Brain Metastases in Very Young Patients with Lung Cancer Are Still Brain Metastases

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In this issue of ONKOLOGIE, Nieder and colleagues retrospectively reviewed 149 patients treated with whole brain irradiation for lung cancer with subset evaluation of 9 patients under the age of 40 [1]. Five of the 9 patients had small cell lung cancer. Median survival was 7 months. Median Karnofsky performance score (KPS) was 70. Only one of 8 patients with complete follow-up information died as a direct result of CNS disease. In conclusion, the very young patients did not achieve a better outcome than intermediate age groups. Radiation provided durable CNS control in nearly all patients, while systemic failures remained the leading cause of death.

The small percentage (6%) of very young patients in this study is consistent with the age distribution of lung cancer in the general population: less than 5% of patients with lung cancer are less than 40 years old [2–4]. Due to these small numbers, studies do not focus on prognosis and therapy of this particular age group. Standard therapy is based on treatment of patients with varying histologies, stage of disease and underlying comorbid conditions.

Younger patients differ from older patients in terms of histology, genetic susceptibility, and gender distribution. Younger patients have a lower male/female ratio than older patients [3–5]. Lung cancer risk is higher in young patients with family history of smoking suggesting a genetic predisposition to lung cancer in patients with early onset of disease [5–7]. Contrary to the dominant small cell histology in the current study, younger patients tend to have a higher incidence of adenocarcinoma [3–5, 8]. In addition to differences in gender ratios, genetic predisposition and histological differences, patients ≤ 40 years may tolerate therapy better and be willing to accept a higher risk of toxicity than patients ≥ 65 . These differences in younger versus older patients with lung cancer support the need to evaluate treatment and outcomes in very young patients separate from older lung cancer patients.

Recursive partitioning analysis (RPA) of RTOG brain metas-

tases trials (61% of patients had lung cancer) identified three prognostic groups [9]. Favorable prognostic factors included KPS ≥ 70 , age < 65 years, controlled primary tumor, and no extra-cranial metastases. Other studies have validated these results [10, 11]. RPA classification has also been validated for small cell lung cancer [12]. Although younger age is a favorable prognostic factor, the age cut off for these studies is 65 years. These studies do not specifically address prognostic factors of very young patients. In the current study [1], very young patients with brain metastases did not achieve a better outcome than intermediate age groups.

Whole brain irradiation in the current study was effective in palliating CNS symptoms and preventing death from CNS disease. Unfortunately these patients had uncontrolled extra-cranial disease. Better systemic therapy may improve outcomes but early detection of disease, when it is potentially curable, and prevention of CNS failures is needed to significantly improve survival.

Prophylactic cranial irradiation (PCI) is accepted as part of standard therapy for small cell lung cancer. PCI has been shown to improve survival in patients with limited disease small cell lung cancer by 5.4% [13]. Additionally PCI has been shown to decrease symptomatic brain failures and improve 1-year overall survival in patients with extensive disease SCLC [14].

Prospective randomized studies have shown that PCI decreases and delays CNS failures in patients with non-small cell lung cancer but studies have not been powered to show a survival advantage [15–17]. Further studies are needed clarify the role of PCI in NSCLC, particularly in high-risk patients. Non-small cell lung cancer patients at highest risk for CNS failures include younger patients. Studies have shown that younger age predicts for an increased risk of brain metastases and earlier brain failures in patients with non-small cell lung cancer [18–21].

Unfortunately, with rare exceptions and regardless of age, histology, and site of primary disease, the prognosis of patients with brain metastases is very poor. Better understanding of the disease process and prognostic factors will help to cus-

tomize therapy and ultimately improve outcomes. Smoking is the most important risk factor for lung cancer in the very young. Preventing young people from smoking will have the most significant impact.

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