Management of Brain Metastases: Neurosurgical Considerations

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Metastatic lesions to the brain occur commonly in oncology patients and portend a very poor outcome, as they often occur in the setting of progressive systemic metastatic disease and can result in neurologic deterioration that may preclude therapy. Therapy of patients with brain metastases requires a combination of measures to achieve local control at the site of metastasis (eg, with surgical resection or radiosurgery) and to reduce the subsequent risk of recurrences elsewhere in the brain (eg, with whole-brain radiation). Successful therapy of extracranial systemic metastases is required for optimal outcomes. Clinical trials are currently underway to define the optimal role of whole-brain radiation and radiosurgery in different subsets of patients. Novel therapies to enhance radiation responsiveness are also under investigation. In the current review, we discuss recent developments in the management of patients with brain metastases.

Rao et al review an extremely important topic in systemic cancer management: brain metastases. As highlighted by the authors, brain metastases and their management have actually received little attention from the standpoint of translational or clinical research. However, the number of patients with brain metastases is certainly much higher than that of primary brain cancers. In fact, the incidence of brain metastases is increasing, as better adjunctive therapy has resulted in longer survival times for these patients. For some cancer survivors, the central nervous system has become the last "bastion" of metastases.

Treatment Options

Therapy for brain metastases currently consists of surgery, radiation, and chemotherapy. This article emphasizes surgery and radiation as the mainstays of treatment, as the effectiveness of chemotherapy has been limited. The authors have highlighted their treatment algorithm for patients with one metastatic lesion, one to four metastatic lesions, and multiple metastases (see their Figure 1). For a single metastasis, they recommend surgical resection for surgically accessible tumors > 3 cm in size, followed by whole-brain radiation therapy (WBRT). Surgical removal of the large tumor will directly remove mass effect and edema from the surrounding brain.

The use of postoperative WBRT is much more prevalent on the East Coast and in the Midwest. On the West Coast, we often treat patients with a radiosurgery boost to the resection cavity, rather than WBRT. The advantages of a tumor bed radiosurgery boost, as opposed to WBRT, include convenience (one outpatient radiosurgery session vs 4 to 5 weeks of daily WBRT), better local control of the resection cavity, and decreased risk of cognitive damage. Although cognitive damage does not always occur with WBRT, its risk in decreasing the quality of life in elderly patients is well known. The potential disadvantage of a radiosurgery boost to the tumor bed alone is subsequent metastasis to other areas of the brain, which WBRT may prevent.

It must be emphasized that a large study comparing the efficacy of tumor resection followed by WBRT to that of tumor resection followed by radiosurgery to the tumor bed has not been performed. Although not mentioned in this paper, some investigators have also looked at the application of carmustine wafers (Gliadel) for local control of the tumor bed, instead of radiation therapy.[1]

For patients with one to four metastatic lesions, the authors recommend radiosurgery to the lesions followed by WBRT. One situation that I often face is the patient with a large lesion requiring surgery (> 3 cm), and up to three other smaller ones. If the large lesion is resectable, I recommend resection of the large tumor, followed by radiosurgery to the tumor bed and the smaller tumors. Patients who experience disease progression with additional metastases are then treated with WBRT. For patients with multiple metastases (more than four tumors) or poor performance status from systemic disease, I would recommend upfront WBRT alone.

Further Considerations

Besides the type of radiation to administer, three other issues are important in the management of
brain metastases. First, not all brain tumors in a cancer patient are metastatic. It is possible that a primary brain tumor such as a meningioma could be present. Breast cancer patients, for instance, may have associated meningiomas.[2] A meningioma on magnetic resonance imaging (MRI) scan can usually be distinguished from an intracerebral metastasis and will have a unique MR spectroscopy profile (i.e., an alanine peak).[3] Patients with hereditary neurologic syndromes such as Turcot syndrome may present with colon polyps and brain tumors.[4]

The second consideration is leptomeningeal disease, which may occur in association with brain metastasis. In these patients, diagnosis is key. In addition to the clinical symptomatology of headaches and cranial nerve deficits, MRI recognition of leptomeningeal enhancement and positive cerebrospinal fluid cytology is necessary to make a positive diagnosis. These patients should be treated with intrathecal chemotherapy (i.e., liposomal cytarabine [DepoCyt]), or with whole-brain irradiation.[5] Patients with leptomeningeal disease may develop hydrocephalus, necessitating the need for a ventriculoperitoneal shunt.

Finally, although chemotherapy has not proven effective in this setting, brain metastasis is a systemic disease. The development of small-molecule chemotherapy, allowing better penetration of the blood-brain barrier, will increase chemotherapeutic options for these patients.

Conclusions

The authors have provided a comprehensive review of the management of intracranial metastases. Central nervous system metastasis is a field that is underserved and understudied. More translational research and clinical trials are needed. As a systemic disease, brain metastasis ideally should be treated with effective chemotherapy. Neurosurgery and radiation provide only local control of the disease.

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