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Mini Review

Treatment of Brain Metastases Using the Current Predictive Models: Is the Problem Solved?

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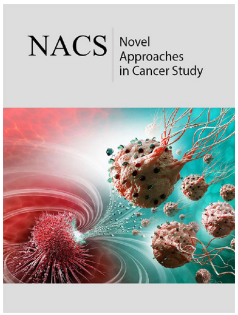

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Opinion

Brain metastases from solid tumours are the most common intracranial tumours [1] and it occur in 40% of patients with cancer [2]. The most common primary tumours that metastasize to the brain are lung(40%),breast (25%) and melanoma (20%) [3]. The incidence is expected to be on the increase, due to improved survival, with use of modern cytotoxic drugs, targeted therapy, immunotherapy and modern radiotherapy techniques, in addition to greater use of magnetic resonance imaging of the brain. Brain metastases are common in the elderly, defined as above 60 years [4], and the interval between diagnosis of the primary and the development of brain metastases is variable, however some reported an average of 19 months [5] and adenocarcinoma is the commonest histology that metastasizes to the brain [6].

Many patients have multiple metastases [7] at diagnosis, although about 20% and 9% have one or two lesions respectively [8]. About half of brain metastases are asymptomatic [9], however two thirds of patients develop symptoms at the time of initial diagnosis or during the course of the disease [10], and the commonest presentations are headache, neurological deficits and seizures [11]. Staging of lung cancer includes whole body FDG PET-CT scan [12] and brain MRI as recommended by National Comprehensive Cancer Network [13]. MRI is more sensitive than contrast enhanced CT scan in detecting brain metastases and in one study about one third of patients with apparently solitary metastases based on CT scan, turned out to have multiple lesions on MRI [14].

Treatment of brain metastasis includes, best supportive care, steroids, whole brain radiotherapy, surgery and stereotactic radiotherapy or a combination of these, depending on the number, size and location of the metastases. Generally speaking, survival is poor, and is less than 2 months for patients treated with steroids only. However, whole brain radiotherapy could extend the survival up to 7 months [15]. Surgery and WBRT improved the survival up to 13.5 months in one study [16]. The average survival after stereotactic radiosurgery is 8.5 to 12.1 months [17,18].

Researchers have investigated some prognostic and predictive factors for the survival of patients with brain metastases. Lagerwaard & Levendag [19] found performance status, age, extracranial metastases and the status of the primary to be the most important factors. Hazuka et al. [20] found that initial presentation with neurologic deficit, multiple metastases to be poor prognostic factors, while solitary lesion, gross total resection and adenocarcinoma subtype improved the survival and at the same time the survival was independent of primary tumour site, presence of active extracranial disease and radiation dose.

Researchers have sought to derive scoring systems or predictive models for better selection of patients with brain metastases who would benefit from treatment and to avoid overtreating those with very poor survival. In 1997 The Radiation Therapy Oncology Group (RTOG) developed the Recursive Partitioning Analysis (RPA) [21], the Grading Prognostic Assessment (GPA) was developed in 2008 [22] and, more recently, disease specific GPAs were developed mainly for lung and breast [23]. RTOG RPA classified patients into 3 classes; Class One, those who have Karnofsky performance score (KPS) of ≥70, age <65, and controlled primary tumour without extracranial metastases, Class 3 patients have KPS <70, all other

patients fall into Class 2, including those with KPS ≥70 but other unfavorable characteristics, such as uncontrolled primary tumour, extracranial metastases, or age ≥65.The median survival for classes 1,2 and 3 were 7.1,4.2 and 2.3 months respectively [21,24,25]. GPA classification excluded the status of extracranial disease acknowledging only its presence or absence, it kept age and KPS and added number of brain metastases and each factor was given values of 0,0.5 and 1. Four prognostic groups were created and the median survival was 2.6 months,3.8 months, 6.9 months and 11 months for GPA scores of 0-1,1.5-2.5,4 and 3.5-4 respectively [26].

Diagnosis-specific graded prognostic assessment was developed after the primary tumour site was shown to be an important prognostic factor in some studies [23]. Despite the availability of diverse scoring systems, there still is a lack of consensus regarding which clinical factors have the major impact in treatment decision-making concerning the use of WBRT. Although those predictive models are very useful for patient selection , yet making a clinical decision based on them is still a challenge as it is difficult to identify patients with very short survival(< 2 months) after WBRT ,also the survival for groups with poor prognostic score based on of RPA OR DS GPA is still heterogonous. I propose looking into another group of predictive models for detection of brain metastases in cancer patients, in particular for the asymptomatic group, and image the brain mainly with MRI to detect limited metastasis which could be treated with focal treatment to improve the survival.

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