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Abstract

Gamma Knife Radiosurgery and Highly Active Antiretroviral Therapy for the Treatment of AIDS-Related Primary CNS Lymphoma. Prospective, Observational, Cohort, Clinical Study

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Abstract

Objectives: Primary Central Nervous System Lymphoma (PCNSL) is a rare and aggressive malignancy characterized by a yearly incidence of 0.5 cases per 100000 people and a prevalence of less than 4% of all brain tumors. The criterion standard for the treatment of newly diagnosed PCNSL remains high-dose chemotherapy in conjunction with palliative whole-brain radiotherapy with a low success rate and many long term side effects. We investigate the role of novel combined approaches using chemotherapy, HAART, and GKRS to have a positive impact on survival rates of PCNSL and PCNSL related to AIDS and in immunocompetent patients.

Methods: This is a prospective, observational, comparative clinical study evaluating the effect and survival rate of patients with a histological diagnosis of PCNSL treated with MTX alone (control) and MTX OR HAART therapy, plus GKRS. A prospective follow-up was completed between 2007-2018. The study received approval from IRB. Eligible patients underwent GKRS and/or a chemotherapy protocol using MTX at the same institution. The diagnosis was confirmed by a pathology report. A priori sample size calculation was performed on the basis of a prior study, which evaluated the survival rate in a sample size of 40 patients. The study implied a sample size of at least 31 subjects per group is necessary to detect the minimal clinically important difference in the mortality rate of 1.5 standard deviations (s = 1.5, a = 0.05, ß = 0.20). The Wilcoxon Rank Sum Test was used for comparison of continuous data between the groups. A comparison of categorical data was performed using Pearson's Chi-square test or Fisher's exact test as indicated. Ordinal ranking scores were compared using the Mantel-Haenszel test.

Results: One hundred twenty-eight patient charts and clinical follow-ups were reviewed. Included 73 chemotherapy and 55 chemotherapy, plus GKRS, patients and 37 GKRS and HAART therapy. The follow-up period was 24 to 55 months (mean 38.1 months). There were no statistically significant differences in patient demographics or histology diagnosis. The median survival rate from initial diagnosis was statistically significant (p = 0.0034) with 26.8 months in the chemotherapy group and 47.6 months in patients receiving chemotherapy, plus GKRS. The signs and symptoms of the patients remained evidently improved within two to six weeks after GKRS and four to 10 weeks after chemotherapy alone. Significant factors contributing to survival greater than 24 months following GKRS were increased marginal dose (odds ratio = 6.5,

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p = 0.031, 95% CI (1.4-18.57)), increase in maximal dose (odds ratio = 1.54, p = 0.012, 95% CI (1.15-2.89)), and increase in the pretreatment Karnofsky score (odds ratio = 5.13, p = 0.008, 95% CI (1.55-85.1)). The side effects attributed to GKRS were minimal.

Conclusions: GKRS is a minimally invasive procedure that allows for the immediate use of systemic chemotherapy and can be an ideal co-adjuvant treatment option in patients with PCNSL. The criterion standard for treatment of newly diagnosed PCNSL remains high-dose chemotherapy in conjunction with palliative whole-brain radiotherapy; however, there may be a role for novel combined approaches using chemotherapy, HAART, and GKRS to have a positive impact on survival rates of PCNSL related to AIDS. The early and accurate combination of therapies may allow for greater tumor control, enhanced overall survival period, and a lesser number of complications.