Risk Factors for Development of Brain Metastases

While brain metastases are common, some patients seem to be at higher risk than others. As previously noted, SCLC has a very high risk of spread to the brain. For NSCLC subtypes, several studies have shown that patients with non-squamous lung cancers have a greater tendency to develop brain metastases than those with squamous cancers, which tend toward more local spread. Here is the figure for development of brain metastases in patients treated for stage IIIA NSCLC out of the Harvard/Dana Farber system (abstract here).

![Risk of Brain Meta for Squamous vs. Non-Squamous NSCLC (Stage IIIA Patients)](click to enlarge)

Another trial just published from UCSF evaluating the stage IIIA NSCLC population also found a high risk (55%) of recurrence in the brain after aggressive treatment, and that the risk of brain metastases was higher for patients with adenocarcinoma vs. squamous cell carcinoma (57% vs 34%, a statistically significant difference (abstract here)). The Boston study also demonstrated that patients who had a good response to pre-operative treatment (chemo, radiation, or a combination of both for all but 3 patient who had unsuspected N2 nodal disease at surgery) and cleared their mediastinal nodes at the time of subsequent surgery had significantly lower risk of developing brain metastases than patients who had N2 nodes positive at the time of surgery:

![Risk of Brain Met Based on Mediastinal Clearance after Induction Therapy (St 11A Plt)](null)

Finally, another trial out of Columbia in NYC was just published in the journal Radiology (abstract here), looking at the clinical variables that predicted for development of brain metastases among 264 patients with full imaging and clinical information available. Like the other studies, they reported that the patients with adenocarcinomas had a higher risk of developing brain metastases than those with squamous cell cancers, and the folks with undifferentiated cancers fall between them (likely actualy a mix of adenocarcinomas and squamous cell cancers). This study also reported that higher nodal stage predicts higher risk of developing brain metastases, and that the risk of brain metastases increased steadily as the size of the primary tumor increased, as shown here:
This study also reported that there was not an association of increased risk with being male or female, with patient age, or with location of the tumor being central or peripheral, toward the outer edge of the lung.

Practically speaking, this doesn’t change our management. At this point, prophylactic cranial irradiation (PCI) is not a standard recommendation after potentially curative treatment for locally advanced NSCLC (topic reviewed in prior post), but with so many trials showing a high risk of “brain first” or “brain only” recurrence in this setting, it’s a very important question. I routinely recommend that my patients who have undergone treatment for stage III NSCLC consider a clinical trial in this setting of PCI vs. observation here, because we don’t know if it will be helpful or harmful or have no effect. I might be particularly inclined to recommend the trial in a patient with an adenocarcinoma, given the consistently higher risk of brain metastases seen in this population, but I recommend this trial for pretty much everyone. We need to see if there is a way to reduce the risk of brain metastases in both NSCLC and SCLC. There will be an important trial presented about PCI in extensive disease SCLC at our big international oncology meeting, ASCO, in early June, so I’ll provide an update when the data are available. In the meantime, I’ll continue the discussion with more on prognosis and management options in the coming posts.