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Puttur Srinivasan Uday Prakash

Scientific supervisor: Ph.D., associate professor N. N. Usova

Educational Establishment
«Gomel State Medical University»
Gomel, Republic of Belarus

THE LATEST TREATMENTS FOR BRAIN TUMORS (GLIOBLASTOMA)

Introduction

A brain tumor is a growth of abnormal cells in the brain. The anatomy of the brain is very complex, with different parts responsible for different nervous system functions. Brain tumors can develop in any part of the brain or skull, including its protective lining, the underside of the brain (skull base), the brainstem, the sinuses and the nasal cavity, and many other areas. There are more than 120 different types of tumors that can develop in the brain, depending on what tissue they arise from.

Goal

To provide an overview on the current treatment methods used to treat brain tumor globally and to provide a better understanding on the advances of new treatment methods used to treat brain tumor and to show how successful these treatment methods are, using clinical trials which have been carried out globally as examples.

Material and methods of research

The search of information was conducted through the research of scientific articles and systematic literature and the results were screened for the relevance review topic and also new articles were added based on the clinical knowledge of the author on the specific area. Statistical information was also obtained from clinical trials conducted on the area of review.

The results of the research and their discussion

Glioblastoma (GBM), also referred to as a grade IV astrocytoma is a fast-growing, aggressive and deadly brain tumor. It invades the nearby brain tissue, but generally does not spread to distant organs. GBMs can arise in the brain de novo or evolve from lower-grade astrocytoma. In adults, GBM occurs most often in the cerebral hemispheres, especially in the frontal and temporal lobes of the brain. GBM is a devastating brain cancer that can result in death in six months or less, if untreated; hence, it is imperative to seek expert neuro-oncological and neurosurgical care immediately, as this can impact overall survival.

Prevalence and Incidence

Glioblastoma is the most common malignant brain and other CNS tumors accounting for 47.7 % of all cases.

Table 1 – Indicates prevalence and incidence of the neuroglioblastoma

Incidence	Age	Gender
3.21/100,000 population	Older > young	Male > female

Survival rate is approximately: 40 % after the first year post diagnosis and 17 % in second year.

Factors associated with glioblastoma risk are prior therapeutic radiation, decreased susceptibility to allergy and impaired immune response. Several hereditary cancer syndromes greatly increase the risk of glioblastoma, including Li-fraumeni syndrome and Lynch syndrome.

Advancement in treatment:

Introduction

In over 40 years median survival has only shown modest improvement , and standard of care treatment often has negative impact on quality of life . Treatment including radiation and chemotherapy takes a heavy toll. Frequently patients cannot tolerate the completion of the prescribed chemotherapy cycles. Thus, there is a great unmet need for a completely different therapeutic approach with better outcome and less toxicity.

A new FDA-approved treatment involving electric fields alternating at 200 kHz called Optune™ therapy is now available for recurrent GBM as monotherapy and in combination with temozolomide for newly diagnosed GBM. It is also being tested in clinical trials for other cancers. Its hypothesized mechanism of action involves disruption of tubulin dimers, mitotic spindles, and cell division by electric field-induced dipole alignment and dielectrophoresis . It has a modest effect on survival, increasing median overall survival by 0.6 month in recurrent GBM, and in newly diagnosed GBM by 31 %.

Oncomagnetic Device

The Oncomagnetic device consists of 3 oncoscillators securely attached to an acrylonitrile butadiene styrene helmet and connected to a microprocessor-based electronic controller operated by a rechargeable battery. Further details regarding the device are given in the Supplementary Appendix. Based on a finite element model-based calculation of the spread of the field and the size and magnetization of the rotated diametrically magnetized neodymium magnets, we estimated that the combined effective field (at least 1 mT in strength) of the 3 oncoscillators covered the entire brain, including the upper part of the brain stem.

Oscillating Magnetic Field Treatment

The treatment consists of intermittent application of an OMF that needs to be generated by rotating permanent magnets in a specific frequency profile and timing pattern to be effective. The patient received this treatment initially in the Peak Center clinic under the supervision of the treating physician and the Principal Investigator (DSB) of this study for the first 3 days. The dose was escalated over this period as follows. On the first day, the treatment was for 2 hours with a 5-min break between the first and the second hour. On the second and third days, it was increased to 2 and 3 2-hour sessions, respectively, with 1-hour breaks between the sessions. The patient's spouse was trained in the use and care of the device on these days. After this initial supervised phase, the treatment was continued at home unsupervised with the same regimen as on the third day, above. The spouse was instructed to maintain a daily log of the conduct and progress of treatment, and any observed treatment and adverse effects.

Data Analysis

Post-contrast T1 anatomical and T2-FLAIR MRI scans at each of the 6 time points were used to determine changes in contrast-enhanced tumor (CET) volume and non-enhanced tumor infiltration, respectively, before and after initiation of treatment. Information on image processing, data normalization and plotting are given in the Supplementary Appendix. Values obtained from pre-treatment clinical scans taken at 2 time points over 3 months before enrollment of the patient were also plotted on the same graph. Because this is a single patient case report, we

could not perform any meaningful statistical analysis. However, to obtain a semi-quantitative assessment of the significance of the trend seen with treatment, we analyzed the changes in CET volume using Bayesian logic, given the observed increasing trend at two pre-treatment time points. Accordingly, we assumed that the chance of increase, decrease and no change in the rate of tumor growth was the same at each time point after treatment initiation to calculate the probability of a decrease at each post-treatment initiation time point.

Discussion

The findings of this study indicate that Oncomagnetic device-based OMF therapy is well tolerated by a patient who has end-stage recurrent GBM with leptomeningeal involvement and has no other available effective treatment options. They also demonstrate a clinically significant reduction in CET volume with reductions in non-enhanced tumor volume and/or edema in T2-FLAIR scans. The temporal profile of changes in CET volume also suggests a correlation with the treatment dose and the presence or absence of treatment. When the treatment dose was higher (6 hours/day for 4 days) we see a tumor volume reduction rate of 2.32 cm^3/day. When it was lower (2 hours/day for 9 days and 3 hours/day for 18 days) the reduction is 1.03 cm^3/day. Moreover, when the treatment was paused for 8 days the decreasing trend reversed and the CET volume increased, instead. Assuming that the ~1.03 cm^3/day decreasing trend had continued until the treatment was paused, we can estimate that the CET volume grew at the rate of 1.26 cm^3/day during the pause. Despite the apparent correlation it is possible that the treatment response is independent of the short-term changes in the treatment dose.

Besides Optune™, the other type of treatment approved by the FDA and recommended as a standard in National Comprehensive Cancer Network guidelines for recurrent GBM is the anti-vascular endothelial growth factor (VEGF) monoclonal antibody, Bevacizumab.Bevacizumab treatment response of reduction in tumour volume on MRI scans has been reported to be lower than is observed in the present study Furthermore, while anti-VEGF drugs in general have mild toxicity profiles and two Phase II trials have shown anti-tumour efficacy a subsequent Phase III trial did not show a significant increase in overall survival

Conclusion

Noninvasive Oncomagnetic device based OMF therapy appears to be a safe and efficacious new modality of treatment against GBM that potentially has many advantages over existing treatments. The present report has the limitation of the treatment being conducted in only a single patient so far. Extending it to more patients in research studies would provide additional information regarding safety and efficacy.

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