Management of Solitary Supratentorial Metastatic Brain Tumours

Thesis

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ABSTRACT

Brain metastases are a common complication in cancer patients. In this work, 30 patients with supratentorial solitary brain metastases are evaluated retrospectively, The modality of therapy: Surgery followed by whole brain radiotherapy. Results of both therapies, including efficacy, toxicity /morbidity and survival, quality of life and cost benefit will be evaluated.

Key Words:

Brain metastases

Surgery

Whole Brain Radiotherapy

INTRODUCTION

Brain metastases are the most common brain tumor seen clinically representing slightly more than half of brain tumor patients and an important cause of morbidity and mortality. They develop in approximately 10% to 30% of adults and 6% to 10% of children with cancer

In adults, the primary tumors most often responsible for brain metastases are lung cancer (50%), breast cancer (15% to 20%), unknown primary tumor (10% to 15%), melanoma (10%), and colon cancer.

In children, the most common sources of brain metastasis are sarcomas, neuroblastoma, and germ cell tumors

Approximately 80% of brain metastases are located in the cerebral hemispheres, 15% in the cerebellum, and 5% in the brainstem ***(Biswas et al., 2006)***.

Clinical Manifestations

The clinical features of brain metastases are extremely variable, and the presence of brain metastases should be suspected in any cancer patient who develops new neurological symptoms**.**

The clinical presentation of brain metastases is similar to that of other brain tumors and includes headache, focal neurological dysfunction, cognitive dysfunction, and seizures

Brain metastases must be distinguished from primary brain tumors, abscesses, demyelination, cerebral infarctions or hemorrhage and progressive multifocal leukoencephalopathy. Moreover brain metastases must be differentiated from the effects of prior treatment, including radiation necrosis ***(Bruce-Staskal & Bouton, 2001)***.

The best diagnostic test for brain metastases is contrast-enhanced Magnetic resonance imaging (MRI). This test is more sensitive than enhanced CT scanning or nonenhanced MRI in detecting lesions in patients suspected of having cerebral metastases, and in differentiating these metastases from other central nervous system (CNS) lesions. There is also new diagnostic methods as MRI spectoroscopy, functional MRI is extremely helpful as it demonstrates the relations of the mass to the eloquent cortical areas and white mater fibers. Further advanced techniques have therefore been com bined with diffusion imaging in this increased sensitivity, most commonly used is MRI spectroscopy which provides information about the metabolic profile inside and in areas around the lesion ***(Han, Huang, Guo, Zhuang, & Han, 2015)***.

In the majority (80%) of patients, brain metastases develop after the diagnosis of primary cancer (metachronous presentation). However, in some patients, brain metastases may be diagnosed before the primary tumor is found (precocious presentation) or at the same time as the primary is detected (synchronous presentation) ***(T. Batchelor & DeAngelis, 1996)***.

Management Goals

A) Symptomatic Therapy

i- Corticosteroids

Corticosteroids produce their antiedema effect by reducing the permeability of tumor capillaries, and are indicated in any patient with symptomatic edema

ii- Anticonvulsants

Seizures are the presenting symptom in approximately 10% to 20% of patients with brain metastases, and occur at some stage of the illness in another 10% to 20% of patients

iii- Treatment of Venous Thromboembolic Disease

Venous thromboembolic disease is common in patients with brain metastases, occurring in approximately 20% of patients. The optimal therapy is unknown ***(T. T. Batchelor & Byrne, 2006)***.

B) Definitive Treatment

I-Surgery

Indications of surgical excision of solitary lesion:

- Lesion is accessible.
- Lesion is symptomatic or life threatening.
- Diagnosis is unknown: alternatively considered as biopsy. e.g. Stereotactic biopsy ***(Tajran & Berek, 2003)***.

Patients with multiple brain metastases generally have worse survival than those with solitary lesions. Multiple brain metastasis are usually treated with radiosurgery without surgery.

In these cases, indications of surgery include:

- One accessible symptomatic and /or life threatening lesion. e.g. post. Fossa or large temporal lesion.
- Multiple lesions that can all be completely removed surgically.
- No identifiable primary ***(Iida et al., 2014)***.

II- Radiation Therapy

i- Overall, conventional whole-brain radiation therapy (WBRT) increases the median survival to 3 to 6 months. Radiation is effective in the palliation of neurological symptoms and also significantly decreases the likelihood of death due to neurological causes**.** The main goal of radiation therapy is to improve the neurological deficits caused by the tumor deposit and induce growth restraint of these metastatic deposits ***(Saito et al., 2006)***

ii - Stereotacic Radiosurgery

Stereotacic radiosurgery is a technique of external irradiation that utilizes multiple convergent beams to deliver a high single dose of radiation to a radiographically discrete treatment volume. Radiosurgery can be performed with high-energy x-rays produced by linear accelerators, with gamma rays emitted by radioactive Cobalt source using the Gamma Knife machine, and, less frequently, with charged particles,

such as protons, produced by cyclotrons**.** Stereotactic radiosurgery is used as a boost to brain metastases after WBRT ***(Boyd & Mehta, 1999***).

iii- Interstitial Brachytherapy

Interstitial brachytherapy involves the implantation of locally active radioisotope into a tumor or the wall of the surgical cavity, with the objective of delivering an additional dose of radiation to the residual tumor while limiting the amount of radiation to the surrounding brain ***(McDermott, Cosgrove, Larson, Sneed, & Gutin, 1996)***.

III- Chemotherapy

Cytotoxic chemotherapy has been considered ineffective for brain metastasis, traditionally because of poor penetration across the blood-brain barrier.

However, cytotoxic chemotherapy could be effective in some specific situation, e.g. macroscopic brain metastasis of chemosensitive disease, such as: small cell lung cancer, germ cell tumor and breast cancer.

Recently, tyrosine kinase inhibitors targeting epidermal growth factor receptor (EGFR), (gefitinib and erlotinib) or human epidermal growth factor receptor 2(HER 2), have a promising activity to brain metastasis of lung cancer with activating EGFR mutations or breast cancer with HER 2overexpression ***(Bai & Han, 2013)***.

V-Hormonal therapy:

This can be used as a part of treatment regimen especially in patients with hormone-responsive tumors, such as breast cancer ***(Wang et al., 2014)***.

Prognosis

The median survival of patients with untreated brain metastases is approximately 1 month. Addition of steroids increases survival to 2 months, whole-brain radiation further improves survival to 3 to 6 months. Favorable prognostic factors include the absence of systemic disease, young age (<60 years old), good performance status (Karnofsky performance status $\geq$ 70), long time to the development of metastasis, surgical resection, and the number of lesions is 3 or less ***(Auchter et al., 1996)***.