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Circulating Tumor Cells (CTC's) May Have a Supportive Role in Management Decisions for Difficult Problems in Patients with non Small Cell Lung Cancer (NSCLC)

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Recently Normanno *et al.*[1] suggested that monitoring of circulating tumor cells in NSCLC patients using a Reverse Transcriptidase-Polymerase Chain Reaction (RT-PCR) technique for EGFR mRNA assessment may add a relatively non-invasive method of determining one of the correlated indicators of therapeutic response. However, quantitative measurement of CTC's alone may have a role to play in therapeutic decisions following definitive therapy in patients with NSCLC. Rolle *et al.*[2], using HEA (human epithelial antibody)-magnetic bead enrichment and laser scanning cytometry serially, i.e., preoperatively, at 2 weeks post-op and at 5 months post-op, recently suggested a correlation of recurrent disease in NSCLC patients with adenocarcinoma undergoing complete resection with a continuous sequential increase of CTC. CTC's were detected at 2 weeks in all patients with the direction of quantitative change correlating with the extent of surgical manipulation (pneumonectomy vs. lesser procedure). However, the favorable prognostic group had decreased CTC's 3-5 months after surgery. Quantitative measurement of circulating tumor cells (CTC's) as an early indicator of response and prognosis in breast cancer using cytokeratin antibodies and immune magnetic technology[3,4] may assist therapeutic decision making.

Data suggest that CTCs are a real-time reflection of tumor characteristics[5] and have been shown to be detectable in all major epithelial carcinomas[6] including lung cancer[1,2,7]. Circulating nucleated cells lacking CD45 and expressing cytokeratin are only rarely detected in non cancer patients (`0.3%) [6] and > 95% of CTC's harvested for patients with malignancy show correlation to malignant genotype[8].

We report use of CTC testing to assist in a difficult management problem in a 75 year old patient with NSCLC (poorly differentiated adenocarcinoma) who had previously undergone left upper lobectomy for stage IIb disease. Nine months following adjuvant therapy with Gemcitabine, Carboplatin and Iressa a new lesion in the left lower lobe was identified. Our initial hypothesis was that if his CTC level was elevated he was more likely to have a significant metastatic burden[9] and, thus, a poor prognosis and, therefore, should not undergo the risk of further thoracic surgical resection. Conversely, if his CTC count was 0 he was more likely to have limited disease volume and potentially would be more likely to derive benefit from complete surgical resection. PET scan and CT scans showed no other sites of disease. His CTC count was 0. He consequently underwent complete nodule resection. A poorly differentiated non-small cell carcinoma morphologically similar to his prior lung lesion was found. This suggested a recurrence of his original tumor; confirmatory mutational profiling was not performed[10]. Two months after surgery the patient's CTC was 13, which is similar to what Rolle found in patients with limited resections[2]. Follow-up testing indicates no evidence of CTC's at 4, 5 and 6 months. Continuing clinical radiographic assessment over the 6 months following his second surgical procedure has not revealed disease recurrence. No further therapy has been administered and the patient continues under closely supervised follow-up.

CONCLUSION

Although as yet unvalidated, results of the CTC assessment helped to support our decision to recommend a second surgical approach and the addition of CTC testing to standard follow-up procedures, may play a role in the patient's future care.

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