Inoperable glioblastoma

For patients harboring inoperable Glioblastoma, due to the anatomical location of the tumor or poor general condition of the patient, the life expectancy is even worse. The challenge of managing Glioblastoma is therefore to improve the local control, especially for non-surgical patients.

Considering the treatment duration and its side effects identification of patients with survival benefit from treatment is essential to guarantee the best achievable quality of life.

The aim of a study by Löber-Handwerker et al. from Göttingen was to evaluate the survival benefit from radio-chemotherapy and to identify clinical, molecular, and imaging parameters associated with better outcomes in patients with biopsied Glioblastomas. Consecutive patients with inoperable Glioblastoma who underwent tumor biopsy at the department from 2005 to 2019 were retrospectively analyzed. All patients had histologically confirmed Glioblastoma and were followed up until death. The overall survival (OS) was calculated from the date of diagnosis to the date of death. Clinical, radiological, and molecular predictors of OS were evaluated. A total of 95 patients with biopsied primary Glioblastoma were enrolled in the study. The mean age was 64.3 ± 13.2 years; 56.8% (54/95) were male, and 43.2% (41/95) were female. Median OS in the entire cohort was 5.5 months. After stratification for adjuvant treatment, a higher median OS was found in the group with adjuvant treatment (7 months, range 2-88) compared to the group without treatment (1 month, range 1-5) log-rank test, $p < 0.0001$. Patients with inoperable Glioblastoma undergoing biopsy indeed experience a very limited OS. Adjuvant treatment is associated with significantly longer OS compared to patients not receiving treatment and should be considered, especially in younger patients with the good clinical condition at presentation [1)].

Adult brainstem gliomas are characterized into subtypes depending on clinicopathologic and radiographic characteristics. Among them, brainstem glioblastoma is the most malignant and has the poorest prognosis, with surgical resection for this condition posing a great challenge and risk. Postoperative synchronous radiotherapy and temozolomide (TMZ) chemotherapy, or “Stupp protocol”, is the standard of care for glioblastomas. However, antiangiogenic therapy, which is widely used for different cancers, is now an alternative treatment for malignant tumors. Angiogenesis is one of the pathological features of glioblastoma and is involved in tumor progression and metastases. Besides, previous studies suggested a better response to antiangiogenic therapy in some solid tumors with TP53 mutation than TP53 wide-type. Apatinib is a novel, oral, small-molecule tyrosine kinase inhibitor that mainly targets vascular endothelial growth factor receptor-2 (VEGFR-2) to inhibit angiogenesis. In addition, apatinib can cross the blood-brain barrier and improve encephaledema. A report by Zhu et al. describes the use of concurrent apatinib and dose-dense TMZ in a clinically inoperable patient who had a refractory brainstem glioblastoma with a TP53 germline mutation. He obtained an ongoing progression-free survival (PFS) of nearly 16.0 months after resistance to TMZ maintenance. Due to the patient's circumstances, apatinib and TMZ was considered an effective and safe treatment method [2)]

Interstitial photodynamic therapy (iPDT) is a minimally invasive treatment relying on the interaction of light, a photosensitizer and oxygen. In the case of brain tumors, iPDT consists of introducing one or several optical fibers in the tumor area, without large craniotomy, to illuminate the photosensitized tumor cells. It induces necrosis and/or apoptosis of the tumor cells, and it can destruct the tumor

vasculature and produces an acute inflammatory response that attracts leukocytes. Interstitial PDT has already been applied in the treatment of brain tumors with very promising results. However, no standardized procedure has emerged from previous studies. Leroy et al. proposed a standardized and reproducible workflow for the clinical application of iPDT to Glioblastoma. This workflow, which involves intraoperative imaging, a dedicated treatment planning system (TPS), and robotic assistance for the implantation of stereotactic optical fibers, represents a key step in the deployment of iPDT for glioblastoma treatment. This end-to-end procedure has been validated on a phantom in real operating room conditions. The thorough description of a fully integrated iPDT workflow is an essential step forward to a clinical trial to evaluate iPDT in the treatment of Glioblastoma. [3].

Muir et al. retrospectively reviewed patients with newly diagnosed, unresectable Glioblastoma who underwent LITT. Progression-free survival (PFS) was the primary endpoint measured in our study, defined as time from LITT to disease progression. Results Twenty patients were identified with newly diagnosed, inoperable Glioblastoma lesions who underwent LITT. The overall median PFS was 4 months (95% CI = 2 - N/A, upper limit not reached). The median progression-free survival (PFS) for patients with less than 1 cm 3 residual tumor (gross total ablation, GTA) was 7 months (95% CI = 6 - N/A, upper limit not reached), compared to 2 months (95% CI = 1 - upper limit not reached) for patients with a lower GTA (p = .0019). The median overall survival was 11 months (95% CI = 6 - upper limit not reached). Preoperative Karnofsky performance score (KPS) less than or equal to 80 and deep-seated tumor location were significantly associated with decreased PFS (HR, .18, p = .03; HR, .08, p = .03, respectively). At the end of 1 month, only 4 patients (20%) experienced persistent motor deficits. LITT is a safe and effective treatment for patients with unresectable, untreated Glioblastoma with rates of survival and local recurrence compared to patients with surgically accessible lesions treated with conventional resection. Careful patient selection is needed to determine if GTA is attainable. [4].

1)
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2)
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