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Radiosurgery for metastatic brain tumors

Abstract Since the life span of patients with metastatic brain tumors is quite limited, the aim of the treatment is to prolong their useful quality of life with minimally invasive therapeutic modalities. Although gamma knife radiosurgery (GKR) is widely used and accepted as a standard therapeutic modality for treating metastatic brain tumors today, there are still several problems to be clarified. The indication of GKR for metastatic brain tumors is based on the size, number of metastases, the state of primary cancer, systemic metastases, general condition of the patient, the radiosensitivity of primary cancer, the effective dose, etc. Although these problems have already been widely documented, the following recent papers have analyzed them more clearly. It seems that GKR is suitable for a single and solitary metastatic tumor of < 3 cm in diameter, with a Karnofsky Performance Score of > 70%, and there appears to be no limitation concerning the histology of the primary cancer and different radiosensitivity. The papers selected also cover the effect of GKR when combined with surgery and/or whole brain radiotherapy, and the limitations of GKR in the treatment of metastatic brain tumors.

Key words Metastatic brain tumor · Gamma knife · Radiosurgery · Lung cancer · Melanoma · Radiotherapy

Introduction

The incidence of metastatic brain tumors has increased recently in parallel with the increasing number of cancer patients. About 20–25% of autopsied patients had brain metastasis. If brain metastasis is not treated, it will be a direct cause of death for the patients. The life span of cancer patients with metastatic brain tumors is generally 3–4 months if no treatment is given after the onset of the initial symptoms. The aim of treatment for metastatic brain tumor patients is to prolong their useful life as long as possible with less invasive therapeutic modalities. The local control of brain metastasis by surgery and/or radiotherapy has historically been demonstrated to prolong the life of the patients. The recently developed gamma knife radiosurgery (GKR) has been proved to achieve the same effect of good local tumor control as surgical removal. The merits of GKR are that focal radiation can be given with minor effect on adjacent normal brain tissue, even deep-seated metastatic tumor tissue that is not suitable for surgical removal can be treated, hospital stays are shortened, and therapeutic morbidity and medical costs are reduced. Local tumor control is quite as good as microsurgical removal, and GKR can treat multiple metastases quite easily. The demerit is that GKR cannot treat a large metastatic tumor mass > 3.5 cm in diameter. In such cases, surgical removal of the tumor
and decompression are required for further treatment. Lung cancer (non-small cell carcinoma) and breast cancer are radiosensitive, while melanoma and renal clear cell carcinoma are rather radioresistant. The following papers have, however, shown quite good effectiveness of GKR, even for these radioresistant tumors. In the last decade, many papers have reported the indication, effectiveness, and complications of GKR. A critical analysis of those papers shows the indication, effectiveness and limitations of GKR more clearly for the treatment of metastatic brain tumors.

[1] Surgery and radiotherapy compared with gamma knife radiosurgery in the treatment of solitary cerebral metastases of small diameter

Information. This study was carried out to compare retrospectively the therapeutic efficacy of surgery plus whole-brain radiation therapy (WBRT) with GKR alone as the primary treatment for solitary cerebral metastases from various cancers. Fifty-two patients were treated by surgery plus WBRT, and 56 patients by GKR alone. Patients with single circumscribed brain metastases, 3.5 cm or smaller in diameter, and stable systemic disease were selected. The primary tumors of the WBRT group were cancers of the lung (n = 17), of the genito-urinary tract (n = 10), of the gastrointestinal tract (n = 3), breast cancer (n = 8), melanoma (n = 16), and other cancers (n = 4). All patients of the WBRT group were treated at the Ludwig-Maximilian University Hospital, Munich. Tumor resection was performed using microsurgical techniques. All patients received WBRT beginning within 2 weeks of surgery at a conventional fractionated dose of 40 Gy plus an additional boost to the tumor bed of 10 Gy. The median hospital stay for surgery was 10 days. Conventional radiotherapy required 5 weeks of treatment and was performed generally on an outpatient basis. All patients of the GKR group were treated at the Gamma Knife Center, Munich. The diagnosis of brain metastasis was based on radiological findings and histological findings in the primary tumor except in 3 patients in whom stereotactic biopsy was performed to establish the histological diagnosis. Any surgical treatment and/or WBRT was not performed before or after GKR. The minimum dose applied to the tumor margin ranged from 14 to 27 Gy (mean 21). The maximum dose ranged from 28 to 54 Gy (mean 41). The radiation dose was determined by the radiosensitivity of the tumor. Melanoma and hypernephroma were considered to be radioresistant tumors, and lung and breast cancers were considered to be more radiosensitive. Multiple isocenters (mean number 7) were chosen to match the tumor volume and shape. In cases of local or distant tumor recurrences, an additional radiosurgical procedure was performed if the patient was in good clinical condition with stable systemic disease.

The patient groups did not differ statistically in terms of age, sex, pretreatment Karnofsky Performance Score (KPS), duration of symptoms, tumor location, histological findings, status of the primary tumor, time to metastasis, and cause of death. However, the GKR group had more melanoma cases (n = 16) than the WBRT group (n = 7). The 1-year survival rate (median survival) was 53% (68 weeks) in the WBRT group and 43% (35 weeks) in the GKR group (P = 0.19). The 1-year local tumor control rates after WBRT and GKR were 75% and 83%, respectively, (P = 0.49), and 1-year neurological death rates were 37% and 39%, respectively, (P = 0.8). The shorter overall survival time in the GKR group was related to higher systemic death rates. A pretreatment KPS of <70% was an unfavorable prognostic factor for survival. Perioperative morbidity and mortality rates were 7.7% and 1.6% in the WBRT group, and 8.9% and 1.2% in GKR group, respectively.

Analysis. This study was not a prospective randomized study but a retrospective analysis. The patients of both groups – conventional surgery plus WBRT and GKR – were, however, well selected, and the results provide us with reliable data to compare the efficacy of the two therapeutic strategies. The study suggests that GKR can be used to achieve local tumor control comparable with that achieved by surgery plus WBRT for single and well-circumscribed metastatic tumors with a diameter of 3.5 cm or less. GKR is a less invasive therapeutic modality than surgery and can be performed either in an outpatient clinic or with only a short stay in hospital. Larger tumors with a diameter of 3.5 cm, however, require surgical removal before GKR. The difference in outcome & or radiosensitive cancers such as lung or breast cancer and radioresistant tumors such as melanoma or hypernephroma requires further study.