### SURGERY FOR BRAIN METASTASES IN SINGAPORE

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#### ABSTRACT

The best possible treatment for a single metastasis to the brain is complete surgical excision followed by whole brain irradiation. A survey was done to determine the proportion of patients with brain metastases who had surgical excision of the lesion. The number of patients with a preoperative diagnosis of cerebral metastases who underwent surgical excision in Tan Tock Seng Hospital from 1985 to 1989 was obtained from the operation records. An average of 11 surgical excisions were done for cerebral metastases annually. To estimate the number of cases of single brain metastases seen annually in Singapore, figures of cases of cancer of the lungs, breast and colorectum from 1978 to 1982 were obtained from the Singapore Cancer Registry. Based on a conservative estimate that 20% of these cancers metastasize to the brain, that 50% are single metastasis and of these, half are suitable surgical candidates, our calculations show that there are at least 67 cases of surgically excisable single brain metastasis in Singapore annually. This means that more than 84% of patients with a single brain metastasis are not getting the best possible treatment. The reasons may be due to patients' fear of operation and to lack of awareness among physicians on advances in the management of brain metastases. Patient education and physician update on recent advances in treatment will allow patients to obtain the best possible treatment.

Keywords : Brain metastasis, Cancer, Surgery

#### INTRODUCTION

About 20% to 30% of patients with systemic cancer develop metastases to the brain<sup>(1,2)</sup>. About 50% of these metastases are single<sup>(3-5)</sup>. Patients with metastases to the brain who are not treated have a poor prognosis with a median survival of about one month<sup>(6,7)</sup>. With corticosteroids, the median survival is two months<sup>(8)</sup>. This increases to six months with whole brain irradiation<sup>(4,8,9)</sup>. With surgery followed by radiation, the period of survival is longer than with radiation alone<sup>(10-13)</sup>.

The first randomised controlled trial of surgery in the treatment of single metastasis to the brain was recently reported by Patchell et al<sup>(14)</sup>. This study of 48 patients showed that surgical removal of a single brain metastasis followed by radiation therapy prolongs survival (overall survival : median 40 weeks versus 15 weeks) and decreases the likelihood of local recurrence in the brain as well as death from neurologic disease. The patients who underwent surgery remained functionally independent longer compared to the group that received radiation only (median 38 weeks versus 8 weeks). This study proves that the best treatment for patients with a single brain metastasis is surgical excision of the lesion followed by whole brain irradiation.

As the incidence of cancer in Singapore has been steadily increasing over the past few years<sup>(15)</sup>, it was felt by the authors that treatment of patients with a single brain metastasis by surgical excision needed to be reviewed. This study was undertaken to investigate our impression that the treatment of single brain metastases has not reflected the advances in our knowledge of this disease entity.

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#### METHOD

The operation records of the Department of Neurosurgery, Tan Tock Seng Hospital from 1985 to 1990 were studied to determine the number of surgical procedures done for patients with a pre-operative diagnosis of brain metastasis. These procedures include craniotomy with gross macroscopic or subtotal excision or biopsy, burrhole biopsy and cerebrospinal fluid shunting procedures. From 1985 to late 1989, the Neurosurgical Department in Tan Tock Seng Hospital was the only major public neurosurgical centre in Singapore. A few patients with single brain metastases were operated in the private hospitals but these patients were mainly foreigners.

To estimate the number of local patients with a single brain metastasis, the number of cases of patients with cancer of the lungs, breast and colorectum from 1978 to 1982 were obtained from the Singapore Cancer Registry<sup>(15)</sup>. Only these cancers were considered as they commonly metastasize to the brain<sup>(3,5)</sup>. The incidence of brain metastases in systemic cancer is reported to be between 20 to 30%<sup>(1,2)</sup>. We used the lowest figure, 20%, in our estimate of the incidence of brain metastases in patients with systemic cancer. Fifty percent of patients with brain metastases have a single brain metastasis<sup>(3-5)</sup> and of these, about 50% are not surgical candidates due to inaccessibility of the lesions, advanced systemic disease or other factors<sup>(11)</sup>. Using these figures we were able to calculate the lowest possible estimate of patient with surgically resectable single brain secondaries.

#### RESULTS

From 1985 to 1989, a total of 77 neurosurgical procedures were done for patients with a pre-operative diagnosis of brain metastases. They included 57 craniotomies. 18 shunting procedures and two biopsies via burrholes. Thus an average of 15 neurosurgical procedures were done annually at the Department of Neurosurgery, Tan Tock Seng Hospital for patients with brain metastases and of these, 11 were surgical excisions.

The total number of cases of cancer of the lungs. breast and colorectum from 1978 to 1982 was 6693, giving an avcrage of 1339 cases annually over the five year period. At least 20% or 268 of these cases will have secondaries to the brain. Of these 268 cases, 50% or 134 cases will have a single brain metastasis and 50% of these or 67 cases are suitable surgical candidates. Thus, we should expect at least 67 patients with a surgically resectable single brain metastasis in Singapore yearly. However, only about 11 patients (16%) had surgical resections annually. This means that more than 84% of patients with a surgically resectable brain secondary were not operated on.

#### DISCUSSION

The presence of metastases in patients with systemic cancer has a poor prognosis as it implies that tumour cells have disseminated throughout the body. Once a tumour has metastasized to the brain, the outcome is rapidly fatal and they die within a month or two if they are not treated. Patients with metastases to the brain may be asymptomatic but the majority will develop focal neurological deficits, seizures or present with signs and symptoms of raised intracranial pressure<sup>(16)</sup>. Death usually results from neurologic complications such as raised intracranial pressure and resultant brain herniation although these patients may also die from the effects of multiple metastases elsewhere in the body<sup>(4,9,11)</sup>.

The majority of secondaries to the brain have a preferential distribution in the superficial distal arterial fields, ie the anatomic watershed areas, as they result from arterial tumoural microemboli which tend to pass as far distally along the arterial tree as their size will permit<sup>(3)</sup>. From a surgical point of view, these tumours are thus superficial and have low surgical risk. There is also a high incidence of metastases in the posterior fossa, because they tend to be symptomatic earlier and also possibly because of retrograde spread via Batson's venous plexus<sup>(3)</sup>. Cerebellar metastases are life threatening but can be removed with low surgical risk.

The goal of surgery in patients with a single brain metastasis is to obtain a local cure for the disease. However we cannot be sure if there are other micrometastases elsewhere. Nevertheless, there are reports of long term survival after surgical excision of a single brain metastasis in the literature<sup>(17)</sup>.

The purpose of surgery is two-fold:

- removal of the mass lesion causing brain compression; and
- ii) histological confirmation of diagnosis.

Surgical removal of mass lesions will prolong life<sup>(10-14)</sup>. Symptoms are alleviated expediently with minimal risk and quality of life is enhanced as the symptom-free interval is prolonged. Total surgical removal of the tumour with post-operative radiation will improve duration and quality of survival as well as reduce the incidence of recurrence of the metastasis. Patients with a synchronous primary lesion may also benefit from surgical resection of both lesions<sup>(18)</sup>.

Surgical techniques currently used in the definitive treatment of cerebral metastases are open craniotomy for surgical excision and computer-assisted stereotactic craniotomy and excision<sup>(19)</sup>. Stereotactic biopsy is used for diagnostic confirmation of deep-seated lesions and its role in local curative surgery is limited.

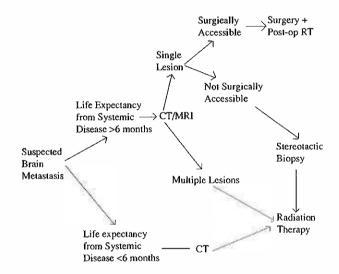
Histological confirmation is important as even with modern imaging modalities such as CT scanning and magnetic resonance imaging, wrong diagnoses may be made. Primary brain tumours or non-neoplastic lesions can co-exist with extracranial cancer. Metastases have been found within primary intracranial tumours such as meningiomas and gliomas<sup>(20,21)</sup>. In Patchell's study, 6 of 54 patients initially entered into the study were found not to have brain metastases on histological diagnosis and were thus excluded from the study<sup>(14)</sup>. This clearly shows the danger of radiating patients without a histological diagnosis.

Puvanendran et al in a prospective study of cerebral metastasis in bronchial carcinoma in Singapore found a 55% incidence (21 out of 36 cases) of brain metastases in patients with bronchial carcinoma<sup>(22)</sup>. Twelve of the 21 (57%) brain metastases were single. Overall 33% of patients had a single brain metastasis. We used a conservative figure of 10% in our estimation of the incidence of single brain metastases.

Our study shows that a very large proportion (at least 84%) of patients with single brain metastasis in Singapore are not treated surgically. This may be acceptable in the past as surgical treatment of brain secondaries was considered controversial due to the poor outlook of the disease and to the lack of any randomised study. A rethink of this issue is now necessary in the light of Patchell's study which shows conclusively that surgical excision of a single brain metastasis followed by radiation will prolong patient survival and quality of life. The risk of surgery is low and the results are almost immediate. There is expeditious alleviation of symptoms with potential for protracted symptom-free interval.

The low surgical rate in Singapore is probably due to patients' fear of surgery and the lack of awareness among physicians on advances in the management of cerebral metastases. Fig 1 gives the best therapeutic approach to patients with brain metastases based on current knowledge. By increasing awareness among physicians on the management of cerebral metastases, we can improve the outlook of those patients with a single metastasis to the brain.

#### Fig 1 - Suggested Therapeutic approach to brain metastasis



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## REACHING NEW HEIGHTS IN CUSTOMER SATISFACTION

It is 8.30am, Monday morning in Johnson & Johnson's office. Everyone is in the conference room. In today's monthly meeting, a number of important issues are discussed. Almost all issues discussed are related to customer satisfaction. "How can we serve our customers better?" "5hould we try this way from now on?" At Johnson & Johnson, everyone is talking about our most important mission – TOTAL CUSTOMER SATISFACTION.

At 11.45am, Caroline and Susan went out to lunch. A little too early? No, we have implemented a flexible lunch schedule so that we have full telephone coverage throughout lunch for customer service function. At 12.30, it was Selvi and Elicia's tum for lunch. This is just one example of how Johnson & Johnson is introducing new policies to serve its customers better.

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