevelopment of the child. Some AEDs are more adopted than others in this age subgroup due to their relative "neuro-safe" profile, like levetiracetam; however, the literature is inconclusive on the subject, and the available data is limited [18]. Indeed, it may not be plausible to reach the singular "definitive" AED of choice because not all patients show the same response pattern to any of the commercially available AEDs, as some of them may very well require multiple lines of AEDs or even require general anesthesia to fully subdue the seizures, as is the case with status epilepticus, although it is not very common in tumor-associated seizures [19].

The clinical course of tumor-associated seizures is dynamic and very often challenging; however, the data on the subject remains scarce and variable[4].

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Understanding the burden of tumor-associated seizure (i.e., prevalence, presentation, and outcomes) and AED utilization patterns in pediatric patients is a critical step in improving the existing protocols for seizure control to decrease the treatment duration, which in turn would minimize the potential for detrimental effects of the seizures on the neurodevelopmental process of the child and also the side effects of the AEDs used. The aim of this study is to evaluate seizure prevalence, AED usage patterns, and changes in AED requirement before and after treatment in a specialized neurology center in Tripoli, Libya.

Methods

This retrospective cohort study was conducted at a specialized pediatric neurology center in Tripoli, Libya. The study included 53 pediatric patients aged ≤16 years with brain tumors who underwent neurosurgical intervention, regardless of tumor histology or grade. Patients with incomplete records regarding seizure history or antiepileptic drug (AED) use were excluded.
Medical records were reviewed by the investigators, and data were extracted using a standardized form. Collected variables included demographic information (age and sex), tumor characteristics (location classified as supratentorial or infratentorial, histopathological diagnosis, and WHO tumor grade when available), and seizure-related variables. Seizure data included presence or absence of seizures at presentation, seizure type according to International League Against Epilepsy (ILAE) classification, and AED utilization patterns, including the number of distinct AED lines required and the type of medications used before and after surgery. AED response was defined as seizure freedom during the first postoperative week without escalation or addition of medications.
The primary outcomes were seizure prevalence and AED utilization patterns, while the secondary outcome was the patient's response to AED therapy. Postoperative seizure and AED data were assessed for up to seven days following surgery to capture the early postoperative period. Data analysis was performed using Jamovi for Windows. Descriptive statistics were reported as frequencies and percentages for categorical variables, and means with standard deviations for continuous variables. The McNemar test was used to compare paired categorical outcomes, specifically AED requirements before versus after surgery, with a two-sided significance threshold of $p < 0.05$. The study protocol was reviewed and approved by the Scientific Affairs Committee at Dar Alsalam Hospital. Informed consent was obtained from the families or legal guardians of all patients included in the study, and all data were handled to ensure complete anonymity and confidentiality.

Results

A total of 53 pediatric patients with brain tumors were included in the study. The mean age at diagnosis was 9.23 years (±4.9**)**, and 77.4% were male. Tumor locations were predominantly supratentorial in 35 patients (65.4%) and infratentorial in 18 patients (36.5%). The distribution of tumor grades according to the WHO classification was as follows: the most frequent tumor grade was grading II tumor (37.1%), followed by grade I (28.6%), and grades III-IV were found in 6 cases each (17.1%). The most common histological subtypes were medulloblastoma (25.5%), followed by astrocytoma (17.6%), and ependymoma (17.6%).

Table 1 Demographics and Tumor Characteristics

Variable	**N (%) or mean ± SD**
Total patients	53
Age (years)	9.23 ± 4.9
Male sex	41 (77.4)
Tumor location: Supratentorial	35(65.4)
Tumor location: Infratentorial	18(34.6)

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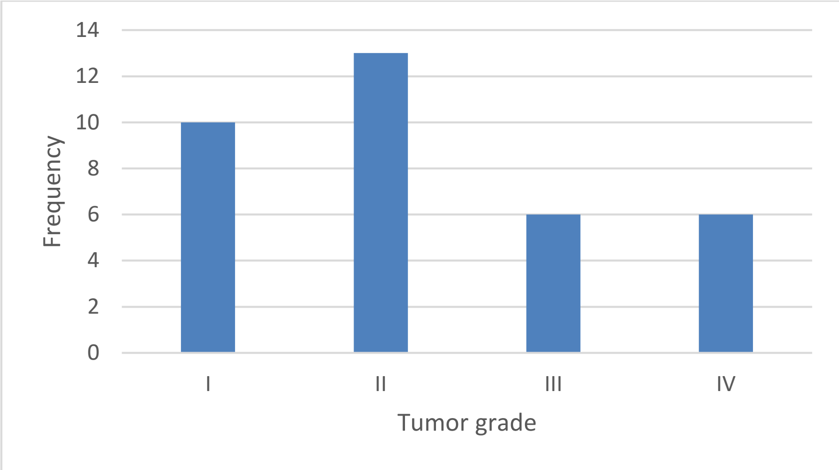

Figure 1 Tumor grade distribution

Seizures were present at presentation in 8 patients (15.1***%). 84.9% of patients were receiving at least one AED before and after the operation. The most commonly prescribed AEDs were phenytoin (75.5***%). In 4 cases, phenytoin was not ideal; in 2, levetiracetam was given alone, and in the other 2, it was given in combination with Tegretol. There was a single case that was treated with Depakine.

When stratified by tumor grade, location, or histology, seizure prevalence and AED utilization patterns varied. For instance, patients with low-grade gliomas had a seizure prevalence of 22.9**%** compared to 0% in high-grade tumors. Supratentorial tumors were associated with a higher seizure frequency (22.9%) than infratentorial tumors (0%) (Figure 2).

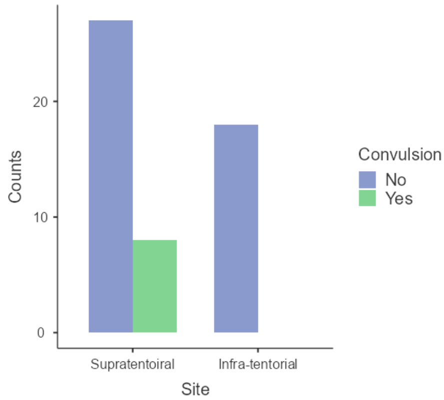

Figure 2. Seizure Distribution According to Tumor Site

No seizures were documented among the 6 patients who received radiotherapy (p =0.28), nor did the 5 patients who received chemotherapy have seizures at the time of presentation (p = 0.425) (Figure 3).

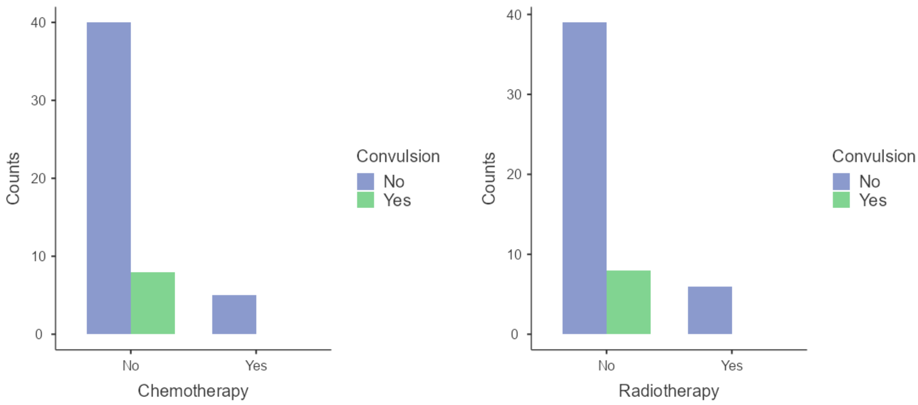

Figure 3. Seizure-Free Outcomes in Radiotherapy and Chemotherapy Groups

Discussion

This study provides insight into the burden of tumor-associated seizures and antiepileptic drug (AED) utilization patterns among pediatric brain tumor patients treated at a specialized neurology center in Tripoli, Libya. In this cohort, seizures were present at diagnosis in 15.1% of patients, a prevalence that falls at the lower end of the wide range reported in the literature. Despite the relatively low seizure prevalence at

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presentation, the majority of patients received AED therapy, reflecting prevalent real-world prescribing practices in pediatric neuro-oncology and underscoring the complexity of seizure management in this population. The observed seizure prevalence is lower than that reported in many pediatric series, where rates between 15% and 34% have been described. This discrepancy may be partially explained by the tumor spectrum in the present cohort, which included a substantial proportion of infratentorial tumors and high-grade lesions, both of which are generally associated with lower epileptogenic potential compared with supratentorial low-grade tumors [20].
Consistent with existing evidence, seizures were more frequent among patients with supratentorial tumors[20]. These findings support the established concept that cortical involvement and slower-growing tumors confer greater epileptogenicity, likely through chronic cortical irritation, disruption of inhibitory neuronal networks, and tumor-related alterations in the peritumoral microenvironment [21,22]. In contrast, no seizures were observed among patients with infratentorial or high-grade tumors at presentation, highlighting the importance of tumor location and biology in seizure risk stratification [23]. A notable finding of this study is the high rate of AED utilization relative to seizure prevalence, with nearly 85% of patients receiving AED therapy before and after surgery. This suggests a widespread use of prophylactic AEDs in pediatric brain tumor patients, even in the absence of documented seizures. While prophylactic AED use remains controversial—particularly given the lack of robust evidence supporting its routine application—this practice likely reflects clinician concern regarding perioperative seizures, limited access to continuous electroencephalographic monitoring, and the potentially catastrophic consequences of uncontrolled seizures in children with intracranial tumors [24].
Phenytoin was the most commonly prescribed AED in this cohort, reflecting its availability, clinician familiarity, and historical role in neurosurgical practice. However, the need to substitute or supplement phenytoin with newer agents such as levetiracetam in selected cases underscores emerging recognition of the limitations of older AEDs [25], particularly with respect to drug–drug interactions, adverse effect profiles, and neurocognitive impact [26]. No seizures were documented in the patients who received chemotherapy or radiotherapy. These two modalities are known to reduce seizure burden among patients with brain tumors [27]. The findings emphasize the variations of tumor-associated seizures between patients and support the need for individualized seizure management strategies based on tumor characteristics, patient factors, and evolving evidence.

Conclusion

Tumor-associated seizures represent a clinically important but heterogeneous complication of pediatric brain tumors. In this retrospective cohort from a specialized pediatric neurology center, seizures were present at diagnosis in a minority of patients, with higher prevalence observed among those with supratentorial and low-grade tumors. Despite the relatively low seizure burden at presentation, antiepileptic drugs were prescribed in the majority of patients, reflecting widespread prophylactic use in clinical practice. Surgical intervention was associated with improved early postoperative seizure control and reduced need for escalation of antiepileptic therapy, supporting the role of tumor resection in mitigating epileptogenic burden. However, the high rate of AED utilization relative to seizure prevalence highlights ongoing uncertainty regarding optimal AED prescribing strategies in pediatric brain tumor patients. These findings underscore the need for individualized seizure management approaches that account for tumor characteristics, patient-specific factors, and potential neurodevelopmental implications of antiepileptic therapy. Prospective studies with standardized protocols and longer follow-up are required to define better evidence-based guidelines for seizure prophylaxis and treatment in this vulnerable population.

Conflict of interest. Nil

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