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Clinical and Surgical Management for Cerebral Astrocytoma

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Abstract

Cerebral astrocytoma is a primary brain tumor originating from astrocytes, the star- shaped glial cells that support and protect neurons. It represents a diverse group of tumors with varying degrees of malignancy, classified according to the World Health Organization (WHO) grading system into grades I through IV. Grade I astrocytomas, such as pilocytic astrocytomas, are generally well-circumscribed and less aggressive, while higher-grade tumors like anaplastic astrocytomas (Grade III) and glioblastoma multiforme (Grade IV) exhibit more aggressive behavior and poorer prognoses. Clinical presentation varies with tumor location and grade but commonly includes headaches, seizures, and focal neurological deficits. Diagnostic evaluation typically involves imaging techniques such as MRI and may be supplemented by biopsy for histological confirmation. Treatment strategies are tailored to the tumor grade and include surgical resection, radiation therapy, and chemotherapy. Despite advances in therapeutic approaches, the prognosis remains variable, with higher-grade tumors generally associated with reduced survival rates. Ongoing research focuses on improving early detection, understanding molecular mechanisms, and developing targeted therapies to enhance patient outcomes.

Keywords:Cerebral astrocytoma,medical treatment,surgical intervention

INTRODUCTION

Gliomas refer to the tumors of glial cells, the supporting cells, of the Central Nervous System (CNS). They are named after the type of the glial cell affected, i.e. astrocytoma, oligodendroglioma, ependymoma. Gliomas are intra-axial neoplasms that have distinct molecular, behavioral and histological variations and thereby each acquire a distinct prognosis.[1] In order to properly manage and grade each type, a criterion for categorization was required. This system of classification, by the World Health Organisation (WHO), has adopted an evolving course since 1926. From grading tumors based on morphology and immunohistochemistry to identifying various molecular associations, has revolutionized the criteria of classification of gliomas and thereby treatment approaches.[2] The course of this evolution is important for a clearer

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understanding of the history of classifying gliomas.[3,4]

Low grade glioma (LGG) is a term used for gliomas grades I and II and was historically categorized into 3 groups based on morphological characteristics; oligodendroglioma, astrocytoma and oligoastrocytoma.[5,6,7] Grading then was based on histological and morphological characteristics. However, several tumor types of identical characteristics were behaving differently and so, new classification criteria were needed to appropriately grade tumors.

In 2016, molecular criteria were introduced to the classification system and new categorization based on isocitrate dehydrogenase (IDH) mutation and codeletion of 1p/19q genes was emerged.[5,8] In 2021, the latest classification of brain tumors was adopted by WHO, being the 5th version overall, and incorporating more of the gene and molecular profiles. However, a "hybrid taxonomy" is now used where some families are classified according to molecular similarities and others by histological similarities while carrying different genetic and molecular variations.[9]

Clinical Presentation of Astrocytomas

The signs and symptoms of brain tumor usually depend on the tumor size, location and its growth rate. The most frequent presenting symptom of LGGs is seizure with an incidence of 60-85%,[10] but other symptoms may include new onset headache, focal neurological deficits or personality changes due to the tumor location in eloquent, typically supratentorial areas in the brain.[1] Patients with optic nerve glioma may experience visual field defects and decrease in visual acuity. They may also experience speech disturbances, vertigo, ataxia, psychiatric symptoms or signs of increased intracranial pressure such as headache, vomiting and nausea.[11] When tumors arise in the hypothalamus, endocrine disturbances such as diabetes insipidus, electrolyte imbalance or precocious puberty may occur.[12]

Astrocytoma is usually a slow growing tumor that tends to cause symptoms to progress slowly and worsen over months or years. Seizure is a common presentation in low grade astrocytoma, but the tumor location and histology influence the risk of seizure occurrence.[13]

Diagnosis

Astrocytomas are a type of brain tumor that originate from astrocytes, a type of glial cell in the brain. These tumors can vary widely in appearance on radiological imaging, depending on factors such as the grade of the tumor, its location, and its size.

The WHO classification of CNS tumors divided them into individual entities: adult-type diffuse gliomas, pediatric-type diffuse low-grade gliomas, pediatric-type diffuse high-grade gliomas and circumscribed astrocytic gliomas.[14]

Here are some general radiologic characteristics of astrocytomas

On CT scan, astrocytomas usually appear as hypodense masses with irregular borders. Depending on the grade of the tumor, associated surrounding edema and enhancement are seen.[15]

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MRI is the modality of choice for assessing astrocytomas. They usually appear hyperintense on T1-weighted images and hypointense on T2 weighted images. In some cases, they may have a cystic component or show areas of necrosis. Diffusion weighted images help in assessing the cellularity of the tumor, as higher-grade tumors show restricted diffusion. On MR spectroscopy, high grade tumors show increased choline levels and decrease NAA levels.

Low grade astrocytomas constitute a subgroup of primary brain tumors originating from astrocytic cells, characterized by slow growth and relatively indolent behavior compared to high-grade gliomas. Despite their low proliferative rate, these tumors can cause significant morbidity and mortality, emphasizing the importance of accurate diagnosis and appropriate management. Radiological imaging, particularly CT and MRI, plays a critical role in the detection, characterization, and surveillance of low-grade astrocytomas.

CT imaging is used as the initial imaging modality for patients presenting with neurological symptoms suggestive of intracranial pathology. Low grade astrtocytomas typically appear as well-defined, hypodense, non-enhancing lesions, reflecting their relatively slow growth and minimal surrounding vasogenic edema and mild mass effect. Calcifications are usually seen more in high grade tumors.

Magnetic resonance imaging (MRI) is considered the imaging modality of choice for evaluating brain tumors due to its superior soft tissue contrast and multiplanar imaging capabilities. Low grade astrocytomas typically demonstrate characteristic findings on MRI, which vary depending on their histological subtype and grade. Low grade astrocytomas usually appear iso- to hypointense on T1 weighted images and typically hyperintense on T2 weighted images. Enhancement is not always present. On the diffusion weighted images, they may show relatively low apparent diffusion coefficient (ADC) values compared to normal brain tissue. MR spectroscopy may demonstrate relatively low choline peaks and high N-acetylaspartate (NAA) peaks, less pronounced compared to high grade tumors. Perfusion weighted images can provide information about the tumor vascularity and blood flow. PWI may show relatively low cerebral blood volume (rCBV) values compared to high-grade tumors.

Pilocytic astrocytomas, a common low-grade variant, often present as cystic lesions with a mural nodule, resulting in a "cyst with a nodule" appearance on imaging. These tumors typically exhibit hypointensity on T1-weighted images and hyperintensity on T2-weighted images, with variable enhancement patterns following contrast administration. Diffuse astrocytomas, on the other hand, present as infiltrative lesions without a distinct border, resulting in ill-defined margins and heterogeneous signal intensity on MRI. Subependymal giant cell astrocytomas frequently arise near the ventricular walls and may demonstrate calcifications, resulting in characteristic hypointense foci on T1-weighted images.

Astrocytoma, IDH-mutant tumors, show isointense to hypointense signal on the T1 weighted images, hyperintense T2 signal that

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incompletely suppresses on FLAIR: T2/FLAIR mismatch sign.

Extent of Resection

Surgical resection plays a central role in the management of gliomas, and there is a growing body of evidence regarding the value of extent of tumor resection to improve overall survival, progression-free survival, time to malignant transformation, and seizure control. Thus, it is important to discuss preoperative surgical planning for low and high grade gliomas, with a focus on the role of extent of resection in improving patient outcomes.

As a result, all patients were able to return to a normal life after surgery with no malignant transformation. Out of 15 patients, only 2 cases were reported to have slight residual deficits and 4 to have tumor recurrence .It has come to some research that when confronted with diffuse and deep seated tumors, a therapeutic benefit to patients is thought to have an extent of resection threshold of 80% and volume of residual less than 10 mL.

Awake Craniotomy versus Craniotomy under General Anesthesia

When dealing with suspected low-grade gliomas in eloquent areas of the brain, it is important to consider using tools such as awake craniotomy and intraoperative mapping. When paired with electrophysiological mapping to identify functional areas and clear cortical windows for resection, these tools offer a highly effective method for safely removing tumors from eloquent regions . Awake craniotomies were shown to be correlated with low intraoperative seizure rates, better postoperative KPS, shorter hospitalizations, more frequent 100% total resections and perioperative complication rates when compared with craniotomies under general anesthesia .

Preoperative Preparation

In Awake surgery you need to select the patient meticulously, it requir es a highly cooperative patient and an experienced surgical team. The patient should meet the anesthesia team before surgery for comfort and to be familiar with the team during surgery. An airway evaluation should be performed in all patients. Control of preoperative anxiety before awake craniotomy is important and can be relieved by proper preoperative counseling about the anesthetic and surgical procedures, therefore preoperative consultation by anesthesiologist is an important process. The anesthesiologist should outline the overall awake craniotomy procedures including the positioning, scalp nerve block, the possible discomfort, and the motor and language tests. A good anesthesiologist-patient relationship is essential, and the anesthesiologist should attempt to alleviate anxiety and discomfort of the patient.

Anesthetic Approaches for Awake Craniotomy

Various anesthetic techniques performed for awake craniotomy. Among them, there are two commonly used anesthetic methods for awake craniotomy: monitored anesthesia care (MAC) and asleep-awake-asleep (AAA) techniques. The anesthesiologists should provide sufficient sedation and analgesia during the initial craniotomy, a rapid and smooth emergence of patients is required for intraoperative

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neurophysiologic test including motor function, language test, and brain mapping.

After cortical and subcortical mapping and labeling the eloquent zones tumor resection take place, sedation is often sufficient until completion of the surgery. The sedation profile during the first stage of awake craniotomy, from skin incision to dura opening, plays a pivotal role in the quality of intraoperative consciousness. The anesthesiologist should restore the consciousness of patient back to the preoperative state for neurophysiologic tests and brain mapping to be performed successfully.

Pre-operative planning

Most of the awake craniotomies for brain tumor resection should be discussed in the neuro-oncology multi-disciplinary team meeting. A proper radiological imaging should be done for surgical planning including diffuse tensor imaging (DTI), and functional MRI (fMRI). A formal speech and motor power assessment evaluation (Muscle Power Scale), which is usually carried out up to 2 days before surgery (baseline) and to be repeated intra-operatively to identify motor errors during stimulation or during functional resection. Although fMRI is increasingly being adopted as a practical preoperative planning tool for brain tumor resection.

A comprehensive neuropsychological evaluation, patient's emotional state and ability to cooperate during awake surgery is usually assessed and meeting the team before surgery is crucial as well, we usually use RAMSES score.

Surgical Technique in Awake Fashion

As with any awake technique, delays and technical problems in the operating theatre should be avoided. The team should be made aware of the presence of an awake patient by a sign on the entrance of the operating room and noise should be kept to a minimum. The operating theatre becomes a crowded place and staff movement should be restricted and a calm atmosphere should be maintained at all times. Patient comfort is very important, we should be asking the patient if they are comfortable and the operating table should be adequately padded and attention paid to head and limb positioning and that should be double checked before draping the patient. It is usually preferable to allow the patient to position themselves on the operating table before institution of sedation or anesthesia so that they may lie in the most comfortable position. If a Mayfield head fixator is used, adequate local anesthesia should be applied prior to application of the pins. Surgical drapes should be positioned allowing the anesthetist constant and unimpeded access to the airway whilst preserving a sterile field. The use of clear drapes reduces the feelings of claustrophobia.

The skull can be drilled and opened without pain or discomfort to the patient since there is no sensory innervation, however the dura is innervated by branches from all three divisions of the trigeminal nerve, the recurrent meningeal branch of the vagus nerve, and by branches of the upper cervical roots.

Challenges during the awake phase

Several complications may be encountered during awake craniotomy: 1) Hypertension can

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be induced by pain, psychological stress, along with hypercapnia or hypoxia. Also, it may be caused by dexmedetomidine (DEX) use.

Post-awake and post-operative care

After the awake part of the surgery has served its part, we can continue the surgery with the patient awake or using spontaneous ventilation under light, with deep sedation, or we can go with full general anesthesia and complete airway control. Normally sedation suffices, but if there is a complicated closure process (extended dural repair, a cranioplasty or very big wound) general anesthesia can be done. However, the patient usually requires lower rates of sedative infusions during the post awake phase than during the pre-awake phase as patients are often fatigued with lower tendency to agitation, and there is a lower level of painful stimuli during skull closure.

After the surgery, the patient should be admitted to an intensive care unit (preferably neurological/neurosurgical intensive care unit) with close neurological monitoring (q1h) for the first 24h.

The standard dose range for radiation therapy is typically between 45 Gy and 54 Gy (1.8 Gy/fr). Higher radiation dose did not improve PFS, nor OS and heightened the risk of radiation necrosis, with the dose being determined based on treatment volume. For tumors with IDH mutation and homozygous CDKN2A/B deletion or a grade 3-4 by morphologic criteria (microvascular proliferation and/or necrosis), a total dose of 60 Gy along with concomitant/sequential temozolomide should be considered, given their comparable prognosis to grade IV gliomas .

Radiotherapy can cause acute side effects like fatigue, weight loss, headache, skin dermatitis, nausea/vomiting, and alopecia. Increased risk of radiation necrosis may occur with higher doses and oligodendroglioma histology. Late effects such as neurocognitive decline and endocrine dysfunction can be severe especially in young adults. Future research may identify patients who can delay RT, potentially improving long-term quality of life (QoL) without compromising overall survival (OS). Additionally, studies may determine those who could benefit from lower RT doses, reduced treatment volumes, or specific delivery techniques.

MATERIAL AND METHODS

The signs and symptoms of brain tumor usually depend on the tumor size, location and its growth rate. The most frequent presenting symptom of LGGs is seizure with an incidence of 60-85% , but other symptoms may include new onset headache, focal neurological deficits or personality changes due to the tumor location in eloquent, typically supratentorial areas in the brain[1].

Patients with optic nerve glioma may experience visual field defects and decrease in visual acuity. They may also experience speech disturbances, vertigo, ataxia, psychiatric symptoms or signs of increased intracranial pressure such as headache, vomiting and nausea[15]. When tumors arise in the hypothalamus, endocrine disturbances such as diabetes insipidus, electrolyte imbalance or precocious puberty may occur .

Astrocytoma is usually a slow growing tumor that tends to cause symptoms to progress

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slowly and worsen over months or years. Seizure is a common presentation in low grade astrocytoma, but the tumor location and histology influence the risk of seizure occurrence.

RESULTS

For tumors located in speech or motor regions, functional magnetic resonance imaging (fMRI) can be highly beneficial before craniotomy, especially when paired with diffusion tensor imaging. Functional MRI measures brain activity by detecting changes associated with blood flow relying on the fact that cerebral blood flow and neuronal activation are coupled. Preoperative fMRI was successful in accurately localizing motor, sensory, and visual cortical areas (91.9%, 91.9%, and 100% respectively) in a prospective series . However, its accuracy in outlining language-associated cortical areas was 85.4%. This study also showed that patients with low grade gliomas had less frequent fMRI inaccuracies than higher grade gliomas. It is also important to note that the use of fMRI along with intraoperative direct cortical stimulation (DCS) allows the achievement of a high resection rate with a mean of 96.7%. With this association, DCS's efficacy is increased, providing valuable information for better surgical planning of intracranial gliomas .Building on that, fMRI showed a high overall sensitivity of 83% and specificity of 82% for the detection of functional cortex next to a focal mass lesion with lower sensitivity for high-grade gliomas compared to low-grade. Diffusion-weighted MRI (DWI) uses the diffusion of water molecules to generate contrast in MR images. Results from a prospective study including 31 patients with gliomas showed higher accuracy of diffusion- and perfusion-weighted MRI in assessing glioma grade as compared to conventional MRI which is useful as a preoperative assessment and surgical planning. The overall sensitivity of perfusion-weighted MRI (PWI) with regional cerebral blood volume of 1.7 was 82.6% when preoperatively assessing high-grade gliomas. Specificity was 75%, positive predictive value (PPV) was 90.48%, negative predictive value (NPV) was 60%, and overall accuracy was 80.65%. As for diffusion-weighted MRI (DWI), sensitivity was reported as 69.57%, specificity as 75%, PPV as 88.8%, NPV as 46.15% and overall accuracy as 71%

DISCUSSION

Lower grade gliomas, especially IDH-mutant, tend to occur more commonly in younger patients. However, occasionally elderly patients are also diagnosed with WHO G2 astrocytoma. Indications for radiation therapy should not differ from those for younger patients. As for hypofractionation (HFRT) usage, it is not a common practice for LGG due to the prolonged survival probability, compared to high-grade gliomas. The data regarding hypofractionation in these patients is limited and minimal.

Radiotherapy can cause acute side effects like fatigue, weight loss, headache, skin dermatitis, nausea/vomiting, and alopecia. Increased risk of radiation necrosis may occur with higher doses and oligodendroglioma histology . Late effects such as neurocognitive decline and endocrine dysfunction can be severe, especially in young adults. Future research may identify patients who can delay RT, potentially improving long-term quality of life (QoL) without compromising overall survival (OS). Additionally, studies may determine those who

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could benefit from lower RT doses, reduced treatment volumes, or specific delivery techniques.

CONCLUSIONS

Grading and classification of astrocytoma are now more focused on the molecular markers rather than the cellular morphology and histology. Once confirmed, the mainstay of treatment is complete resection, if possible. Awake craniotomies may aid the surgeon to ensure maximal resection while preserving adequate function. The decision of whether or not to assign the patient for radiation should be individualized per case, and the decision should be performed by a multidisciplinary team to outweigh benefits vs side effects of radiotherapy.

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