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Review

Brain tumor-associated epilepsies in adulthood: Current state of diagnostic and individual treatment options

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Abstract

Brain tumors are one of the most frequent causes of structural epilepsy and set a major burden on treatment costs and the social integrity of patients. Although promising oncological treatment strategies are already available, epileptological treatment is often intractable and requires lifelong epileptological care. Therefore, treatment strategies must be adapted to age-related needs, and specific aspects of late-onset epilepsy (LOE) must be considered. The practical implementation of individual decisions from tumor boards and the current state of the art in scientific knowledge about pathological mechanisms, modern diagnostic procedures and biomarkers, and patient-individualized treatment options into practical epileptological disease management is a prerequisite.

This narrative review focuses on the current work progress regarding pathogenesis, diagnosis, and therapy. Exemplarily, interdisciplinary approaches for optimized individualized therapy will be discussed, emphasizing the combination of neurological-epileptological and oncological perspectives.

Introduction

25–60 % of brain tumor patients suffer from epileptic seizures [1], often requiring long-term patient care for the treatment of the brain tumor and epilepsy, respectively. Epilepsy in brain tumors often has a complex and multifocal etiology. Additionally, in most cases, the best treatment strategy for each patient must be individually adapted, especially to age-related needs. Advances in pathogenesis, diagnosis, and therapy will be discussed, and interdisciplinary approaches to optimized individual therapy will be exemplified.

Section snippets

Epidemiology

The incidence rate for all brain tumors is about 10.82 (95 % CI: 8.63–13.56) per 100,000 person-years [2]. According to Miller and coworkers, brain tumors occur in different age groups with the following distribution [3]:

- Birth - 14 years: 3.87/100,000.…
- 15-19 years: 2.60/100,000…
- 20-39 years: 3.39/100,000…
- 40-64 years: 7.96/100,000…
- 65 years: 21.26/100,000.…

The incidence of brain tumor-associated epilepsy is about 4 % [4]. Seizures are the first symptom in 35–50 % of brain tumors [5]. Supratentorial…

Pathogenesis of brain tumor-related epilepsy

The pathogenesis of brain tumor-associated epilepsy is complex. Important multifactorial mechanisms are briefly summarized, distinguishing between alterations of the peritumoral environment and intrinsic tumoral mechanisms. Peritumoral edema, ischemia, acidosis, inflammation, necrosis, and ionic disbalance are pathogenic. Furthermore, functional alterations of neurotransmitters (e.g., glutamate and GABA), as well as aberrant neuronal plasticity (BDNF) and altered transcription of genes (e.g.,…

Seizure semiology and frequency

Concerning potentially localizing indicators in seizure semiology, a study on 100 patients with tumor-related epilepsies in northern Italy showed initial seizures to be tonic-clonic in 48 %) without clear initial focal signs in more than half of the patients, focal motor (26 %), complex partial (10 %), and somatosensory (8 %). Most patients (60 %) had isolated seizures or a low seizure frequency at the onset of the disease, whereas high seizure frequencies or status epilepticus were observed in …

Diagnostics

Depending on the histological diagnosis, tumor grade, and localization, brain tumors cause persistent or progressive neuronal dysfunctions. The resulting motor, sensory, autonomic, and/or cognitive deficits usually guide the diagnostic workup and often allow an initial indication of the involvement of aberrant brain structures. For the epileptological workup, negative symptoms, in particular, can pose a challenge for the correct classification [19]. For example, there are anecdotes about…

Classification of brain tumors

Epilepsy-associated brain tumors are now considered in the context of a new hybrid classification, which has led to an integrated pheno-genotypic tumor classification. The following are analyzed: (a) tumor origin (mother tissue), (b) degree of malignancy, and (c) molecular characteristics to be assigned to the tumor entity (gene amplification, deletion, translocation, gene product, receptor). The molecular signature is important for diagnosis and treatment. One example is the study by Stone and …

Anti-seizure-medication (ASM)

In contrast to many other clinical seizure situations, treatment with an ASMs is indicated after the first seizure in brain tumors.

Previously used, so-called *older* ASM such as carbamazepine (CBZ), phenytoin (PHT), and phenobarbital (PB) have been replaced by mostly non-hepatic enzyme-inducing and neurocognitively less disadvantageous successor substances like Levetiracetam, Valproate, Lacosamide, Lamotrigine, Zonasemid, Perampanel, and Clobazam [[27], [28], [29], [30]]. GBP, Lacosamide,…

Seizures prognosis

Approximately 60 % of patients with brain tumor-associated epilepsy do not become seizure-free with the first ASM, and 40 % of these patients become seizure-free with a second ASM in monotherapy or polytherapy [28].

In the course of the entire treatment, patients with neuroepithelial tumors achieved long-term seizure control in 80 % and without ASM in 41 %; patients with ganglioglioma or oligodendroglioma were seizure-free in 90 %, with astrocytoma II (66 %) and pilocytic astrocytoma (61 %) [8]. …

Aging and brain tumor-associated epilepsies

With increasing age at the time of tumor identification, the risk of late-onset epilepsy (LOE) also increases. The work of Lin et al. determines higher-grade gliomas to be recognized at older ages [92]. The average age at diagnosis of WHO grade IV glioma was 46.3, WHO grade I gliomas 21.9 years, and WHO grade II, III 33.6, and 38.9 years, respectively. The appropriate classifications of age groups were 0–14 years (pediatric group), 15–47 years (youth group), 48–63 years (middle-aged group), and …

Psychosocial factors

Brain tumor-associated epilepsy can have a significant impact on the quality of life and the need to cope with the disease. Any physical or mental impairments and possible social restrictions on participation in normal life pose a major psychological and social challenge, making it difficult to maintain fitness to drive, work, and social activities.…

The future challenge of building interdisciplinary bridges

Improvements in diagnostics and individual treatment options for brain tumor-associated epilepsies should be accompanied by cooperative research approaches that integrate neurological, epileptological, and neuro-oncological expertise. The focus here would be on facilitating the transition of an oncological-epileptological assessment into neurological practice.

In view of the progressively increasing life expectancy, tumor-associated epilepsies in older age are also increasingly becoming the…

Conclusions

The diagnosis and treatment of brain tumor-associated epilepsy requires interdisciplinary cooperation due to its complexity. Today, high-resolution, non-invasive and invasive diagnostic procedures are available in epilepsy centers. Non-enzyme-inducing and mood-enhancing ASMs are preferred. Possible interactions of

ASMs with chemotherapeutics and other drugs can reduce the antitumoral and anti-ictal effects or lead to side effects. It is currently being investigated which ASMs inhibit both…

Key points

- New insight into pathogenesis…
- Antitumoral effects of ASM…
- Multimodal quantitative noninvasive presurgical evaluation…
- Histo-molecular marker for pre- and postoperative seizure prognosis…
- Age-related characteristics of tumor-associated epilepsies…

…

Declaration of competing interest

The authors declare no conflict of interest.…

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