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Comprehensive Review of Glioma Tumors, And Surgical Treatment

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Abstract: **Glioma or Glioblastoma (GBM) is the most typical primary malignant brain tumor, comprising 16% of all main brain and main nervous system neoplasms, Current neurosurgical innovations aim to enhance our structural, functional and physiologic understanding of the surgical area of interest in order to prevent possible neurological morbidity throughout resection.**

Objective: Current review was conducted to overview the surgical procedures of gliomas resection management, we intended to highlight some different approaches for different gliomas and different locations of the brain, also to discuss the outcomes of resection procedures as management method.

Methodology: Literature search was conducted by using electronic databases such; Medline (Pub Med), and Embase for relevant articles concerning Gliomas and surgical management. This review was carried on August 2017.

Conclusion: Gliomas are open to an aggressive surgical approach. though Glioblastoma is not a disease that can be treated with surgical treatment alone, however securely carried out optimum surgical resection is shown to considerably increase development overall and free survival while making the most of quality of life. there is growing evidence favoring substantial surgical resection and increasing interest in the function of chemotherapy total elimination can boost survival, improve the patient's lifestyle, and use a favorable long-lasting diagnosis.

Keywords: Gliomas, brain tumor, surgical treatment.

1. INTRODUCTION

Glioma or Glioblastoma (GBM) is the most typical primary malignant brain tumor, comprising 16% of all main brain and main nervous system neoplasms [(1)]. The average age-adjusted incidence rate is 3.2 per 100,000 population [(2,3)]. Although GBMs occur practically solely in the brain, they can likewise appear in the brain stem, cerebellum, and spine. Sixty-one percent of all primary gliomas happen in the 4 lobes of the brain: frontal (25%), temporal (20%), parietal (13%), and occipital (3%) [(4)]. Glioblastoma (GBM; World Health Organization grade IV glioma) is the most prevalent and lethal main intrinsic brain tumor [(5)]. Unlike other solid tumor cell types, GBM commonly invades the surrounding brain but seldom metastasizes to other organs [(5)].

Inning accordance with the World Health Organization (WHO), glioblastoma is the most common main brain neoplasm [(6)]. It consists of 15% of all intracranial neoplasms and 60-75% of astrocytic tumors [(7)]. The term glioblastoma multiforme (GBM) was previously synonymous with glioblastoma, however "multiforme" is presently no longer a part of the WHO category [(8)]. The abbreviation, GBM, is still typically used and accepted in the literature to refer to glioblastoma. Glioblastoma is obtained particularly from the astrocyte cell type, in which the cellular development is uncontrolled and tumor development happens. Examples for the WHO grading system of astrocytomas can be seen on (**Table 1**) [(9)]. Grade 1 astrocytomas are considered benign and sluggish growing. Surgical excision is typically considered curative, nevertheless gross total resection (GTR) can in some cases be limited by adhesions the tumor might have with surrounding eloquent anatomy [(9)].

Although still a matter of debate, many authors presently advocate surgery in the treatment of supratentorial Low-grade-glioma (LGGs) [10,11,12,13]. However, it seems that glioma resection must be the most comprehensive possible to have a genuine impact on the nature of this sort of tumor [14].

However, a main tenet of neurosurgical oncology is that survival can improve with greater tumor resection, this principle needs to be tempered by the capacity for functional loss following an extreme elimination. Current neurosurgical innovations aim to enhance our structural, functional and physiologic understanding of the surgical area of interest in order to prevent possible neurological morbidity throughout resection. Emerging imaging innovations, as well as cutting edge intraoperative techniques, can assist in extent of resection while lessening the associated morbidity profile. Specifically, the value of mapping motor and language pathways is reputable for the safe resection of intrinsic tumors.

Table 1: astrocytomas based of WHO grade

WHO grade for astrocytomas
Grade 1
Pilocytic astrocytoma; subependymal giant cell astrocytoma
Grade 2
Pilomyxoid astrocytoma; pleomorphic xanthoastrocytoma
Grade 3
Anaplastic astrocytoma
Grade 4
Glioblastoma; gliosarcoma

Current review was conducted to overview the surgical procedures of gliomas resection management, we intended to highlight some different approaches for different gliomas and different locations of the brain, also to discuss the outcomes of resection procedures as management method.

2. METHODS AND MATERIALS

Literature search was conducted by using electronic databases such; Medline (Pub Med), and Embase for relevant articles concerning Gliomas and surgical management. This review was carried on August 2017. Following keywords were used "Glioblastoma", "glioma", "astrocytoma" and "glioblastoma multiform", Combined with "Surgery", "resection" and "neurosurgical management". We restricted search to only English published studies with human subject.

3. DISCUSSION

Glioma tumors are histologically separated into Grades I through IV according to the World Health Organization (WHO) criteria. Grade I tumors generally have a good diagnosis and more frequently take place in kids [15,16], and Grade II tumors are defined on histologic assessment by hypercellularity: These Grade II tumors have a 5 – 8-year median survival. Grade III astrocytoma tumors (anaplastic astrocytoma tumors) are identified on histologic assessment inning accordance with hypercellularity, along with nuclear atypia and mitotic figures (**Figure 1**). Anaplastic astrocytoma has a 3-year mean survival [16,17]. Grade IV gliomas, likewise known as GBMs, are defined on histologic assessment inning accordance with hypercellularity, nuclear atypia, mitotic figures, and evidence of angiogenesis and/or necrosis (**Figure 2**). The mean survival for patients with GBM tumors is 12 - 18 months [15], and older patients (> 60 years of age) normally have a survival that is rather shorter than the typical.

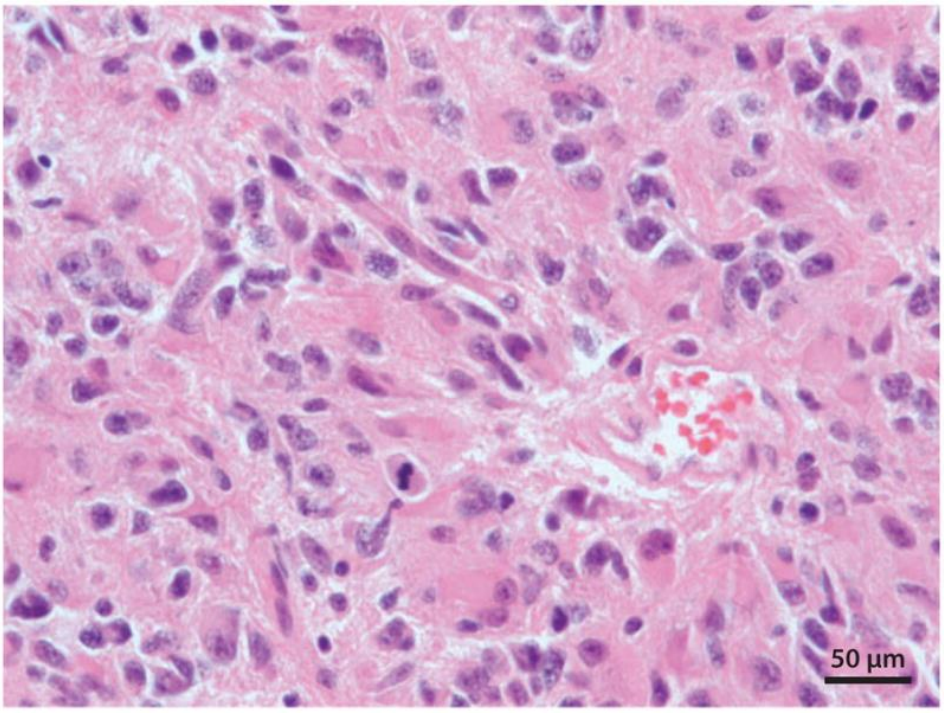

Figure 1: Anaplastic astrocytoma (World Health Organization Grade III)

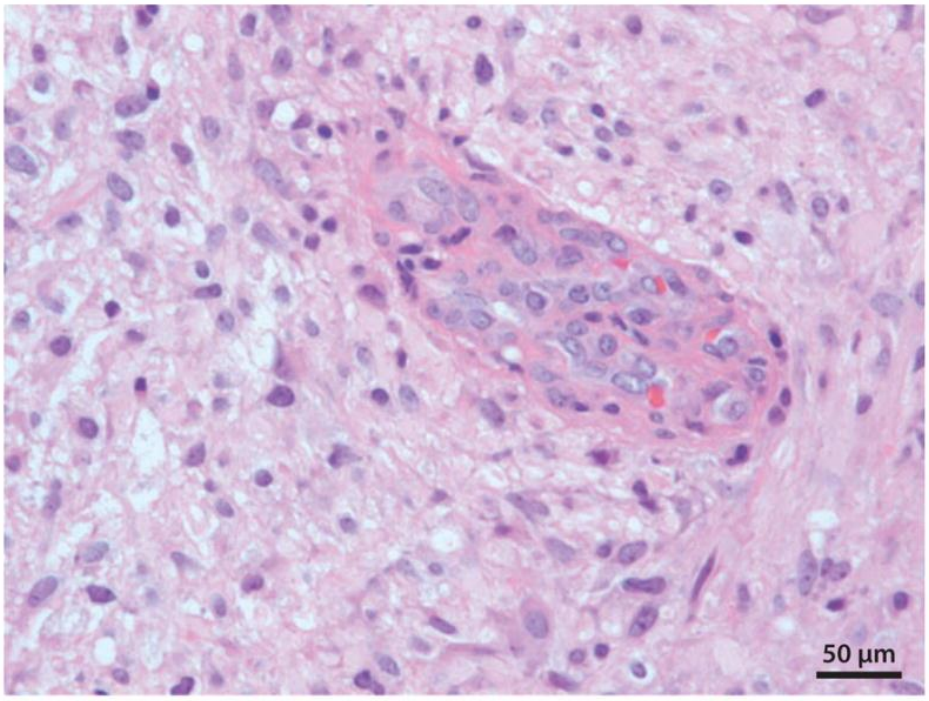

Figure 2: Glioblastoma tumor (World Health Organization Grade IV)

- **Surgical resection of Gliomas in general:**

The major advantages of re-resection are fast palliation of symptoms and histological medical diagnosis. Few research studies supplied data of re-resection as sole treatment method. A randomized study compared the implantation of BCNU-impregnated polymers, versus placebo polymers after re-resection [(18)]. Median survival was 31 weeks versus 23 weeks, i.e. significantly much better for the BCNU group. In a smaller sized research study, where 24 patients with GBM went through re-resection alone, average survival was 14 weeks [(19)]. In a lot of other trials, postoperative radio- and/or chemotherapy were administered. The effect of re-resection by itself is not totally clear. Barker et al. reported the outcomes of re-resection plus individual extra treatment (chemotherapy in 85% of cases) for GBM [(20)].

The newly released literature verifies the figures from the BCNU wafer trial, i.e. average survival of 23 weeks after re-resection alone [21]. The study population included 38 patients with recurrent GBM. The typical period between very first and second resection was 10 months. Mean survival from initial diagnosis was 13 months. The only favorable prognostic factor was Karnofsky performance status (KPS) > 80%. The BCNU wafer outcomes were extended by a dose escalation trial with 44 patients (32 GBM, average KPS 80%) [22]. Compared to the original 3.8% concentration, a maximum-tolerated dose (MTD) of 20% was found. Typical general survival was 36 weeks. It was 31 weeks in the initial randomized trial. It appears possible that higher doses of BCNU may a little improve survival because no patient received less than 6.5% BCNU by weight. This hypothesis needs testing in a randomized contrast. Re-resection plus intracavitary application of paclitaxel and carboplatin encapsulated in a liquid crystalline cubic stage system was reported by von Eckardstein et al. [23]. Cubic stages have a gel-like structure. Hence, much better protection of irregular resection cavities might be achieved. The initial experience is restricted to 12 patients with frequent GBM. Their average survival was 28 weeks (16.5 months from initial diagnosis).

Stylli et al. reported the results of re-resection followed by photodynamic treatment [24]. Prior to surgery, haemetaporphyrin derivate was injected i.v. The principle is that this sensitizer is used up by the tumor cells. After optimum resection, the tumor bed area receives irradiation by laser light of the proper wavelength, leading to activation of the retained sensitizer and destruction of recurring tumor cells. Fifty-five patients with frequent GBM and 29 with frequent astrocytoma were treated. Typical KPS and other prognostic elements were not reported. Median survival was unexpected, i.e. 59 weeks for GBM and more than 5 years for AA. PFS again was not reported. Earlier outcomes with this approach were less favorable. The 5 GBM patients included in the series by Schmidt et al. [25] had a relapse-free survival time of 2 - 9 months (median 4 months).

Other groups studied the intratumoral delivery of representatives via stereotactically positioned catheters. The outcomes of a dose-escalation trial of convection-enhanced shipment of interleukin-4 Pseudomonas exotoxin (NBI-3001) in 31 patients with a KPS > 50% have been published [26]. Twenty-five patients had GBM. The MTD was 6 μg/ ml × 40 ml. Grade 3 or 4 central nerve system (CNS) toxicity was seen in 22% of patients at this dosage level. Median survival was 36 weeks (25 weeks in patients with GBM). A similar method was evaluated in a phase I trial by Sampson et al. [27]. The immunotoxin utilized (TP-38) was a recombinant chimeric protein made up of the epidermal development aspect receptor (EGFR)-binding ligand changing growth factor-α and a genetically engineered form of the Pseudomonas exotoxin, PE-38. TP-38 was instilled over 50h. Sixteen out of 20 patients had GBM (average age 54 years, KPS 60-- 100%). At the time of the report, the MTD had actually not been reached. Two patients experienced radiographic reactions. Mean survival was 23 weeks (19 weeks in patients with recurring disease and 33 weeks in others). A better outcome was observed after re-resection with intralesional shipment of autologous lymphokine-activated killer cells in 40 patients with GBM [28]. Typical survival was 39 weeks (17.5 months from initial medical diagnosis of GBM). Chiocca et al. performed a stage I trial of re-resection and intracerebral injections of the oncolytic adenovirus ONYX-015, a virus that can still reproduce in a reasonably selective fashion in tumor cells [29]. From 24 patients, 17 had GBM. Mean KPS was 90%. The MTD was not reached. Mean time to progression was relatively brief, i.e. 7 weeks. However, mean survival was 27 weeks.

Another technique is delivery of the herpes simplex infection thymidine kinase (HSV-tk) gene by re-resection, injection of vector producing cells into the nearby brain, positioning of an Ommaya tank for further cell injection 7 days after surgery and treatment with repeat cycles of ganciclovir, a nucleoside prodrug which is activated by HSV-tk. Prados et al. dealt with 30 patients inning accordance with this protocol in a stage I/II research study [30]. Average survival was 37 weeks. Another report of debulking and adenoviral vector-based HSV-tk gene shipment plus ganciclovir consisted of 14 patients [33]. Eleven had GBM, average KPS was 80%. Average survival was 17 weeks. Already, also thinking about previous outcomes of a negative randomized trial and other smaller investigations evaluated by Pulkkanen and Yla-Herttuala [34]], HSV-tk gene treatment has not led to the expected efficacy. Lang et al. performed gross overall resection followed by p53 gene treatment via injection of an adenovirus vector in a stage I trial [35]. Fifteen patients were registered (13 GBM, median KPS 90%). In all patients, exogenous p53 protein was identified in astrocytic tumor cell nuclei. Transfected cells resided usually within 5 mm of the injection site. Toxicity was minimal. Mean PFS was limited to 13 weeks, while typical survival was 43 weeks.

Surgical Resection of Low Grade Glioma (LGG):

The lack of pathognomonic imaging for LGG and the requirement for molecular, chromosomal, and histopathologic characterization of tumors mandate tissue acquisition for precise medical diagnosis, prognostication, and management. Needle biopsy specimens have been related to a greater than 50% misdiagnosis rate [34,35]. Surgical resection (vs biopsy

alone) manages a much better chance to characterize, grade, and study tumor tissue to make sure appropriate medical diagnosis, treatment, and prognostication. Regardless of the lack of a randomized regulated trial, the proof for the advantages of comprehensive surgical resection is growing. In 2001, Keles et al. [36] reviewed the literature and concluded that a prevalence of the evidence preferred more extensive resection for patients with LGG. Since then, a number of extra long-lasting institutional research studies have been published favoring substantial surgical resection [37,38,39]. Smith et al. [39] retrospectively analyzed results in 216 patients who went through surgical resection for LGG at UCSF between 1989 and 2005, from a total of more than 800 patients treated for LGG during that period. Since such patients usually have complicating elements and addition may puzzle the interpretation of the results, patients who went through biopsy were specifically omitted. On multivariate analysis, degree of resection (EOR) was significantly connected with enhanced OS but not PFS. Five-year survival in patients with a minimum of 90% EOR was 97%, whereas it was 76% in those with less than 90% EOR [39]. In 170 patients dealt with surgically at Johns Hopkins Hospital in between 1996 and 2007, McGirt et al. [37] similarly discovered that gross total resection (GTR; based upon independent radiologist interpretation) was separately related to enhanced OS and PFS compared to subtotal resection (5-year OS: 95% vs 70%, P=0.017; median time to development: 7 vs 3.5 years, P=0.043). These research studies recommend GTR is preferable, not all tumors are amenable to GTR. Predictors of incomplete tumor resection consist of tumor participation of the corticospinal system, big tumor volume, and oligodendroglioma histopathologic type [40].

In addition to OS and PFS, cognitive and quality-of-life outcomes after surgical resection must be thought about, particularly due to the fact that issues relating to these outcomes have actually thwarted the interest for radiotherapy. Surgery might transiently exacerbate baseline deficits; most patients return to baseline or improve upon preoperative cognitive function within 3 months [41]. Additionally, advances in intraoperative technology (eg, neuronavigation) and pre- and intraoperative brain mapping strategies (eg, practical MRI, magnetic source imaging, and subcortical and cortical stimulation mapping) now allow neurosurgeons to customize resections to specific practical brain architecture, decreasing the threat of irreversible deficit to less than 2% and making sure that patients' lifestyle is protected [42,43]. Duffau et al. [43] discovered that LGG patients operated on with the assistance of cortical stimulation had a considerably lower permanent deficit rate, a greater GTR rate, and a survival advantage compared with patients who were operated on without intraoperative mapping. In fact, the authors found that mapping may be utilized to determine dynamic modifications in individual patients' functional brain architecture, enabling more extensive tumor resections utilizing a multistaged surgical technique [44]. Making surgical treatments much safer and more comprehensive, advances in brain mapping also have made surgical treatment an option for more patients [43]. In particular, there has actually been substantially increased interest in the surgical management of insular gliomas, which are challenging from a structural and eloquence viewpoint but can be resected with just a 6% risk of postoperative deficit [45].

Microsurgical Technique for Insular glioma resection:

The insular area remains one of a lot of difficult areas for the aggressive resection of LGGs or HGGs [3,8]. These tumors are entrenched in eloquent tissue and surrounded by microvasculature serving crucial language and motor systems [12,14].

All microsurgical eliminations were approached through 1 or more transcortical corridors. Tumor area and hemispheric supremacy determined the choice of either basic (50 procedures [43.5%] or awake (65 procedures [56.5%] anesthesia. Our protocol for awake neuroanesthesia has actually been explained elsewhere [46]. Patients are placed in a semilateral position with the head turned parallel to the floor. For tumors inhabiting the posterior element of the insula, a 15 ° upward head turn permits tumor resection below the lip of practical cortex overlying the posterior insula (**Figure 3**). The vertex of the head is tipped 15 ° towards the flooring or toward the ceiling when the tumor is predominantly below or above the sylvian crack, respectively. After a tailored craniotomy, cortical and subcortical language, motor, and sensory mapping are carried out as required and according to previously reported procedures [46]. Once functional areas have actually been recognized, transcortical windows above and below the sylvian crack are created through nonfunctional cortex, taking care to preserve a minimum of a 1-cm margin from any functional website. This "windowing technique" permits tumor removal along the course of the uncinate fasciculus, generating supra- and infrasylvian resection cavities that are eventually connected to one another below the skeletonized sylvian vessels. Finally, identification of the lenticulostriate arteries10 and motor mapping of the internal capsule permits delineation of the median border of resection for the most parts[46].

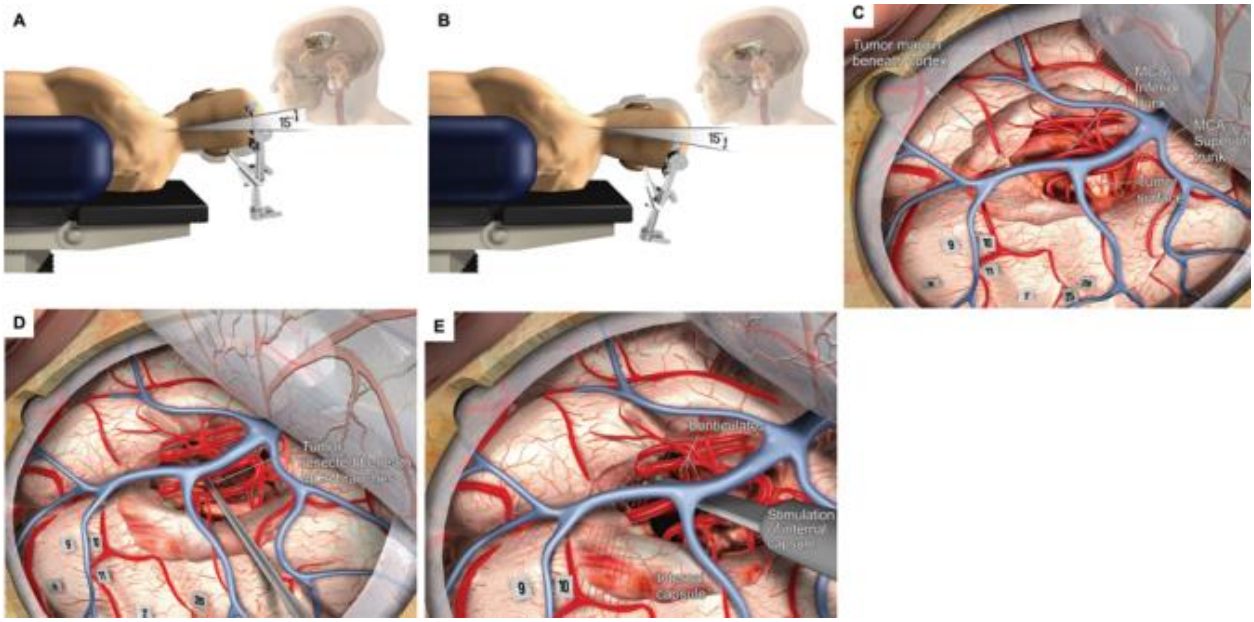

Figure 3: Drawings depicting patient positioning and the microsurgical technique for transcortical resection of an insular glioma. For tumors primarily above the sylvian fissure

4. CONCLUSION

Gliomas are open to an aggressive surgical approach. though Glioblastoma is not a disease that can be treated with surgical treatment alone, however securely carried out optimum surgical resection is shown to considerably increase development overall and free survival while making the most of quality of life. there is growing evidence favoring substantial surgical resection and increasing interest in the function of chemotherapy total elimination can boost survival, improve the patient's lifestyle, and use a favorable long-lasting diagnosis.

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