Pediatric low-grade glioma

Epidemiology

Pediatric low-grade glioma epidemiology.

Classification

Pediatric Low-Grade Glioma Classification.

Clinical features

Low-grade gliomas, especially glioneuronal tumors, are a common cause of epilepsy in children. Seizures associated with low-grade pediatric tumors are medically refractory and present a significant burden to patients. Often, morbidity and patients´ quality of life are determined rather by the control of seizures than the oncological process itself and the resolution of epilepsy represents an important part in the treatment of LGGs. The pathogenesis of tumor-related seizures in focal LGG tumors is multifactorial, and mechanisms differ probably among patients and tumor types. Pediatric low-grade tumors associated with epilepsy include a series of neoplasms that have a pure astrocytic or glioneuronal lineage. They are usually benign tumors with a neocortical localization typically in the temporal lobes and other supratentorial locations. Gangliogliomas and dysembryoplastic neuroepithelial tumors (DNET) are the most common entities together with astrocytic gliomas (pilocytic astrocytomas and pleomorphic xanthoastrocytoma) and angiocentric gliomas, and dual pathology is found in up to 40% of glioneuronal tumors. The treatment of low-grade gliomas and associated epilepsy is based mainly on resection and the extent of surgery is the main predictor of postoperative seizure control in patients with a LGG. Long-term epilepsy-associated tumors (LEATs) tend to be well-circumscribed, and therefore, the chances for a complete resection and epilepsy control with a safe approach are very high. New treatments have emerged as alternatives to open microsurgical approaches, including laser thermal ablation or BRAF inhibitors. Future advances in identifying seizure-related biomarkers and molecular tumor pathways will facilitate targeted treatment strategies that will have a deep impact both in oncologic and epilepsy outcomes [1)].

Seizure-related biomarkers in PLGGs:

Seizures are a common symptom in children with low-grade gliomas, particularly those located in the temporal lobe or near the cortex. Researchers have been investigating various biomarkers that might predict seizure occurrence or help in management. Some key points include: a) BRAF alterations: The BRAF V600E mutation, common in PLGGs, has been associated with a higher likelihood of seizures in some studies. This could potentially serve as a biomarker for seizure risk. b) Glutamate signaling: Altered glutamate signaling has been implicated in both glioma growth and epileptogenesis. Markers of glutamate pathway dysregulation could potentially predict seizure risk. c) Inflammatory markers: Tumor-associated inflammation may contribute to seizure activity. Markers of inflammation in the

tumor microenvironment or cerebrospinal fluid might correlate with seizure risk. d) MicroRNAs: Some studies have explored the potential of specific microRNAs as biomarkers for seizure risk in gliomas, though this research is still in early stages for pediatric patients.

Molecular tumor pathways in PLGGs:

Understanding the molecular pathways involved in PLGGs has revolutionized our understanding of these tumors. Key pathways include: a) MAPK pathway: This is the most commonly altered pathway in PLGGs. Key alterations include:

BRAF alterations (V600E mutation, KIAA1549-BRAF fusion) NF1 mutations (in neurofibromatosis type 1-associated PLGGs) FGFR1 alterations

b) PI3K/AKT/mTOR pathway: Sometimes activated in conjunction with MAPK pathway alterations. c) IDH mutations: Rare in pediatric gliomas but can occur in older children/adolescents. d) H3K27M mutations: More common in midline gliomas but can rarely occur in PLGGs. e) CDKN2A deletions: Associated with more aggressive behavior in some PLGGs. f) TERT promoter mutations: Rare in PLGGs but can occur, especially in older children. These molecular alterations not only help in classification and prognostication but also guide targeted therapies. For instance, BRAF inhibitors have shown promise in BRAF V600E mutant tumors. It's worth noting that the relationship between these molecular pathways and seizure occurrence is an active area of research. Some alterations, like BRAF V600E, may be associated with both tumor behavior and seizure risk, potentially serving as both prognostic markers for the tumor and predictive markers for seizures.

Treatment

see Pediatric Low-grade glioma treatment.

Outcome

The determinants of outcomes for adult survivors of pediatric Low-grade glioma (PLGG) are largely unknown.

Pediatric LGG patients have a high survival rate; 90–95 % will be alive 10 years after diagnosis [2) 3)].

This high overall survival includes many patients with residual tumor, and some of these tumors never grow once they have been diagnosed. Nevertheless Low-grade glioma can cause significant morbidity in combination with treatment-related late effects. It is increasingly acknowledged that pediatric LGG is often a chronic disease.

Case series

Pediatric low-grade glioma case series.

References

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