Single brain metastasis –
What is the role of microsurgery in times of radiosurgery?

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Introduction

The incidence of brain metastases is approximately 14 cases per 100,000 population per year. In about one third of all cases this is a single lesion. The occurrence of brain metastases still marks a stage of cancer disease with a dismal prognosis. Numerous therapy protocols consider this situation to be part of the final stage of disease – many therapeutic protocols are terminated with the occurrence of brain metastases. However, surgery and radiosurgery are both effective modalities for the treatment of single brain metastases.

Radiosurgery has been shown to allow a local control of the disease in up to 90%, even in cases where multiple metastases have to be treated radiosurgically (either within one session or in subsequent treatments) [1–7]. Therefore, a debate has been revolving around the question of which metastases have to be treated with microsurgical resection at all. For selected patients harbouring a single and resectable metastasis (with a Karnofsky performance score of $\geqslant$70) and a stable systemic disease, microsurgical tumour resection plus whole brain radiotherapy (WBRT) has been shown to be more effective than WBRT alone [8,9,7].

Another open question is whether radiosurgery or microsurgery leads to a higher local control rate and which modality is associated with less therapy related morbidity [10]. Using data from the literature and our own prospective randomised study, a treatment algorithm for singular brain metastases has been developed after a synopsis of both treatment concepts.

Microsurgery

The widespread use of refined diagnostic facilities like high field MRI has improved the detection of single brain metastases even of small size. The use of image guided surgery techniques (e.g. image guided neuronavigation devices) and/or intraoperative ultrasound in conjunction with microsurgical dissection techniques greatly enhanced the results of mircosurgical treatment. Even lesions in functionally relevant areas ('eloquent brain areas') can now be safely removed with the aid of intraoperative mapping/electrophysiological monitoring devices which allow safe dissection within the cortex. However, the deeper the lesion is located, the higher the risk of the surgical intervention. Even a small angular deviation of the trajectory of approach can mislead the surgeon. In this situation it may not only be hard to find the lesion, but procedure related morbidity due to dissection of non-affected brain areas will increase. As a consequence, for very deep seated lesions, additional and alternative therapeutic modalities have been sought.

Careful micro-dissection of brain metastases should be done at the border of the metastasis which is facilitated by the fact that brain metastases per se are non-invasive into the adjacent brain tissue. En bloc dissection and removal may reduce the likelihood of cancer cell spillage with subsequent metastatic spread. Especially in very large tumours and in lesions with partially cystic or liquid content, this may be difficult, and any injury to the tumour mass can cause contamination with metastatic cancer material. Therefore, post resection radiotherapy of the resection cavity has been advocated in order to improve local control rate after microsurgical removal. The concept of microsurgery involves post-surgical radiotherapy, mostly as whole brain radiotherapy, with a local boost at the resection site (surgery plus WBI). This should lead to high local control rates in conjunction with good control for distant disease.

Radiosurgery

High dose single shot irradiation of a very focussed lesion has been termed stereotactic radiosurgery (SRS). Due to physical/technical limitations, single session radiosurgery is limited to lesions of a small volume with a diameter of up to 3.5 cm. Following these guidelines, radiosurgery could be offered as an effective outpatient treatment modality with a tumour control rate between 60 and 90%. Treatment related morbidity consists of 'malignant radiation necrosis exceeding the target volume with concomitant extensive brain edema which might be long lasting even under steroid medication. In addition, functional deficits in case of location in eloquent areas and epileptic seizures might occur [11]. SRS in single brain metastases has proved to be more efficient than WBI alone [12].

The concept of radiosurgery is to target one or few lesions only (mostly one to three, sometimes up to five). Multiple lesions can be treated either in one session or in few sessions targeting one or two at a time [11]. Therefore, radiosurgery aims to achieve a high local control rate without taking care of distant areas of the brain. In this approach, subsequent metastases at distant sites may be subject to additional radiosurgical sessions. Thus, a purely radiosurgical treatment concept might involve several treatment sessions in subsequently evolving lesions and not treating the 'hole brain disease' at the time of initial diagnosis since whole brain radiotherapy by itself is a toxic treatment. There is still a dispute going on revolving around whether SRS should be followed by WBI, similar to the concept in microsurgical therapy. Further studies have to be awaited to clarify this issue. SRS plus additional WBI did not prolong overall survival compared to SRS alone, although the rate of new distant brain metastases is higher without WBI [13–15]. Especially in so-called 'radioresistant' primaries, adjuvant WBI after SRS may be withheld without additional risk for the patient. Here, subsequent sessions of SRS (so-called 'salvage SRS') may follow once additional lesions appear (this concept, however, requires regular follow-up scans of the brain) [16].

Since previous whole brain radiotherapy and a history of chemotherapy (especially protocols containing platinum compounds) markedly increase the risk of radiation induced damage of radiosurgery, this method should be indicated very restrictively in these patients.

A proposed treatment algorithm: A neurosurgeon's perspective

Patients with controlled systemic disease and single brain metastasis with a diameter of 3.5 cm or more should be subject to microsurgical removal using image guided surgery and, if necessary, under electrophysiological monitoring. Deep seated lesions, whenever amenable to radiosurgery due to their size, should be treated in this way. Superficial small size lesions are also good candidates for radiosurgery.

Any space occupying lesion in the posterior fossa causing mass effect, especially with concomitant hydrocephalus, should be subjected to microsurgical removal since any (even temporary) increase of the lesion volume due to post radiosurgical swelling or increase of the perifocal edema might cause an acute rise of intracranial pressure within the posterior fossa with subsequent decompensating hydrocephalus which, in conjunction, may lead to a neurological/neurosurgical emergency.

SRS in patients with previous WBI may increase the risk of radionecrosis depending on dose of irradiation and target volume [17]. According to our experience, previous whole brain radiotherapy, a history of chemotherapy with platinum or taxane compounds as well as vascular disease (e.g. in conjunction with diabetes mellitus) are risk factors for radionecrosis as a late side effect of radiosurgery. The risk increases with the size of the lesion so that in patients displaying the above mentioned risk factors microsurgery might be considered even in the case of smaller lesions as soon as these are located in critical areas.

A situation that might involve a combination of both treatment modalities could be the case of one large metastatic lesion in conjunction with a few small ones (up to five) being possible candidates for radiosurgery. In this case, removal of the larger lesion with radiosurgical treatment of the remaining small ones should be considered. In this situation additional whole brain radiotherapy might reduce the risk of distant disease within the CNS.

Conflict of interest statement

None declared.

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