Intracerebral neutron brachytherapy for hemispheric glioblastoma multiforme

A pilot study

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Abstract

The University of Kentucky Brain Tumor Study and Research Group has developed a new treatment protocol of interstitial brain brachytherapy using Californium-252 neutron source implantation in 1980. Only patients with malignant gliomas were eligible for this pilot study. Nine patients entered the Phase I trial of the protocol study between November 1980 and October 1981. According to the design of the protocol, all patients who had a verified histologic diagnosis of glioblastoma multiforme underwent postoperative intracerebral Cf-252 neutron source implantation, followed by 6000 cGy of external photon beam irradiation. The purpose of this pilot study was to test the feasibility of interstitial Cf-252 neutron source implantation and only one implant afterloading applicator was used for brachytherapy. The implant applicator was placed in the center of tumor and the procedure was performed under CT guidance. In the assessment of the procedure, Karnofsky functional performance status, intellectual status, neurological examination, CT scans, and complications were used. All patients tolerated the procedure well and no serious complications were encountered. Despite the quality of these early treatments, there was some evidence of short-term benefit in duration of survival of the patients. We believe that further technical improvement to achieve an adequate isodose distribution to cover the tumor volume might result in longer duration improvement in survival.

Introduction

The extremely poor prognosis and survival of patients with malignant glioma has been well documented in the literature (1, 2), with greater than 50% mortality within 6 months, and 90% mortality within one and an half years (3, 4).

Chemotherapy has been employed in treatment for more than two decades. However, there is no consistent evidence that any chemotherapeutic agent has improved the life expectancy or quality of survival compared with surgery and postoperative radiotherapy (5). Malignant gliomas do not metastasize outside of the central nervous system except in very rare instances. Treatment failure is the result of locally recurrent or persistent disease in the cranial fossa. The treatment results of glioblastoma multiforme by surgery, photon radiotherapy, hypoxic radiosensitizers, hyperbaric oxygen or fractionated radiotherapy are so disappointing that any new treatment justifies a trial if there is a reasonable chance of success and acceptable toxicity. This pilot study aimed to assess our early efforts to test the feasibility and side effects of interstitial Cf-252 implants in malignant glioma patients (6).

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Materials and methods

Only the patients who had the histologic diagnosis of malignant glioma were eligible for interstitial Cf-252 neutron irradiation. Nine primary brain tumor patients whose histologic diagnosis was glioblastoma multiforme were entered into this pilot study during the period of November 1980 to October 1981 at the University of Kentucky Medical Center. All of nine patients underwent a single tube implantation into a glioblastoma in their brain and received ~6000 cGy external irradiation uniformly to the whole brain (6). The details on nine patients treated with a single applicator are reviewed in this study. Criteria of eligibility for this study were (1) histologic diagnosis of glioblastoma multiforme should be established by the neuropathologist at this institution, (2) performance of the patients of 30% or greater by Karnofsky Performance criteria, (3) 79 years of age or younger, (4) hemispheric location of the tumor and (5) consent to participate in this study by the patients and/or their family.

All patients underwent craniotomy and tumor resection. After the incision sites healed and the histologic diagnosis of glioblastoma multiforme was confirmed, the patients underwent intracranial implantation in the center of the tumor bed as judged by 2D CT scans, using a stainless steel tube. For localization of tumor and positioning of the applicator, CT scans were utilized (Fig. 1) and a ventricular catheter. The implant applicator was a single metal tube with one closed sharp end termed 'icepick' (Fig. 2), and placed after the tumor site was established. Following applicator placement in the tumor bed, verification X-rays were obtained (Fig. 3). One or two Cf-252 radioactive sources were afterloaded for 6–8 hours. Neutron dosimetry has been discussed elsewhere (6) and was calculated taking into account the higher relative biological effectiveness, (RBE) of neutrons by $D_{req} = RBE_n \cdot D_n + RBE_r \cdot D_r$, where $RBE_n = 6.0$. In addition to interstitial neutron irradiation, the patients received ~6000 cGy of external photon radiation to