Original Article

Histopathologic Characterization of Brain Tumour Related Epilepsy and Review of Pathogenic Mechanisms

Sujata Chaturvedi[1,*], Ishita Pant[1], Kavita Rawat[1], Pragyan Sarma[2]

[1]Department of Pathology, Institute of Human Behaviour and Allied Sciences, Delhi, India
[2]Department of Neurosurgery, Vardhman Mahavir Medical College and Safdarjung hospital, Delhi, India

***Correspondence:** drsujatacv@gmail.com

DOI
10.21276/apalm.3550

Article History
Received: 16-03-2025
Revised: 20-06-2025
Accepted: 17-07-2025
Published: 20-08-2025

How to cite this article
Chaturvedi S, Pant I, Rawat K, Sarma P. Histopathologic characterization of brain tumour related epilepsy and review of pathogenic mechanisms. Ann Pathol Lab Med. 2025;12(8):A232-A239.

Abstract

Background: Brain tumour related epilepsy (BTRE) may occur in 40% to 60% of brain tumours. Its incidence is highly dependent on the location and type of tumour. With the underlying molecular mechanisms getting unravelled, treatment strategies are being designed accordingly. This retrospective study was undertaken to profile the histopathology samples received in our department with the clinical diagnosis of brain tumour related epilepsy.
Methods: A retrospective study of 193 brain tumour related epilepsy cases received over a period of last 10 years (2014-24) was done. Histopathology records were revisited and the details of tumour type and grade, location and demographic details were mapped and analysed. These findings have been presented and brief review of molecular mechanisms in brain tumour related epilepsy has also been incorporated where applicable.
Results: Of the 193 seizure associated brain tumour cases, 182 (94.30%) comprised of primary central nervous system tumours and 11 (5.7%) comprised of tumours metastatic to the brain. In our series, maximum cases were found in young male adults within the age group of 21-40 yrs. Commonest location was intraparenchymal (frontal) and commonest tumour was adult type diffuse glioma.
Conclusion: Collation of clinical, demographic and histopathology findings is necessary in brain tumour related epilepsy for identifying the common patterns and developing management strategies accordingly.

Keywords: Brain tumour-related epilepsy; histopathology; central nervous system; seizures

Introduction

Epileptic seizures due to brain tumours have been described since the 19th century. The direct relationship between seizures and brain tumour was first reported by John Hughling.[1] Epilepsy plays a very important role in adversely affecting the quality of life in patients already coping with brain tumours. It represents the most common co-morbidity in patients with diffuse low-grade gliomas, as much as in >80% of cases as compared with high grade gliomas and brain metastases.[2] Brain tumours in frontal, parietal and temporal lobes are associated with a higher risk of seizures compared to other locations.[3] The presence of seizures in patients with brain tumours implies favourable and unfavourable factors. New-onset seizures represent an early warning sign for the presence of a brain tumour and count as a good prognostic factor for survival; however, seizure onset at a later time, is frequently associated with neurosurgical procedures or progression of the lesion.[4]

The pathogenesis of tumour related epilepsy remains poorly understood. This review attempts to summarize the possible mechanisms of tumour-related epilepsy. This knowledge may provide guidance in the search for newer strategies for the surgical and medical treatment of tumour-related epilepsy.

Materials and Methods

A retrospective analysis of histopathology records available in our department was done for the last ten years. This included histopathology requisition forms, histopathology reports and, in some cases, copies of radiology reports. A total of 193 brain tumour cases associated with seizures were retrieved from department's last 10-year records (2014-2024). Details available for these cases were analyzed for tumour location, type and grade of tumour and demographic profile. Broad classification category of the tumour (WHO 2021) was taken into account while analyzing our seizure associated cases. Tumours received prior to 2021 classification were reclassified as per 2021 classification in order to maintain uniformity of nomenclature. Since it was a retrospective analysis of records and no linked identifiers were used, the same was exempted from Ethics Review as per ICMR guidelines.

Results

Of the 193 brain tumour related epilepsy cases, histologically reported upon during last 10 years, 182 (94.30%) comprised of primary central nervous system tumours and 11 (5.7%) comprised of tumours metastatic to the brain. Besides seizures, there were complaints of headache, altered behaviour, vomiting, blurring of vision and hearing loss. Age and gender distribution of these 193 cases is given in Table 1. Maximum cases were in the age group 21-40 yrs, followed by 41-60yrs, 61-80 yrs, 0-12 and least common in age group >81 yrs. [Table 1] Overall, brain tumour related epilepsy was 1.6 times more common in males (118/193) in comparison to females (75/193). Location, as available in clinical notes mentioned on histopathology requisition form is detailed in Table 2. Maximum cases were located in the cerebral hemispheres and, in some, more than one lobe was involved. Frontal lobe was most frequently involved (82/193) followed by frontoparietal location (21/224), temporal (19/193) and then parietal (16/193). [Table 2] Histopathological typing of epilepsy related tumours has been summarized in [Table 3]. Location wise histopathology in all 193 cases reported is detailed in [Table 4]. Figures 1, 2 and 3 give a pictorial representation of histopathology diagnoses and age distribution for the major cerebral locations. Cerebral locations formed the major group of brain tumour related epilepsy and in these locations, majority of the cases occurred in age group 21-40 years and adult type diffuse gliomas were most frequently seen. [Figure 1-4]

Table 1: Distribution of cases according to age and gender

Age (Years)	Male	Female
0-20	17	8
21-40	58	35
41-60	35	28
61-80	7	4
>80	1	0
Total	**118**	**75**

Table 2: Distribution of cases according to location

Location	Number of cases
Frontal	82
Temporal	19
Parietal	16
Cerebellum	5
Others	30
Lesions involving >1 Lobe	41
TOTAL	**193**

Discussion

Occurrence of epilepsy in patients with CNS tumours is challenging to manage and contributes significantly to the burden of morbidity and already deteriorating quality of life. In order to identify potential therapeutic targets and develop strategies there is a need to map CNS tumours vis à vis epilepsy and also understand the underlying mechanisms involved in brain tumour related epilepsy.

With the progress of research methods and technologies, brain tumour related epilepsy has been deeply explored, especially in terms of its pathogenesis and the corresponding brain neural network. However, there is still a lack of sufficient attention and systematic research on the pathogenesis, clinical diagnosis and treatment of brain tumour related epilepsy. Through this

Table 3: CNS tumours associated with epilepsy

CNS Lesions	Number of cases
Adult-type diffuse glioma	124
Circumscribed astrocytic glioma	4
Glioneuronal and neuronal tumor	5
Ependymal tumors	3
Embryonal tumors	1
Meningioma	37
Sellar region tumors	3
Cranial and paraspinal nerve tumors	1
”Mesenchymal, non-meningothelial tumors”	2
Haematolymphoid tumors involving the CNS	2
Metastatic carcinoma	11
Total	**193**

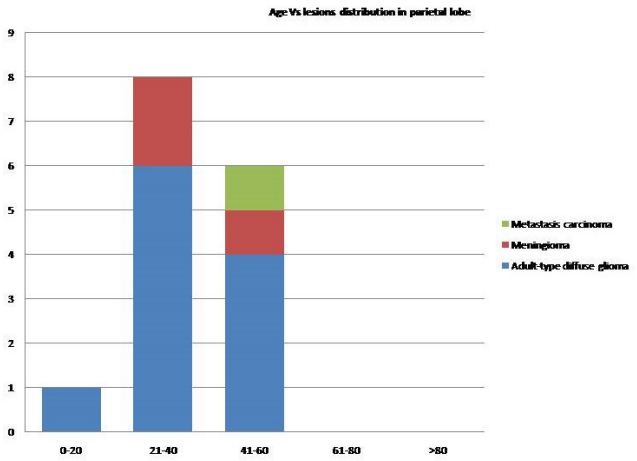

Figure 1: Showing age vs lesions distribution in frontal lobe

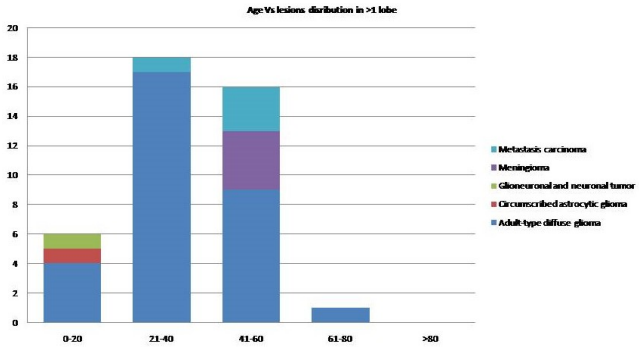

Figure 2: Showing age vs lesions distribution in parietal lobe

retrospective study of 193 brain tumour patients, correlation between age, sex and histopathological type and different WHO tumour grades of patients with brain tumour related epilepsy were tried to be established along with brief pathophysiology of brain tumour related epilepsy.

Various studies have showed that age, sex, tumour location, histopathological type and WHO grade were the influencing factors of glioma with brain tumour related epilepsy and the results of our study were also consistent with the previous studies. Our study showed that the risk of brain tumour related epilepsy was higher in young men adults than in women and the risk of seizure decreased with age, which shows concordance with the study by Wang et al as they also observed in their study that risk of brain tumour related epilepsy is higher in young male than in female and the risk of seizure also decreased with age.[5]

Gliomas can occur in any part of the brain. However, frontal, temporal, parietal gliomas are most likely to be associated

Table 4: Location, histological subtypes and grade of epilepsy associated tumors (n-193)

Location, Histological Subtypes	M	F	Grade 1	Grade 2	Grade 3	Grade 4
Frontal (Male: 57, Female: 25)						
Adult-type diffuse glioma	47	16	0	36	17	10
Circumscribed astrocytic glioma	0	1	1	0	0	0
Glioneuronal and neuronal tumor	2	0	2	0	0	0
Ependymal tumors	0	1	0	1	0	0
Meningioma	6	6	12	0	0	0
Haematolymphoid tumors involving the CNS	0	1	0	0	0	1
Metastatic carcinoma	2	0	0	0	0	2
Temporal (Male: 11, Female: 8)						
Adult-type diffuse glioma	9	2	0	6	5	0
Circumscribed astrocytic glioma	1	0	1	0	0	0
Glioneuronal and neuronal tumor	0	1	1	0	0	0
Ependymal tumors	1	0	0	1	0	0
Meningioma	0	1	1	0	0	0
”Mesenchymal, non-meningothelial tumor”	0	1	1	0	0	0
Haematolymphoid tumors involving the CNS	0	1	0	0	0	1
Metastatic carcinoma	0	2	0	0	0	2
Parietal (Male: 8, Female: 8)						
Adult-type diffuse glioma	6	6	0	7	5	0
Meningioma	1	2	3	0	0	0
Metastatic carcinoma	1	0	0	0	0	1
Cerebellum (Male: 3, Female: 2)						
Circumscribed astrocytic glioma	0	1	1	0	0	0
Embryonal tumor	0	1	0	0	0	1
Meningioma	1	0	1	0	0	0
”Mesenchymal, non-meningothelial tumor”	1	0	1	0	0	0
Metastatic carcinoma	1	0	0	0	0	1
Other (Male: 20, Female: 10)						
Adult-type diffuse glioma	5	3	0	3	1	4
Glioneuronal and neuronal tumor	1	0	1	0	0	0
Ependymal tumors	1	0	0	1	0	0
Meningioma	10	6	13	3	0	0
Sellar region tumor	2	1	3	0	0	0
Cranial and paraspinal nerve tumor	1	0	1	0	0	0
>1 Lobe (Male: 26, Female: 15)						
Adult-type diffuse glioma	18	12	0	14	11	5
Circumscribed astrocytic glioma	1	0	1	0	0	0
Glioneuronal and neuronal tumor	1	1	1	1	0	0
Meningioma	2	2	3	1	0	0
Metastatic carcinoma	4	0	0	0	0	4

with brain tumour related epilepsy, while occipital and supratentorial gliomas are less likely to have brain tumour related epilepsy.[6] Our results showed that brain tumour related epilepsy was most likely to occur in gliomas involving the frontal lobe and multiple lobes. Human language, consciousness, and motor functions are closely related to Frontal lobe, temporal lobe and parietal lobe, thus lesions in these areas could cause abnormal discharge of these brain functional areas, leading to epilepsy. In studies by Weller et al and Chen et al showed that low grade tumours like diffuse astrocytoma and oligodendroglial tumours were common tumours located in the cerebral hemisphere of young patients (frontal, temporal and parietal lobes were common) and epilepsy was one of the most common clinical symptoms.[6, 7]

In our study also, most common locations were the cerebral hemispheres and most common tumours were adult type diffuse gliomas which presented with epilepsy as most common symptom and thus shows concordance with other studies.

Seizures were more common in low-grade gliomas than in high-grade gliomas as showed in various previous studies by Pallud and Van et al.[8, 9] The results were similar to those in our study, which showed that brain tumour related epilepsy was present in lower grade gliomas (like adult type diffuse astrocytoma) at 63% and in higher grade gliomas at 22%. This

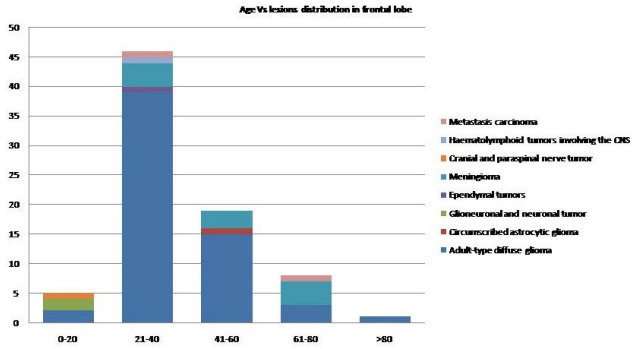

Figure 3: Showing age vs lesions distribution in temporal lobe

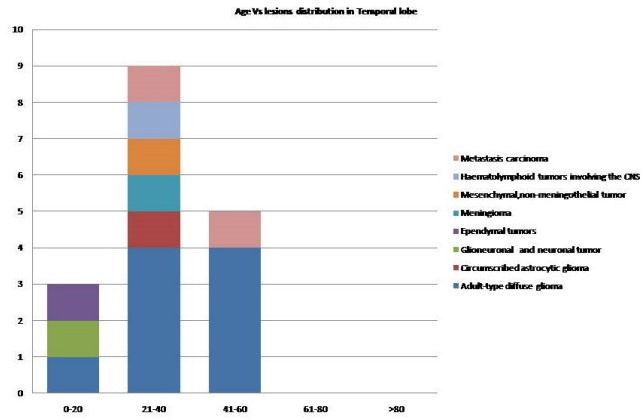

Figure 4: Showing age vs lesions distribution in ¿1 lobe

may be related to the faster growth rate of high-grade glioma, which will cause severe ischemic and hypoxic damage to the surrounding tissues and tumour tissues themselves, making them less likely to form epileptogenic foci. Other studies had suggested that high grade gliomas release excessive amounts of the neuroexcitatory transmitter glutamate, which was neurotoxic and could lead to neuronal death in large quantities, so high-grade gliomas were less likely to have seizures.[10]

Current studies have indicated that epilepsy is associated with many factors and they can be broadly divided into 1. tumour related and 2. related to factors in the peritumoural area.[2] A brief review is presented below:

Tumour related factors: Many tumour related factors have been implicated in brain tumour related epilepsy. Primary among these are tumour location, histology, genetic factors and alteration in blood brain barrier. A brief overview of these factors are made here. In a study by Seidel et al brain tumours located in frontal, parietal, temporal and limbic regions are associated with a higher risk of seizures.[2] In our series too, the maximum number of cases were located in the frontal or fronto-parietal regions followed by temporal and parietal. Besides macroscopic localization, the histologic localization also has a bearing on occurrence of epilepsy in patients harbouring brain tumour. Location and proximity to the cortical grey matter are considered important factors in the development of brain tumour related epilepsy,[4] subcortical location with tumour growth in deep midline structures is less likely to result in seizures.[11] Correlation has also been found between location and histology. Glioneuronal and astrocytic tumours are more commonly found in temporal locations and oligodendroglial tumours are more likely to be located in frontal lobe. Pathogenesis of seizures varies with histology. Tumours with well differentiated cells can overexpress neurotransmitter receptors and neuropeptides, compromising the balance between excitation and inhibition. The associated dysplastic disorganization of the adjacent cortex contributes to the mechanism of seizure generation. Slow-growing tumours could produce an epileptogenic milieu by partial deafferentation of cortical regions, thus causing a denervation hypersensitivity.[12, 13, 14] In contrast, the highly infiltrative nature of fast growing, high grade tumours damages the subcortical network essential for electrical transmission.[15] It can also be hypothesized that some commonalities may be there in the pathways of tumourigenesis and epileptogenesis in brain tumour related epilepsy.[16]

Disturbances in the integrity and functioning of blood brain barrier lead to neuronal hypersynchronization and epileptiform activity. Disruption of blood brain barrier seen in brain tumours also contributes to seizure activity. Low grade gliomas, which disrupt the blood brain barrier but do not destroy the subcortical network are more likely to be associated with seizures.

Genetic factors are also known to play a role in brain tumour related epilepsy. Genes such as Leucine-rich glioma-inactivated 1 (LGI1) a tumour suppressor gene and Phosphatase and tensin homolog (PTEN) critical for inhibition of oncogenic

transformation have been associated with gliomas and epilepsy. Genomic and chromosomal instability may also make the tumour epileptogenic.[17]

Peri tumoural region: As for the tumour related aspects contributing to brain tumour related epilepsy, certain changes have been observed in the peri tumoural tissue which play a role in brain tumour related epilepsy. This region shows significant changes as compared to the normal brain tissue which may, likely, contribute to brain tumour related epilepsy. N-acetyl aspartate is a neuronal marker and its concentration correlates with neuronal density and neuronal function. N-acetyl aspartate decrease is observed in many diseases like tumour, stroke, multiple sclerosis, epilepsy, hyp-/anoxia, inflammation, dementia and trauma, and higher levels have been recorded during brain development and maturation Magnetic Resonance Spectroscopy has shown lowered levels of N-acetyl aspartate in peri tumoural areas. Low frequency magnetic activity has also been recorded on magneto encephalography in the peri tumoural regions.[18] Research related to examining functional connectivity and brain network topology has shown increased theta band connectivity in brain tumour patients with epilepsy.[19] Studies have been made comparing the peri tumoural region in patients with and without epilepsy and significant differences have been noted. Persistent neurons in the white matter, inefficient neuronal migration and changes in synaptic vesicles have been noted in peri tumoural region of brain tumour related epilepsy cases.[20] Peri tumoural pyramidal neurons have been reported to have decreased inhibitory and increased excitatory synapses and these may have a role in epileptogenesis.[21]

Many metabolic changes occur in the tumoural and peri tumoural region which may be contributing to brain tumour related epilepsy. Decreased perfusion within the tumour leads to hypoxia and elevated metabolism of tumour cells because of increased proliferation causes acidosis. This, along with direct compression, causes hypoxia and acidosis in the peri tumoural region also. Glial cell swelling and damage occurs making the astrocytic cell membrane permeable to inward flow of sodium and risk of epilepsy. Increased metabolism of proliferating tumours also reflected by increased lactate production detected by Magnetic Resonance Imaging and Spectroscopy and Positron Emission Tomography.[22]

As is known, ion channels provide the basis for the nervous system's intrinsic electrical activity. They are involved in the unique biology of gliomas pertaining to peri tumoural pathology and seizures, diffuse invasion, and treatment resistance.[23] Elevated sodium and calcium levels in the extracellular peri tumoural space may contribute to neuronal hyperexcitability. Acidic microenvironment facilitates sodium channel activation and inward movement of sodium ions.[24] Similarly potassium channels, too, are known to play a significant role in ictogenicity. Of the approximately 80 potassium channel types, about 10% are known to be associated with epilepsies if genetically mutated. They can impact from the direct control of neuronal excitability or indirect effects via metabolism.[25] Increased densities of calcium (Ca) channel have been reported in epileptic tissue. Extracellular potassium concentrations impact membrane potential and can lead to epilepsy.[26] Magnesium (Mg2+) stabilizes neuronal excitability by blocking Ca influx. Decreased extracellular concentrations of Mg can also lead to epileptiform discharges. Chloride (Cl) dysregulation also occurs in neuronal networks contributing to epilepsy.[27]

Imbalance between excitatory and inhibitory neurotransmitters may lead to brain tumour related epilepsy. Glutamate is an excitatory and GABA an inhibitory neurotransmitter. Glutamate acts on postsynaptic membranes by interacting with ionotropic/metabotropic receptors leading to discharge of excitatory signals. Increase in number of such receptors has been seen in peri tumoural areas of gangliogliomas and Dysembryoplastic Neuroepithelial Tumours with associated brain tumour related epilepsy.[28] Receptors for GABA, which can inhibit neuronal firing, have been found to be down regulated. In peri tumoural tissue of brain tumour related epilepsy cases reduced GABA-ergic neurotransmission has been noted.[29]

There are other amino acid transmitters also which, supposedly, play a role in tumoural epileptogenesis. Kynurenic acid, a metabolic product of L-tryptophan has an anticonvulsant and antiexcitotoxic effect by acting as an antagonist to Glutamate receptors. Gliomas have been to shown to have lower levels of kynurenic acid leading to disinhibition of excitatory glutamate receptors like NMDA.[30] Gliomas have also been shown to have lower levels of noradrenaline (NA) and serotonin which are metabolic derivatives of amino acid L-tyrosine and tryptophan respectively. NA and serotonin have an intrinsic inhitory and anti epileptogenic effect.[29] Their lower levels seen in many tumours contributes to brain tumour related epilepsy.

Activation of both, innate and adaptive, immunity mechanisms and induction of associated inflammatory processes involving astrocytic and microglial cells has been seen in brain tumour related epilepsy especially those associated with glioneuronal tumours.[31] The inflammatory cascades lead to release of many types of cytokines. They can have pro or anti inflammatory effect. Interleukin (IL)-1β and IL-8 are proinflammatory cytokines that activate additional cytokine cascades and increase seizure susceptibility and organ damage, whereas IL-1 receptor antagonist and IL-10 act as anti-inflammatory cytokines that have protective and anticonvulsant effects.[32] Cytokines also contribute to epileptogenesis by acting through Gap Junctions (GJs). Gap junctions are ubiquitously expressed in neurons and glia forming a functional syncytium that extends throughout the brain. They are crucial membrane channels and play an important role in cell-to-cell communication between neuron-neuron, astrocyte-astrocyte and neuron-astrocyte. Connexins (Cx) are the major component of gap junctions. The major types expressed in CNS are: Cx32, Cx36 and Cx26 in neurons; Cx43, Cx30, Cx30, Cx45, Cx40 and Cx32 in astrocytes and Cx32 and Cx45 in oligodendrocytes. Inflammation associated cytokines are known to act on gap junctions with some

causing their upregulation. This increases the number of new electrical synapses and electrical conductivity leading to expansion of synchronized firing of neurons and epilepsy. High expression of Cx43 has been reported in low grade gliomas and their peri tumoural region.[33] In contrast, most high grade astrocytomas exhibited a reduction in Cx43 immunoreactivity. Cx32 immunoreactivity has been observed in the neuronal component of glioneuronal and oligodendroglial tumours.[13] In our series, though immunolabeling for connexins was not done but brain tumour related epilepsy was found to be more in low grade tumours.

The importance of mapping brain tumour related epilepsy and understanding the underlying mechanisms has a bearing on treatment strategies. Approximately one third of patients with brain tumour related epilepsy are resistant to anti-epileptic drugs. The possible reasons for this can be the biochemical milieu of tumoural and peri tumoural regions, drug interaction with chemotherapeutic drugs and increased expression of multidrug resistance-related proteins in tumours.

Since brain tumour related epilepsy involves not only the tumour related factors but also the peri tumoural ones, it needs to be assessed whether lesionectomy or extended lesionectomy is needed. Of the traditional anti-epileptic drugs, valproic acid is thought to inhibit epileptic discharges by stabilizing neuronal membranes and enhancing GABA transmission. However, no role of prophylactic anti-epileptic drugs has been seen in preventing brain tumour related epilepsy.[34] Newer anti-epileptic drugs like levetiracetam, lamotrigine, topimarate, gabapentin, and pregabalin bring many advantages in brain tumour related epilepsy management as they have the ability to target the pathogenic mechanisms briefed in the preceding paragraphs. They can affect neurotransmission causing GABA receptor agonism &/or NMDA receptor antagonism. Ion channel modulation can also be achieved by newer anti-epileptic drugs. Some studies have recommended use of levetiracetam and lamotrigine as first line anti-epileptic drugs in brain tumour related epilepsy as they not only act through mechanisms mentioned above but also have lesser drug interactions with chemotherapeutic agents.[35]

Conclusion

Even though epilepsy is commonly seen in patients with brain tumours, it is only recently that the underlying mechanisms of brain tumour related epilepsy are being unravelled and being used to develop treatment strategies. Our analysis of cases of brain tumour related epilepsy received in our department over the last 10 years was carried out to collate their clinical and histological features and present a brief update about the underlying mechanisms and basis of treatment strategies.

Acknowledgements: None

Funding: Nil

Competing Interests: There is no conflict of interest involved.

References

1. Slegers RJ, Blumcke I. Low-grade developmental and epilepsy associated brain tumors: a critical update. Acta Neuropathol Commun 2020; 8: 27
2. Seidel S, Wehner T, Miller D. Brain tumor related epilepsy: pathophysiological approaches and rational management of antiseizure medication. Neurol Res Pract 2022; 4: 45
3. Zhang J, Yao L, Peng S, Fang Y, Tang R, Liu J. Correlation between glioma location and preoperative seizures: A systematic review and meta-analysis. Neurosurgical Review 2018; 42(3):603-618
4. You G, Sha Z, Jiang T. The pathogenesis of tumour-related epilepsy and its implications for clinical treatment. Seizure 2012; 21(3):153-59
5. Wang Z, Yang W, Wang Y, Aili Y, Wang Z. Correlation of Clinicopathological Factors with Brain Tumour-Related Epilepsy in Glioma. Dis Markers. 2022 Sep 30:2022:4918294
6. Chen DY, Chen CC, Crawford JR, Wang SG. Tumor-related epilepsy: epidemiology, pathogenesis and management. J Neurooncol 2018; 139(1):13–21
7. Weller M, van DBM, Tonn JC, Stupp R, Preusser M, Cohen JME et al. European Association for Neuro-Oncology (EANO) Task Force on Gliomas. European Association for Neuro-Oncology (EANO) guideline on the diagnosis and treatment of adult astrocytic and oligodendroglial gliomas. Lancet Oncol 2017; 18(6):315-329
8. Pallud J, McKhann GM. Diffuse Low-Grade Glioma-Related Epilepsy. Neurosurg Clin N Am. 2019;30(1):43-54
9. Van BMS, Wilms EB, Vecht CJ. Epilepsy in patients with brain tumours: epidemiology, mechanisms and management. Lancet Neuro. 2007; 6(5):421-430
10. Sørensen MF, Heimisdóttir SB, Sørensen MD, Mellegaard CS, Wohlleben H, Kristensen BW et al. High expression of cystine-glutamate antiporter xCT (SLC7A11) is an independent biomarker for epileptic seizures at diagnosis in glioma. J Neurooncol 2018;138(1):49-53
11. Chang EF, Potts MB, Keles GE, Lamborn KR, Chang SM, Barbaro NM et al. Seizure characteristic and control following resection in 332 patients with low grade gliomas. Journal of neurosurgery 2008; 108(2):227-235
12. Wolf HK, Roos D, Blumcke I, Pietsch T, Wiestler OD. Perilesional neurochemical changes in focal epilepsies. ActaNeuropathol 1996; 91: 376-384

13. Aronica E, GorterJA, Redeker S. Distribution, characterization and clinical significance of microglia in glioneuronal tumours from patients with chronic intractable epilepsy. NeuropatholApplNeurobiol 2005; 31:280-289
14. Van Breemen MS, WilmsEB, Vecht CJ. Epilepsy in patients with brain tumours: epidemiology, mechanisms, and management Lancet Neurol 2007; 6:421-430
15. Norden AD, Blumenfeld H. The role of subcortical structures in human epilepsy. Epilepsy Behav 2002; 3:219-231
16. Berntsson SG, Malmer B, Bondy ML, Qu Mingqi, Smits A. Tumor-associated epilepsy and glioma: are there common gentic pathways? ActaOncol 2009;48: 955-963
17. Adhikari S, Walker BC, Mittal S. Pathogenesis and management of brain tumor related epilepsy. In: Gliomas [Internet]. Brisbane (AU): Exon Publications; 2021 Apr 30. Chapter 12
18. Chernov MF, KuboO, Hayashi M, Izawa M, Maruyama T, Usukura M, et al. Proton MRS of the peritumoral brain. J NeurolSci 2005; 228:137-142
19. Douw L, van Dellen E, de Groot M, Heimans JJ, Klein M, Stam CJ, Reijneveld JC. Epilepsy is related to theta band brain connectivity and network topology in brain tumor patients. BMC Neurosci. 2010 Aug 23;11:103.
20. Beaumont A, Whittle IR. The pathogenesis of tumour associated epilepsy. ActaNeurochir Wien 2000;142: 1-15
21. McNamara JO. Emerging insights into the genesis of epilepsy. Nature 1999;399: 15-22
22. Schaller B. Influences of brain tumor-associated pH changes and hypoxia on epileptogenesis. ActaNeurolScand 2005; 111: 75-83
23. Elias AF, Lin BC, Piggott BJ. Ion Channels in Gliomas-From Molecular Basis to Treatment. Int J Mol Sci 2023;24(3):2530
24. Kraft R, Basrai D, Benndorf K, Patt S. Serum deprivation and NGF induce and modulate voltage-gated Na (+) currents in human astrocytoma cell lines. Glia 2001; 34: 59-67
25. Boyle, Y., Johns, T. G., & Fletcher, E. V. (2022, October 1). Potassium Ion Channels in Malignant Central Nervous System Cancers. Cancers . MDPI.
26. Avoli M, Louvel J, Pumain R, Kohling R. Cellular and molecular mechanisms of epilepsy in human brain. ProgNeurobiol 2005;77: 166-200
27. Sontheimer H. An unexpected role for ion channels in brain tumor metastasis. ExpBiol Med (Maywood) 2008;233: 779-791
28. Aronica E, Yankaya B, Jansen GH, Leenstra S, Veelen CW, Gorter JA et al. Ionotropic and metabotropic glutamate receptor protein expression in glio-neuronal tumours from patients with intractable epilepsy. NeuropatholApplNeurobiol 2002; 27: 223-237
29. Haglund MM, Berger MS, Kunkel DD, Franck JE, Ghatan S, Ojemann GA. Changes in gamma-aminobutyric acid and somatostatin in epileptic cortex associated with low grade gliomas. J Neurosurg 1992;77: 209-216
30. Hwa GG, Avoli M. The involvement of excitatory amino acids in neocortical epileptogenesis:NMDA& non NMDA receptors. Exp Brain Res. 1991; 294: 691-695
31. Vezzani A, Lang B, Aronica E. Immunity and Inflammation in Epilepsy. Cold Spring Harb Perspect Med. 2015 Dec 18;6(2):a022699.
32. Youn Y, Sung K, Lee I. The role of cytokines in seizures: interleukin (IL)-1β, IL-1Ra, IL-8, and IL-10.Korean J Pediatr 2013; 56 (7): 271-274
33. Li Q, Li QQ, Jia JN, Liu ZQ, Zhou HH, Mao XY. Targeting gap junction in epilepsy: perspectives and challenges. Biomedicine & Pharmacotherapy 2019; 109: 57-65
34. Glantz MJ, Cole BF, Forsyth PA, Recht LD, Wen PY, Chamberlain MC et al. Practice parameter:anticonvulsant prophylaxis in patients with newly diagnosed brain tumors. Report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology 2000; 54: 1886-1893
35. Vecht CJ, van Breemen M. Optimizing therapy of seizures in-patients with brain tumors. Neurology. 2006 Dec 26;67(12 Suppl 4):S10-3.