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## Circulating Tumor Cells as an Indicator of Postoperative Lung Cancer: A Case Report

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**Conflict of interest:** None declared

**Patient:** Male, 50  
**Final Diagnosis:** Lung cancer  
**Symptoms:** None  
**Medication:** —  
**Clinical Procedure:** Surgery and chemotherapy  
**Specialty:** Oncology

**Objective:** Challenging differential diagnosis





**Background:** Circulating tumor cells (CTCs) are tumor cells that are shed from primary tumors and circulate in the peripheral blood. CTCs, as a surrogate of micro-metastasis, can be a useful clinical marker, but their clinical significance remains unclear in lung cancer. We now report a case of lung cancer in which the count of CTCs was useful in monitoring postoperative recurrence.

**Case Report:** A 50-year-old man had undergone right upper lobectomy for lung cancer (pT1bN2M0, stage IIIA adenocarcinoma), followed by cisplatin-based adjuvant chemotherapy. After the patient's operation, we initiated monitoring of CTCs using CellSearch, and documented the change in the CTC count along with the development of cancer recurrence and response or progression to chemotherapy given for recurrent disease.

**Conclusions:** The CTC count may be useful in monitoring blood of patients with lung cancer.

**MeSH Keywords:** Adenocarcinoma • Carcinoma, Non-Small-Cell Lung • Neoplastic Cells, Circulating

**Full-text PDF:** <http://www.amjcaserep.com/abstract/index/idArt/898934>

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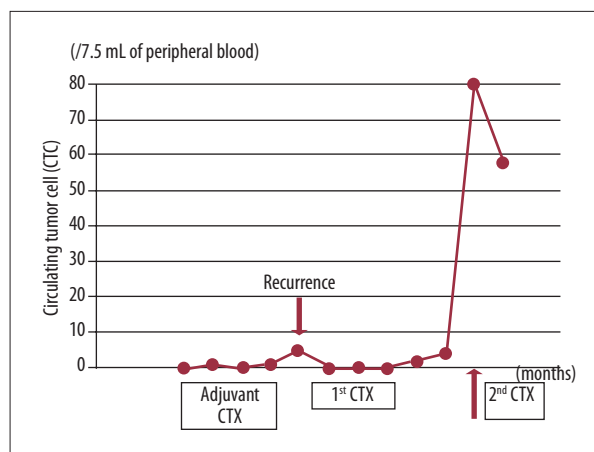
## Background

Circulating tumor cells (CTCs) are tumor cells that are shed from primary tumors and circulate in the peripheral blood. CTCs, as a surrogate of micro-metastasis, can be a useful clinical marker [1–3], but their clinical significance remains unclear in lung cancer. There are various CTC isolation methods. The CellSearch system (Veridex, LLC) is the first and the only technology that has been approved by the US Food and Drug Administration for clinical CTC testing in metastatic prostate, breast, and colorectal cancers. Using a magnetic field, CellSearch captures CTCs from blood samples by using ferrofluid nanoparticles with antibodies that target epithelial cell adhesion molecules. Once the CTCs are isolated, the system labels the cells with cytokeratin monoclonal antibodies, CD45, and 4',6-diamidino-2-phenylindole (DAPI). CTCs are then identified if cytokeratin and DAPI staining is positive, and CD45 staining is negative, as well as by other morphology features. Reports have validated CellSearch for CTC identification in metastatic breast, prostate, and colorectal cancer, with a cutoff set at 5, 5, and 3, respectively, of CTCs detected by CellSearch per 7.5 mL peripheral blood sample [4–6].

Here, we present a case in which the count of CTCs evaluated with CellSearch was useful in monitoring postoperative recurrence and response to chemotherapy.

## Case Report

A 50-year-old male patient, who was a smoker, underwent left upper lobectomy for adenocarcinoma of the lung (pT1b-N2M0, stage IIIA, driver mutations were negative) and postoperative adjuvant chemotherapy (four cycles of cisplatin-docetaxel). After the adjuvant chemotherapy, he enrolled in the clinical trial, “A feasibility study of postoperative adjuvant chemotherapy using platinum-based chemotherapy followed by maintenance TS-1 for completely resected pathologic stage II-III A non-small cell lung cancer with a biomarker study of circulating tumor cell.” Informed consent was obtained from all study patients, including our case study patient. We initiated measuring the CTC count at the start of the study, and the CTC count during the chemotherapy (TS-1) was “0 or 1,” indicating the presence of 0 or 1 CTCs in 7.5 mL of peripheral blood at room temperature. Two years after surgery, multiple lymph nodes were observed on computed tomography (CT), and the CTC count was elevated to “5” (Figure 1). Thus, the study patient received four courses of first-line chemotherapy (cisplatin, pemetrexed, and bevacizumab). After each chemotherapy course was finished, the level of CTCs was “0” and his CT after completion of the four cycles of chemotherapy showed the metastasis was reduced by 50%. Although CTCs disappeared after completion of the first-line chemotherapy, the CTC count



**Figure 1.** Graph showing the trend of circulating tumor cells (CTCs). The level of CTCs increased at the time of recurrence, and new lesions appeared in the liver and brain.

was again elevated to “80,” along with development and progression of distant metastases in the brain and the liver. After two cycles of second-line chemotherapy (carboplatin-nanoparticle paclitaxel) and whole brain radiation, the level of CTCs was “58.” Although the second-line chemotherapy provided a modest effect with some decrease in the CTC-count, the patient died of exacerbation of interstitial pneumonia induced by chemotherapy, and diagnosed by the findings on the CT scan that indicated reticular shadow and bronchoalveolar lavage fluid indicating lymphocytosis.

## Discussion

In the present case, the CTC count changed in accordance with tumor recurrence as well as response or progression to chemotherapy (Figure 1), suggesting that the CTC count may be useful in monitoring the blood of patients with lung cancer. In addition, this case showed that CTC count is likely to be useful as a therapeutic monitoring tool, even for lymph node only metastasis. Even though the patient’s CT scan showed metastases at the time of recurrence only in the lymph nodes, the CTC count was 5. A literature search did not find any other reports showing the relationship between the CTC count and lymph node metastasis. In other types of cancers, there have been numerous reports that include measurement of CTC count and that found it to be useful in therapy evaluation and prognosis [1–3]. However, for lung cancer, reports of CTC count as a useful evaluation marker of disease is scant. Among the many available blood-based biomarkers, serum carcinoembryonic antigen (CEA) has often been used as a biomarker for lung cancer, especially for adenocarcinoma in clinical practice. Tanaka et al. [3] reported that when comparing the CTC test and CEA test for diagnostic performance, the CTC

test had insufficient performance because of its low sensitivity. On the other hand, they reported that the CTC test had a significant diagnostic performance for predicting the absence or presence of distant metastasis, whereas serum CEA showed an insufficient performance.

Future prospective studies are needed to confirm the clinical significance of CTC count in the diagnosis and treatment of patients with lung cancer.

## References:

1. Bidard FC, Peeters DJ, Fehm T et al: Clinical validity of circulating tumour cells in patients with metastatic breast cancer: A pooled analysis of individual patient data. *Lancet Oncol*, 2014; 15: 406–14
2. de Bono JS, Scher HI, Montgomery RB et al: Circulating tumor cells predict survival benefit from treatment in metastatic castration-resistant prostate cancer. *Clin Cancer Res*, 2008; 14: 6302–9
3. Tanaka F, Yoneda K, Kondo N et al: Circulating tumor cell as a diagnostic marker in primary lung cancer. *Clin Cancer Res*, 2009; 15: 6980–86
4. Cristofani M, Budd GT, Ellis MJ et al: Circulating tumor cells, disease progression, and survival in metastatic breast cancer. *N Engl J Med*, 2004; 351: 781–91
5. Cohen SJ, Punt CJ, Iannotti N et al: Relationship of circulating tumor cells to tumor response, progression-free survival, and overall survival in patients with metastatic colorectal cancer. *J Clin Oncol*, 2008; 26: 3213–21
6. de Bono JS, Scher HI, Montgomery RB et al: Circulating tumor cells predict survival benefit from treatment in metastatic castration-prostate cancer. *Clin Cancer Res*, 2008; 14: 6302–9

## Conclusions

This case suggested that CTC count may be useful in monitoring the blood of patients with lung cancer. Additional case studies are needed.