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Brain tumor (Glioma), Impact of Immunohistochemistry in Prognosis and Prediction Radiation Oncologist Perspective

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Abstract

Primary brain tumors are rare and uncommon tumors comprising only 1.6 percent of cancers, although Metastatic brain tumors are more common entity. Primary CNS neoplasm's are a challenging group of tumors to treat given their varied patterns of behavior and subsequent varied clinical outcomes. This chapter will focus on the treatment of both adult low-grade gliomas (LGGs) and adult high-grade gliomas (HGGs), with an emphasis on radiation therapy techniques, Signs and symptoms of intracranial tumors depends upon types and histology as well as grade of tumors, Some tumors causes problems by their intracranial extension only for example Glioms, Menangiomas, Pituitary tumors other brain tumors like Primary CNS Lymphomas, Germ cell tumors as well as Primitive Neuroendocrine tumors (PNET) have strong prediction of leptomeningeal spread, among all primary brain tumor Gioblastoma multiforme (GBM) is the most common primary brain tumor and one of the most lethal in nature due to its infiltrative nature because of this GBM overall survival with surgical resection alone is 3 to 6 month only but if we add adjuvant radiotherapy after surgery its overall survival extends up to 1 year furthermore if we add alkalizing agents chemotherapy its overall survival goes up to 1.5 years.

Keywords

Gioblastoma multiforme (GBM); Primitive Neuroendocrine tumors (PNET); Primary brain tumor

Introduction

American society of Radiation oncology (ASTRO) assembled the group experts in order to develop guidelines for the management of GBM, Their recommendations were, and 1-Fractionated radiotherapy improves overall survival compared with chemotherapy. 2- Radiation must given 3 to 6 weeks after the brain tumor surgery. 3- Adding Temozolamide TZM as concurrent or as adjuvant treatment improves overall survival and progression free survival compare to radiotherapy alone, and this the current standard of care treatment in patients under age of 70 years. 4- Patients younger than 70 years of age must be offered fractionated radiotherapy up to total dose of 60 Grey for High grade glioma.5- Among the elderly patients there is no evidence that conventional radiotherapy 60Gy is superior to hypofractionated radiotherapy dose 40Gy / 15 fractions over 3 weeks. 6- Brain tumor patients with Methyl Guanine DNA Methyl transferase gene (MGMT) promoter methylation gene hypofractionated radiotherapy in combination with Temozolamide TZM more effective compare to those who do not show MGMT gene on immunohistochemistry test after surgery [1-3].

Patients with poor performance status (low KPS less than 60%) hypofractionated radiotherapy alone or Temozolamide alone is an useful option of treatment, Although GBM is diffusely infiltrative disease but partial brain radiotherapy (tightly conformal radiotherapy) leads no worse survival than whole brain radiotherapy here target volume of radiotherapy includes gross tumor/resection cavity with adequate margin without including the edema.

Brain tumor Immunohistochemistry and molecular markers

Majority of glioma are according to WHO updated classification graded as grade 4 Glioblastoma multiforme GBM and grade3 tumor as Anaplastic Astrocytoma or Anaplastic Oligodendroglioma, Other category is low grade glioma LGG as grade 2 Astroctoma or low grade oligodendrogioma, After surgical resection of brain tumor tissue required to send for immunohistochemistry in order to predict adjuvant treatment outcome of this deadly disease (Figure 1).

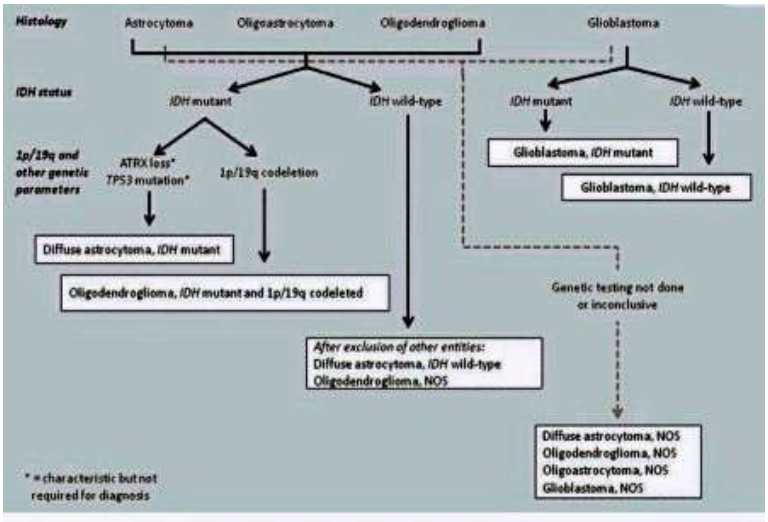

Figure 1: Immunohistochemistry of glioma tumors.

Molecular Markers

IDH I/2 mutations (Isocytrate dehydrogenase 1or 2 mutations) shown to be very important for low grade glioma LGG, it is found that IDH mutant glioma could be further divided into two category one that carries Ip 19q codeletions called oligodendroglioma having good prognosis other category those lacking 1p19q codeletion fall under Astrocyoma category having poor prognosis [4].

The codeletions of chromosomal arms 1p 19q happens as result of translocation this was having clinical significance as those tumors carrying these deletions were shown to respond favorably to both radiotherapy as well as alkylating agents chemotherapy either Temozolamide or PCV (Procarbazine, CCNU, Vincristine) regime, So patients with this molecular profile of glioma were identified as good prognosis and better treatment outcome.

Cycline Dependent Kinase Inhibitors (CDKN) 2A/B

Homozygous deletion of CDKN 2A/B leading to cell dysregulation and have been identified as poor prognostic factor in IDH Mutant and TP53 Mutant astrocytoma.

Methyl Guanine DNA Methyl Transferase Gene MGMT: Methylation of promoter region of O^6 Methyl Guanine DNA methyl transferase in GBM shown to be very important for the response of Temozolamide treatment, but on contrary to that there is no change in response with MGMT gene for radiotherapy treatment [5].

Prognosis Factors For Glioma Tumors

Histological diagnosis after surgery biopsy report if high grade gllioma worst prognosis despite all treatment modalities but if low grade oligodendroglioma prognosis is good, KPS score if more than 60% we can presume good prognosis, younger age patients of glioma do better than older age patients, female do better in compare with male gender [6,7].

Radiotherapy Planning for Brain Tumors

For glioma radiotherapy planning CT/MRI scan to be done after 21 days (3 weeks) of primary tumor surgery in order to avoid large oedma after surgery in radiotherapy port, radiation oncologist must include these structures in radiotherapy planning along 5mm to 10mm margin these structures are, Adjacent Dura, Inner bone flap, brain tumor cavity, Dural sinus adjacent to cavity, any enhancing structure lies in vicinity of surgical tract along precisely excluding the brain edema after combining all above mentioned structure and adding adequate margin we formulated clinical tumor volume CTV, After that we go for multiplanner evaluations to make an Planning tumor volume PTV and deliver radiotherapy (Figure 3,4).

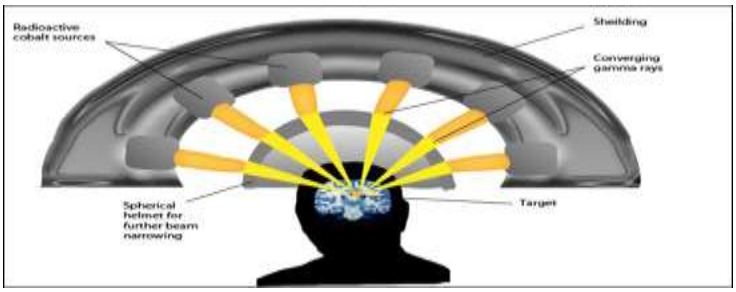

Figure 3: Radiation treatment of brain tumor/ brain mets with Cobalt based stereotactic radio surgery.

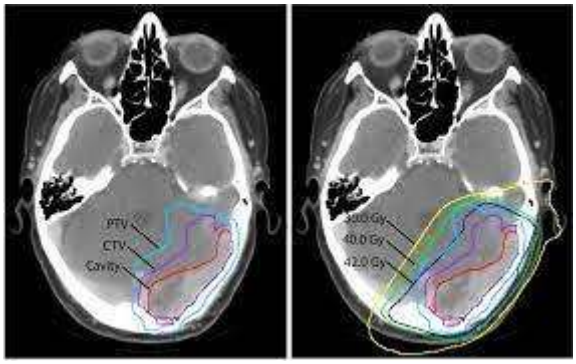

Figure 4: Post-operative radiotherapy to brain mets cavity.

Conclusion

After surgical resection of brain tumor tissue required sending for immunohistochemistry in order to predict adjuvant treatment outcome of this deadly disease. Implementation of contouring guidelines for the unique infiltrative nature of malignant glioblastoma in the daily practice of radiation oncology is critical in the milieu of decreasing target volume expansions, smaller PTV due to daily image guidance carry adequate tightly target dosing, and providing equally effective local control, overall survival in compare to wider field coverage.

Conflict of Interest

None.

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