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A comprehensive review on glioma

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ABSTRACT

Gliomas are essential mind tumors that are thought to get from neuroglial stem or forebear cells. Based on their histological appearance, they have been generally delegated astrocytic, oligodendroglial or ependymal tumors and relegated WHO grades I–IV, which show various levels of danger. Gigantic advancement in genomic, transcriptomic and epigenetic profiling has brought about new ideas of arranging and treating gliomas. Diffusely invading gliomas in grown-ups are presently isolated into three overall tumor bunches with particular normal chronicles, reactions to therapy and results: isocitrate dehydrogenase (IDH)- freak, 1p/19q co-erased tumors with generally oligodendroglial morphology that are related with the best visualization; IDH-freak, 1p/19q non-co-erased tumors with for the most part astrocytic histology that are related with transitional result; and IDH wild-type, for the most part higher WHO grade (III or IV) tumors that are related with helpless guess. Gliomas in youngsters are atomically particular from those in grown-ups, the lion's share being WHO grade I pilocytic astrocytomas described by encompassed development, good anticipation and incessant BRAF quality combinations or transformations. Ependymal tumors can be atomically partitioned into particular epigenetic subgroups as indicated by area and visualization.

Keywords: Gliomas, oligodendroglial, neurological tumors, Epilepsy or Seizure or Convulsant.

INTRODUCTION

Glioma is that the commonest variety of central system (CNS) neoplasm that originates from glial cells. within the u. s., there are six cases of gliomas diagnosed per 100,000 people per annum. Gliomas are very diffusely infiltrative tumors that affect the encircling brain tissue. Glioblastoma is that the most malignant type while pilocytic astrocytomas are the smallest amount malignant brain tumors. within the past, these diffuse gliomas were classified into different subtypes and grades supported histopathologies like a diffuse astrocytoma, oligodendrogliomas, or mixed gliomas/oligoastrocytomas. Recently, gliomas were classified supported molecular and genetic markers.These advances have more specific prognostic and therapeutic benefits for patients with gliomas. additionally to molecular and genetic markers, gliomas are classified in grade I to IV supported the degree of proliferation indicated by the mitotic index and also the presence or absence of necrosis.[1]

HISTORY

The clinical history of patients with glioblastoma multiformes ($_{GBMs}$) usually is brief, spanning but 3 months in additional than 50% of patients, unless the neoplasm developed from a lower-grade astrocytoma. Note the following:

The most common presentation of patients with glioblastomas may be a slowly progressive neurologic

deficit, usually motor weakness. However, the foremost common symptom experienced by patients is headache. Alternatively, patients may present with generalized symptoms of increased intracranial pressure (ICP), including headaches, nausea and vomiting, and cognitive impairment. Seizures are another common presenting symptoms.

ETIOLOGY

There are three common sorts of gliomas, which are classified supported the phenotypic cell characteristics: astrocytomas, ependymomas, and oligodendrogliomas. These cell gliomas are further classified to low grade, atypical, and high-grade tumors supported cell morphology, mitotic activities, and molecular marker. the globe Health Organization (WHO) grading system utilizes molecular markers that have shown to own significant prognostic and therapeutic implications.[2]

Astrocytomas: Originated from astrocytes and may be encapsulated, preserving clear borders between normal and tumor cells, or infiltrative, indicating advanced grade. Low grades are common in children while high grades are common in young adults and older patients.

Oligodendrogliomas: Originated from oligodendrocyte cells. These are less infiltrating than astrocytomas and are common in adults.

Ependymomas: Originated from ependymal cells which are found lining the ventricular cavities and therefore the central canal of the medulla spinalis. These are common within the pediatric patient population.

PATHOPHYSIOLOGY

Over the past decade, the concept of various genetic pathways resulting in the common phenotypic endpoint (i.e, glioblastoma multiforme) has gained general acceptance. Genetically, primary and secondary glioblastomas show little overlap and constitute different disease entities. Studies are getting down to assess the prognoses related to different mutations. a number of the more common genetic abnormalities are described as follows:

Loss of heterozygosity (LOH): LOH on chromosome arm 10q is that the most frequent gene alteration for both primary and secondary glioblastomas; it occurs in 60-90% of cases.

This mutation appears to be specific for glioblastoma multiforme and is found rarely in other tumor grades. This mutation is related to poor survival. LOH at 10q plus 1 or 2 of the extra gene mutations appear to be frequent alterations and are possibly major players within the development of glioblastomas.[3]

p53: Mutations in p53, a tumor suppresser, were among the primary genetic alterations identified in astrocytic brain tumors. The p53 gene appears to be deleted or altered in approximately 25-40% of all glioblastoma multiformes, more commonly in secondary glioblastoma multiformes[4].

TOXICOKINETICS

There are some epidemiological studies suggesting that radiation and a few radiofrequency waves can increase the possibility of redeveloping high-grade gliomas. However, these studies lack specificity to gliomas. However, advances within the biology and genetics of gliomas have revealed that low-grade gliomas transform into high-grade gliomas by altering the genetic makeup of low-grade gliomas. Therefore, one can hypothesize that environmental and treatment-related toxicokinetics can play a job within the transformation of low-grade gliomas.

DIAGNOSIS

The diagnosis of glioma are Abscess, Demyelination, Gliosis, Infarct, Metastasis.

TREATMENT

1. Surgery: Grade I: These gliomas are surgically curable. Grade II: a secure gross total resection and radiographic follow-up are acceptable current practices. Grade III: a secure gross total resection, concomitant chemoradiation, and radiographic follow-up for recurrence are a suitable treatment. Grade IV (glioblastoma): a secure gross total resection, concomitant chemoradiation, and radiographic follow-up for recurrence are an appropriate treatment.
2. Chemoradiation: Currently, Stupp protocol may be a standard of look after Grade III-IV gliomas. The protocol consists of radiotherapy and concomitant chemoradiation employing a total of 60 Gray to 2 Gray per daily fraction over 6 weeks and temozolomide.
3. Treatments for Recurrence: Options for recurrent gliomas include re-operation with Gliadel wafers and targeted therapy like angiogenesis inhibitors or immunotherapy. The effectiveness of of these adjuvants therapies is in development.
4. Others Treatments: High-grade glioma patients are vulnerable to seizures, malignant edema, and complication related immobility. Therefore, these patients need antiepileptic medications, deep thrombosis (DVT) prophylaxis, and steroids before, during, and after the course of treatments to avoid cerebral edema.

Upon initial diagnosis of glioblastoma multiforme (GBM), standard treatment consists of maximal surgical

resection, radiotherapy, and concomitant and adjuvant chemotherapy with temozolomide[5].

Evidence suggests that in patients over 60 years old, treatment with temozolomide is related to longer survival than treatment with standard radiotherapy,

and for those over 70 years old, temozolomide or hypofractionated radiotherapy is related to prolonged survival than treatment with standard fractionated radiotherapy. the advance in survival with temozolomide is enhanced in patients with MGMT promoter methylation.[6]

MEDICAL TREATMENT

RADIATION THERAPY

Radiation therapy additionally to surgery or surgery combined with chemotherapy has been shown to prolong survival in patients with glioblastoma multiformes compared to surgery alone. The addition of radiotherapy to surgery has been shown to extend survival from 3-4 months to 7-12 months [7]

Dose response relationships for glioblastomas demonstrate that a radiation dose of but 4500 cGy leads to a median survival of 13 weeks compared with a median survival of 42 weeks with a dose of 6000 cGy. The responsiveness of glioblastoma multiformes to radiotherapy varies. In many instances, radiotherapy can induce a phase of remission, often marked with stability or regression of neurologic deficits likewise as diminution within the size of the contrast-enhancing mass. Unfortunately, any period of response is short-lived because the tumor typically recurs within 1 year, leading to further clinical deterioration and therefore the appearance of an expansile region of contrast enhancement.[8]

CHEMOTHERAPY

Temozolomide is an orally active alkylating agent that's used for persons newly diagnosed with glioblastoma multiforme. it absolutely was approved by the u. s. Food and Drug Administration (FDA) in March 2005. Studies have shown that the drug was well tolerated and provided a survival benefit. Oral alkylating agent converted to MTIC at physiologic pH; 100% bioavailable; approximately 35% crosses the barrier. Indicated for glioblastoma multiforme combined with radiotherapy. Significant overall survival improvement was demonstrated in patients treated with temozolomide and radiation compared with radiotherapy alone. Carmustine - Alkylates and cross-links DNA strands, inhibiting cell proliferation. Gefitinib - An anilinoquinazoline. Indicated as monotherapy to treat locally advanced or metastatic non-small cell carcinoma after failure of both platinum-based and docetaxel chemotherapies. The mechanism isn't fully understood. Inhibits tyrosine kinases intracellular phosphorylation related to transmembrane cell surface receptors.

Nitrosoureas: BCNU (carmustine)-polymer wafers (Gliadel) were approved by the FDA in 2002. Though Gliadel wafers are utilized by some for initial treatment, they need shown only a modest increase in median survival over placebo (13.8 vs. 11.6 months) within the largest such clinical trial trial, and are related to increased rates of CSF leak and increased intracranial pressure secondary to edema and mass effects.[9]

ANTICONVULSANTS

Phenytoin - Acts to dam sodium channels and forestall repetitive firing of action potentials. As such, it's a really effective anticonvulsant. First-line agent in patients with partial and generalized tonic-clonic seizures. Carbamazepine - Like phenytoin, acts by interacting with sodium channels and blocking repetitive neuronal firing. First-line agent in patients with partial and tonic-clonic seizures. Serum levels should be checked and will be approximately 4-8 mcg/Ml.

CORTICOSTEROIDS

Dexamethasone - Postulated mechanisms of action in brain tumors include reduction in vascular permeability, cytotoxic effects on tumors, inhibition of tumor formation, and decreased CSF production.

ELECTRIC FIELD THERAPY

The Optune device uses low-intensity, intermediate-frequency, alternating electric fields (tumor- treating fields) to focus on dividing cells in glioblastoma multiforme while generally not harming normal cells. The tumor-treating fields are generated via electrodes placed directly on the scalp. to focus on the tumor, array placement relies on the individual patient's resonance imaging results.[10]

Optune, also called the NovoTTF-100A System, was initially approved in 2011 to be used in glioblastoma multiforme that had recurred or progressed after treatment. In October 2015, the FDA expanded approval to incorporate use of the device in conjunction with temozolomide chemotherapy within the first-line setting. Approval was supported an open-label, randomized phase 3 trial in 700 patients, during which median overall survival was 19.4 months with use of the device plus temozolomide, versus 16.6 months with chemotherapy only

CONCLUSION

Characterization of the genetic and epigenetic alterations in gliomas has led to protein structure-function studies that have elucidated both how the signaling pathways are altered and their effect on cell proliferation, survival, and invasion. These studies clearly indicate the complexity of the regulation of those processes and suggest a dynamic process during which the cells of the tumor respond during a context-dependent manner to their microenvironment by cooperation and cross talk among receptors and intersecting signaling pathways. They also indicate how the tumor cells can promote invasion through remodeling of their microenvironment. Importantly, knowledge of those genetic alterations has allowed scientists to make rodent models to check the

importance of such alterations in vivo, to work out whether or not they are necessary for gliomagenesis or tumor progression

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