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Arbiter:

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The decision whether to administer radiotherapy to the brain of elderly patients harbouring intracranial neoplasms is an increasingly important issue. Cranial radiotherapy is the mainstay of treatment for both primary malignant and metastatic brain tumours. The most common primary brain tumour in the older age group is malignant glioma, particularly glioblastoma multiforme. There is significant epidemiological evidence that the incidence of this tumour is rising in general, particularly in the elderly population. This rising incidence is likely due to a combination of factors including improved neuro-imaging, a more aggressive diagnostic approach to new neurological symptoms in elderly patients, and a true change in the incidence of these diseases independent of better ascertainment [1,2]. With improved therapies leading to longer survival of patients with systemic cancer, there is an increased development of central nervous system (CNS) metastatic disease because a greater proportion of patients survive long enough to develop these intracranial complications [3].

Brandes and colleagues and Grau and Verger both acknowledge that the biology of malignant gliomas is more aggressive in older patients. In every single major prospective study of malignant gliomas, age is recognised as a critical and independent prognostic factor [1]. It is usually the most important prognostic factor, having a stronger impact on survival than either performance status or histopathology. It is very clear that these diseases have a different behaviour from the identical tumour in younger patients, and molecular pathology is beginning to categorise the genetic differences of malignant gliomas in the two age groups. Treatment of glioblastoma in the elderly rarely controls disease for longer than a few months. This is also true for whole-brain radiotherapy for brain metastases.

Neurotoxicity from radiation therapy has been divided into three different categories according to the temporal relationship of the neurological syndrome to the radiotherapy. Different syndromes are outlined in detail

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by Brandes and colleagues, but it is the late-delayed reactions that are most important. It is only these toxicities which are permanent, irreversible and can lead to significant disability. These sequelae, which include radiation necrosis and leucoencephalopathy, can only be appreciated once significant disease control has been achieved; otherwise patients die of tumour progression and treatment-related toxicity is not manifested. Because remission from either primary or metastatic brain tumors is usually so brief, even after a course of definitive radiotherapy, the true incidence of late-delayed radiotherapeutic complications in these elderly patients is largely unknown. Nevertheless, they remain a concern since their effects can be so devastating and are potentially worse than the brain tumour itself.

At the Memorial Sloan-Kettering Cancer Center, we have developed an approach for elderly patients with primary or metastatic brain tumours that attempts to balance current effective treatment for these diseases with a reduced potential for radiation-related toxicity [1]. For elderly patients (i.e. those greater than age 65 years) with malignant gliomas, we administer a full course of standard radiotherapy to a total of 60 Gy to patients who have had extensive surgical debulking, and who have a good performance status. Because the radiotherapy is to a limited field, particularly with conformal treatment planning, most older patients tolerate it reasonably well and do not develop serious delayed toxicity before tumour progression. Older patients who are in good clinical condition but have more extensive tumours, such as bilateral neoplasms or lesions in critical areas which limit surgical accessibility, are offered a short course of radiotherapy, such as 300 cGy in 10 fractions, to achieve maximal palliation in the shortest period of time. The advantage of this regimen is the speed with which it is completed and its reasonable efficacy; however, the higher daily fraction increases the risk for late toxicity in addition to the larger port size to accommodate these lesions. These patients do not live long enough to manifest late neurotoxicity and, consequently, the shorter course of treatment offers a greater potential to relieve suffering than to cause harm. Elderly patients, particularly those over the age of 75 years, with extensive tumours that cannot be resected, who are in poor clinical condition, may not be treated with radiotherapy at all, and their symptoms managed with corticosteroids alone. Radiation toxicity is not the limiting factor in these patients; rather, their extremely poor outcome and short survival from tumour progression are the reasons for withholding therapy.

Because brain metastases are treated with whole-brain radiotherapy, these patients are even more vulnerable to the late toxic effects of cranial radiotherapy, particularly cognitive impairment [3]. Consequently, we look to avoid such treatment in these patients, often by trying to identify an alternative approach.

Older patients with one or sometimes even two metastases may undergo resection but not receive postoperative whole-brain radiotherapy despite recent evidence that this improves neurological disease control [4]. Many of these patients will live long enough (greater than 1 year) to exhibit cognitive impairment as a consequence of a standard course of whole-brain radiotherapy. Alternatively, such patients may be treated with stereotactic radiosurgery if they have few metastatic lesions, or with systemic chemotherapy if they harbour a chemosensitive primary tumour [5]. Unfortunately, many elderly patients with brain metastases have too many lesions, or have lesions in eloquent areas of brain which are not amenable to such focal treatments. The only reasonable therapeutic option in these patients may be a course of whole-brain radiotherapy. In this situation, we often make a decision on an individual basis given the patient's clinical condition and the overall state of their primary disease. Many elderly patients with multiple brain metastases will benefit from whole-brain radiotherapy, with amelioration of symptoms but without suffering any significant neurological side-effects. Frequently, the treatment is only temporarily effective and patients succumb from progressive intracranial or systemic tumour. If a patient is thought to have a good chance of long survival because of a good performance status and well-controlled systemic disease, a more protracted course of radiotherapy may be considered to reduce the risk of delayed neurological sequelae.

A reasonable alternative to standard whole-brain radiotherapy should be sought in many patients, particularly in older individuals. Sometimes there is no alternative treatment, and in those situations patients and family members must be counselled by the physician about the pros and cons of undertaking such a treatment in an older individual. Patients and family alike need to understand that sometimes even successful treatment with control of intracranial disease can result in a pyrrhic victory if the patient is left severely compromised by the treatment itself.

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