CLINICAL VIGNETTE

Aggressive Management of Stage IV Colon Cancer for Long-term Survival

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The patient is a 60-year-old Caucasian male who originally presented at the age of 54 with acute onset abdominal pain, and was found to have a perforated, right-sided colon cancer. He was taken to the operating room emergently, and a right hemi-colectomy was performed. Pathology showed an invasive adenocarcinoma with mucinous features (T4), and 0 out of 31 (N0) sampled lymph nodes showing metastatic involvement. A post-operative staging CT scan showed a sub-centimeter right lower lobe lung nodule of indeterminate significance, with no other suspicious lesions for metastatic disease. Therefore, his final staging was determined to be high risk, stage II colon cancer, and adjuvant chemotherapy was started with infusional 5-FU along with oxaliplatin (FOLFOX).

After completing 6 months of chemotherapy, a CT was repeated and showed no significant change in the right lower lobe nodule. Six months later, a full year after his original presentation, a repeat CT showed progression of this nodule to just under 2 cm. A biopsy showed adenocarcinoma with mucinous features, consistent with his original colon cancer diagnosis. Since the lung lesion was the only area of visible metastatic disease, he was taken back to the operating room, and a wedge resection of this lung lesion was performed, with clean margins. His tumor was sent for molecular markers, and was found to have a mutated Kras, elevated ERCC1, and low TS. This profile helped predict that infusional 5-FU with irinotecan (FOLFIRI) and bevacizumab would be the most effective first line treatment option for our patient with recurrent colon cancer. He was treated with another full six months of therapy, with scans showing no visible disease upon completion. Subsequently, he was changed to capecitabine (oral 5-FU) with bevacizumab for 6 more months, then continued on bevacizumab alone for another full year.

Bringing him just beyond his 3 years from his original diagnosis.

After completion of all his therapy, a collective decision was made to give him consolidative radiation therapy to the tumor bed in the right lower lobe in hopes of preventing any further local recurrences within his thorax. Since completion of his radiation therapy, he has been off all active treatment, and free of any visible disease for over 2 years. At the time of this publication, his survival with stage IV colon cancer with lung metastasis has surpassed 5 years.

Discussion

Patients with metastatic colorectal cancer (CRC) are living on average twice as long as they were in the 1990's, primarily due to significant advancements in cytotoxic therapies. However, even with all the advancements in the treatment of stage IV CRC over the past decade, five year survival is still in the single digits[1]. This has led to a more aggressive, multidisciplinary approach to these patients, in hopes of prolonging survival. For instance, resection of liver metastasis in combination with effective chemotherapy has been shown to improve survival times in CRC patients, making this an accepted clinical practice[2]. Resection of lung metastasis has not been as widely adopted; therefore we will review some of the published data here.

Estimates of isolated lung metastasis in CRC patients range from 1.7% - 7.4%[3]. Several single institution studies have shown 5-year survival rates of 21% - 61.4% in resected patients with CRC[4-6]. However, what is not clear is whether this improvement is due to the metastasectomy or selection bias. Recently, a large retrospective study extracted data from a database of over 1400 patients with CRC from three institutions to determine whether or not lung metastasectomy

improves survival outcomes[7]. CRC patients with lung metastasis that were treated with no lung resection had a survival of 31.5 months, while those that had the addition of surgical resection to their management, lived 72.4 months. Although this is not a prospective, randomized, phase III trial, the dramatic difference in survival strongly suggests that surgery does play an active role in the management of these patients. Multiple prognostic factors have been associated with improved prognosis with metastasectomy, amongst these are limited number of nodules, normal carcinoembryonic antigen (CEA) level, absence of involved regional lymph nodes, and metachronous rather than synchronous presentation[8].

The question of how to manage these patients after resection is just as difficult. There are no prospective trials, using current chemotherapy regimens, showing significant improvement. There is retrospective data from 121 patients undergoing pulmonary metastasectomy, in which 73% of patient received post-operative chemotherapy using modern regimens (ie FOLFOX, FOLFIRI, or 5-FU)[9]. The two-year disease free survival was significantly higher in those who received chemotherapy compared to those who did not. Optimal regimen or duration was not clear. Currently, the guidelines from the National Comprehensive Cancer Network (NCCN) recommend a six-month course of either an oxaliplatin or irinotecan containing regimen after lung metastasis resection.

Our case and discussion confirms that we should not consider all stage IV CRC patients the same, and subject them to an indeterminate course of chemotherapy with no true hope of long term survival. Instead, we should try to tease out potential cases that may benefit from further surgical resection in conjunction with our cytotoxic treatments. In this manner, with use of a multidisciplinary approach, our patients will have a reasonable chance to fight this disease.

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