Application of invasive microwave hyperthermia for the treatment of gliomas*

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Summary

Twenty five cases of gliomas of the brain were operated upon by debulking the tumour masses. Following this, microwave hyperthermia was given by heating a measured volume of Ringer’s solution instilled into the tumour cavity. This was followed by a ‘dry treatment’ without Ringer’s solution. The follow up of these cases revealed that 11 cases have died and 14 cases are alive post-operatively. For those that are alive, the follow up period ranges from 21 to 41 months with the mean survival period of 31.1 months; in this group, 12 cases have a Kanofsky scale of 80-100, i.e. they are fully independent. The other two cases have a score of 50 or under and they need institutional care.

In this study, we believe that the first order effect of microwave hyperthermia is predominantly thermal and in the published literature, and in this investigation, there is no clear evidence that microwave radiation produces any other beneficial and quantifiable effect on the tissue.

Introduction

In 1866, a German physician Dr. W. Busch reported the disappearance of a two-year facial sarcoma in a patient who had developed high fever secondary to two episodes of erysipelas [1]. Twenty seven years later, Coley described 38 patients with advanced cancer who had high fever secondary to erysipelas bacterial toxins with improvement. This gave birth to ‘Coley’s toxin’ [2]. In 1898 Westermark advocated local heating of the tumour [3]. In 1918 Rohdenburgh reviewed the literature and reported 166 patients whose cancer regressed spontaneously, of these 72 had developed high fever or had received local heat application [4]. Muller in 1913 described 100 patients with advanced cancers who were treated with both radiation and heat with good results. This was further supported by animal studies [5]. Warren in 1935 introduced the era of physical hyperthermia for cancer therapy. He treated 32 terminal tumour cases with diathermy or radiant heat energy to a rectal temperature of 41.5 °C. There were no cures, but there was immediate improvement lasting from 1 to 6 months [6].

In recent years, the treatment of cancer patients by hyperthermia has attracted much attention and with encouraging results [7–14]. In vitro and vivo hyperthermia has been shown to kill large populations of cells and its effect has many features that may be regarded as complementary to those of x-ray. Two factors have stimulated the resurgence of interest in thermotherapy, they are the relative failure of surgery, x-ray and chemotherapy to control cancer

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adequately, and recent advances in instrumentation. This has encouraged a new look at microwave hyperthermia modalities which may offer the advantage of direct rather than blood-mediated heating of tissue. It should be noted that these advantages derive primarily from the heat energy deposited by the microwave radiation and there appears to be no evidence of any additional therapeutic effects. The main interest in microwave hyperthermia is based on the fact that unlike very short wavelength radiation, this form of energy is non-ionising and its effect is purely thermal.

The treatment of brain glioma with microwave therapy is still in its infancy and it will be some time before its impact is felt in the full treatment of gliomas. Sutton in 1971 reported encouraging results of thermotherapy induced by using a miniature heat probe inserted intracranially into the experimental glioma. Later, he implanted the heat probe into recurrent human gliomas and supplemented the treatment with chemotherapy [15–16]. Salcman and Samaras in 1981 published a paper on the biophysical aspects of treatment of brain tumours with thermotherapy using microwave radiation [17]. Since then, several papers on the treatment of malignant brain tumours with localized microwave thermotherapy have appeared in the literature [17–21]. In this paper, we wish to present our experience with this form of treatment applied to 25 cases of gliomas.

**Method**

Details of this method have already been reported [21]. The method consists of craniotomy and debulking of the tumour mass, including the removal of the surrounding oedematous tissue, until normal tissue is reached [22]. Bleeding from the tumour bed is carefully controlled. The microwave antenna fabricated from a 2 mm diameter coaxial cable is positioned in the middle of the debulked tumour cavity which is filled with a known volume of Ringer's solution. In a separate experiment, the time required for a specific volume of the Ringer's solution to reach 42 °C temperature is determined and a calibration graph of volume against time is plotted. At the periphery of the cavity, the temperature is measured using thermisters. Due to the finite conductivity of the Ringer's solution, the temperature at the centre of the tumour cavity will be higher. The microwave power is adjusted to ensure that the temperature does not exceed 44 °C at the periphery of the cavity. The nominal output power in the microwave generator used here is 10 Watts at a frequency of 2.45 GHz.

Our patients were treated with three ‘wet treatments’, i.e. a known amount of Ringer's solution was instilled in the cavity and heated to a temperature of 42 °C–44 °C and left in the cavity for 2 minutes; this treatment was repeated three times. This is to ensure that the heat penetrates into the crevasses of the debulked tumour cavity and along the blood vessels where tumour cells may be lodged. In order to have a uniform method, the warm solution was removed after each treatment; the bed of the tumour cavity is examined carefully and any fresh blood oozing from the tumour bed is sucked out and bleeding points are coagulated.

After the ‘wet treatment’ has been completed, the wall of the tumour is sprayed with the Ringer's solution and the cavity is heated until the wall temperature reaches 44 °C. In this procedure, we make sure that the antenna is in the middle of the cavity and not touching the brain tissue. If necessary, self-retaining retractors can be applied to prevent the tumour wall from collapsing.

Two weeks after surgery, post-operative C.T. scan is done and if no tumour tissue is left behind the patient is discharged but visits the outpatient clinic for a regular check up. The C.T. scan is repeated every six months. During these visits, the patients undergo neurological examination and these results are compared with the data obtained before treatment. This gives a score on the Karnofsky Scale.

**Clinical details**

Twenty five patients who were diagnosed by C.T. scan and pathologically verified after operation to be suffering from cerebral gliomas were the subject of this investigation. The treatment philosophy was explained to each patient and they all gave a written