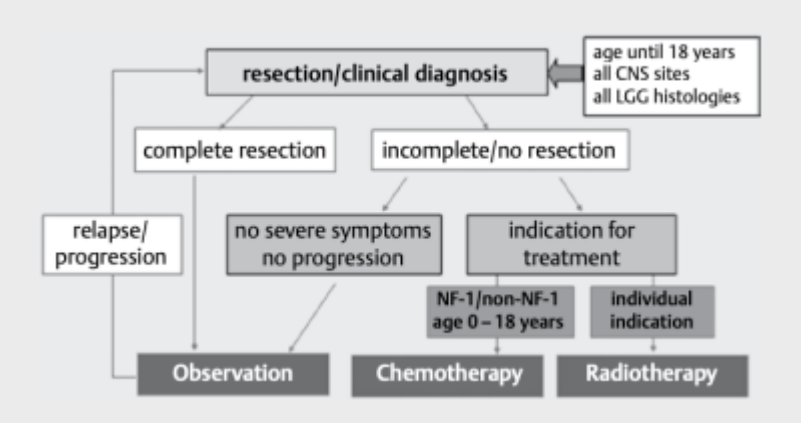
Pediatric Low-grade glioma treatment



Low-grade gliomas (LGGs) constitute the largest, yet clinically and (molecular-) histologically heterogeneous group of pediatric brain tumors of WHO grades I and II occurring throughout all pediatric age groups and at all central nervous system (CNS) sites. The tumors are characterized by a slow growth rate and may show periods of growth arrest. Around 40% of all LGG patients can be cured by complete neurosurgical resection and are followed by close observation. In case of relapse, the second resection often is possible. Following incomplete resection, observation is recommended, as long as there is no radiologic tumor growth and the patient does not suffer from significant, tumor-related symptoms. This also applies to patients with a diagnosis of LGG on the basis of radiological criteria. By contrast, clinical worsening and/or radiologic progression are an indication of treatment with either chemo- or radiotherapy. Overall survival is around 90%, and many patients survive with residual tumor, i. e. they suffer from chronic disease. All patients need comprehensive neuro-oncological care, the principles, and details of which are summarized in the current guidelines. These represent the standard of care for diagnostic work-up (including neuroimaging and neuropathology), and for therapeutic decisions (including the indications to non-surgical treatment) as well as concepts for neurosurgical intervention, chemotherapy, and radiotherapy as well as surveillance and rehabilitation. The current treatment algorithm was compiled by members of the LGG working group of the SIOP-E brain tumor group (SIOP-E-BTG) and is based upon the results of previous European LGG studies and international reports [1)].

Within the multidisciplinary tumor board, all decisions concerning biopsy or resection at the time of diagnosis and progression must be carefully made weighing the potential risk of surgery vs. the therapeutic benefit of elucidating the histologic and molecular subtype of the tumor [2)].

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Since 2006 the German federal joint committee (G-BA, Gemeinsamer Bundesausschuss) has established that in line with all other pediatric hematological and oncological diseases – newly diagnosed Low-grade gliomas (LGG) patients must be treated within the current active society of pediatric oncology and hematology (Gesellschaft fuer paediatrische Onkologie und Haematologie, GPOH) trial or registry to ensure high quality standards of care and use of established referral systems [4)].

Pediatric Low-grade gliomas (LGG) that are unresectable often require adjuvant chemotherapy such as carboplatin/vincristine. Small phase II studies have suggested equivalent efficacy of single agent 4-weekly carboplatin. A single-institution retrospective review captured all patients aged 0 to 18 years diagnosed with LGG between 1996 and 2013 and treated with carboplatin monotherapy. The response and survival according to tumor site was compared to published results for multi-agent chemotherapy. Of 268 children diagnosed with LGG diagnosed in this period, 117 received chemotherapy and 104 children received single agent carboplatin as first line chemotherapy. All patients received carboplatin at 560mg/m2 , four-weekly for a median of 12 courses. The mean age at diagnosis was 5.8 years (range 3m-16y) and 32% had neurofibromatosis type 1. With a mean followup of 54 months, 86% of patients achieved stabilisation or better (SD/PR/CR). 3-year progression free survival (PFS) 66% (95% C.I. 57% - 76%), and 5-year PFS was 51% (95% C.I. 41% - 63%). 5-year overall survival was 97%. Multivariate analysis showed poorer PFS for those with chiasmatic/hypothalamic tumors. In this retrospective analysis single agent carboplatin shows comparable efficacy to historical multiagent chemotherapy for the treatment of patients with unresectable LGG. Equivalent outcomes are achieved with less chemotherapy, reduced side effects and fewer hospital visits. Further research is required to establish the place of this simplified regimen in the up-front treatment of unresectable LGG [5].

Measures

Tumor measurement is important in unresectable pediatric low-grade gliomas (pLGGs) to determine either the need for treatment or assess response. Standard methods measure the product of the largest 2 lengths from transverse, anterior-posterior, and cranio-caudal dimensions (SM, cm). This single-institution study evaluated tumor volume measurements (VM, cm) in such pLGGs. Of 50 patients treated with chemotherapy for surgically inaccessible pLGG, 8 met the inclusion criteria of having 2 or more sequential MRI studies of T1-weighted Fast-Spoiled Gradient Recalled acquisition. SM and VM were performed by 2 independent neuroradiologists. Associations of measurement methods with defined therapeutic response criteria and patient clinical status were assessed. The mean tumor size at the first MRI scan was 20 cm and 398 cm according to SM and VM, respectively. VM results did not differ significantly from SM-derived spherical volume calculations (Pearson correlation, $P<0.0001$) with a high interrater reliability. Both methods were concordant in defining the tumor response according to the current criteria, although radiologic progressive disease was not associated with clinical status (SM: $P=0.491$, VM: $P=0.208$). In this limited experience, volumetric analysis of unresectable pLGGs did not seem superior to the standard linear measurements for defining tumor response [6].

Targeted therapy for pediatric low-grade glioma

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References

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