Pediatric high-grade glioma

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Pediatric high-grade gliomas (pHGGs) are a type of brain tumor that primarily affects children and adolescents. These tumors are classified as high-grade because they are aggressive and tend to grow rapidly. pHGGs originate from glial cells in the brain, which are supportive cells that provide structure and nourishment to neurons. The most common type of pHGG is known as a glioblastoma multiforme, which is also seen in adults.

Classification

see High-grade glioma classification.

Midline pediatric high-grade glioma.

Hemispheric pediatric high-grade glioma.

Age Group: As the name suggests, pHGGs primarily affect children and adolescents. They are most commonly diagnosed in individuals under the age of 18, with the highest incidence occurring in children between the ages of 5 and 10.

Aggressive Nature: pHGGs are highly aggressive tumors that tend to infiltrate surrounding brain tissue. They are characterized by rapid growth and can cause significant pressure on the brain.

Symptoms: The symptoms of pHGGs can vary depending on the tumor's location within the brain. Common symptoms may include headaches, seizures, nausea and vomiting, changes in behavior or personality, weakness or paralysis, and problems with coordination or balance.

Diagnosis: pHGGs are typically diagnosed through a combination of imaging tests, such as magnetic resonance imaging (MRI) or computed tomography (CT) scans, and a biopsy to examine a sample of the tumor tissue. Molecular testing may also be performed to identify specific genetic mutations that can inform treatment decisions.

Treatment

Pediatric high-grade glioma treatment

Prognosis: The prognosis for pHGGs is generally poor due to their aggressive nature. Despite aggressive treatment approaches, these tumors often recur, and long-term survival rates are relatively low. However, advances in research and treatment strategies continue to improve outcomes for some patients.

Research and Clinical Trials: Ongoing research efforts are focused on developing more effective treatments for pHGGs. Clinical trials offer opportunities for patients to access innovative therapies and contribute to the advancement of knowledge about these tumors.

It's important to note that each case of pediatric high-grade glioma is unique, and treatment plans are tailored to individual patients based on factors such as tumor location, size, and genetic characteristics. Pediatric neuro-oncologists and multidisciplinary teams of healthcare professionals play a crucial role in managing and treating these challenging tumors

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High-grade gliomas (HGG) represent one of the most common central nervous system (CNS) tumors among adults. This contrasts significantly to the pediatric population where HGG only comprise approximately 8–12% of all primary CNS tumors [1].

In adults, HGG often arise from a Low-Grade Glioma (LGG) that has undergone malignant transformation, but this phenomenon is exceedingly rare in pediatric patients [2].

Similar to the adult experience, however, pediatric HGG are characterized by their aggressive clinical behavior and account for a significant amount of morbidity and mortality among children with brain tumors. HGG typically arise from astrocytic origins, including glial, oligodendrocytes, and ependymal cells [3].

Since pediatric HGG histologically resemble adult HGG, historically, it was believed that these were similar tumors. New biologic, molecular, and genetic data suggest that pediatric HGG are distinct from adult HGG [4].

Outcome

A population-based study confirms previously reported study results that found worse survival outcomes for malignant diffuse gliomas in girls in the age group 0-9 years. Additionally, in a study, Hoogendijk et al. pinpoint this difference to girls with midline pHGGs aged 0-4 years. They provide insight into the possible underlying mechanisms contributing to sex survival differences in pHGG patients. With first-line treatment has no impact on the higher risk of dying for girls, but age and tumor characteristics have a neutralizing effect. The results of this population-based study serve as a basis for future pre-clinical and clinical studies to further unravel the underlying mechanisms responsible for the survival gap between sexes in midline pHGG [5]

Despite numerous treatment approaches, outcomes have remained dismal with most series showing 5-year survival outcomes ranging from 15 to 35% and the far majority of children succumbing to their disease [6) 7) 8) 9)].

A study suggests that the outcome of HGGs in children and adolescents after high-dose chemotherapy and autologous stem cell transplantation (HDCT/auto-SCT) is encouraging if the patient could achieve CR or PR before HDCT/auto-SCT [10)].

Case series

2017

Lee et al., retrospectively reviewed the medical records of 30 patients with High Grade Gliomas (HGGs) (16 glioblastomas, 7 anaplastic astrocytomas, and 7 other HGGs) between 2006 and 2015. Gross total resection or near total resection was possible in 11 patients. Front-line treatment after surgery was radiotherapy (RT) in 14 patients and chemotherapy in the remaining 16 patients including 3 patients less than 3 years of age. Eight of 12 patients who remained progression free and 5 of the remaining 18 patients who experienced progression during induction treatment underwent the first high-dose chemotherapy and autologous stem cell transplantation (HDCT/auto-SCT) with carboplatin + thiotepa + etoposide (CTE) regimen and 11 of them proceeded to the second HDCT/auto-SCT with cyclophosphamide + melphalan (CyM) regimen. One patient died from hepatic veno-occlusive disease (VOD) during the second HDCT/auto-SCT; otherwise, toxicities were manageable. Four patients in complete response (CR) and 3 of 7 patients in partial response (PR) or second PR at the first HDCT/auto-SCT remained event free: however, 2 patients with progressive tumor experienced progression again. The probabilities of 3-year overall survival (OS) after the first HDCT/auto-SCT in 11 patients in CR, PR, or second PR was 58.2% ± 16.9%. Tumor status at the first HDCT/auto-SCT was the only significant factor for outcome after HDCT/auto-SCT. There was no difference in survival between glioblastoma and other HGGs. This study suggests that the outcome of HGGs in children and adolescents after HDCT/auto-SCT is encouraging if the patient could achieve CR or PR before HDCT/auto-SCT [11)].

2015

McCrea et al. retrospectively reviewed institutional databases evaluating all patients ≤21 years with high grade glioma treated between 1988 and 2010. Kaplan-Meier curves and log-rank statistics were used to compare groups univariately. Multivariate analyses were completed using Cox proportional hazards regression models.

Ninety-seven patients were identified with a median age of 11 years. Median overall survival (OS) was 1.7 years, and median PFS was 272 days. Location was significant for OS ($P < .001$). Patients with gross total resection (GTR) had a median OS of 3.4 years vs 1.6 years for subtotal resection and 1.3 years for biopsy patients ($P < .001$). Female patients had improved OS ($P = .01$). Female patients with GTR had a mean OS of 8.1 years vs 2.4 years for male patients with GTR and 1.4 years for all other female patients and male patients ($P = .001$). PFS favored patients ≤3 and ≥13 years and females ($P = .003$ and .001).

OS was significantly correlated with the location of the tumor and the extent of resection. GTR significantly improved overall survival for both glioblastoma multiforme and anaplastic astrocytoma

patients, and female patients showed a much larger survival benefit from GTR than male patients [12].

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