PROGNOSTIC SIGNIFICANCE OF CIRCULATING TUMOR CELLS IN PATIENTS WITH COLORECTAL CANCER AND LIVER METASTASES

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Background: Despite the reduction in colorectal cancer (CRC) incidence rates in recent years, this tumor remains the most common gastrointestinal cancer in Western countries. CRC is a systemic disease (stage IV) in about 20% of patients, and metastases are most commonly found in the liver and lung. Unfortunately, patients undergoing surgery for CRC liver metastases are at risk for tumor recurrence. Several prognostic criteria have been proposed to improve patient selection for liver resection and adjuvant or neoadjuvant chemotherapy, including specific molecular or genetic assay and circulating tumor cells (CTC) dissemination detection. CTC can be revealed by reverse transcription-polymerase chain reaction (RT-PCR) based on mRNA detection. Since blood contains RNAse able to rapidly destroy extracellular RNA, the detection of mRNA can be accepted as an indicator of the presence of CTC. The aim of this study was to evaluate whether the presence of CTC in blood may predict tumor recurrence in patients who underwent resection for CRC liver metastases (LMs). The Fisher exact probability test, relative risk (RR) and associated 95% confidence interval (CI) calculation were used to analyze results.

Methods: Preoperative blood samples were obtained from 12 patients (8 men, 4 women, median age 67 years, range 58-72 years) with stage IV CRC and LMs. Blood samples were examined by immunomagnetic enrichment with RT-PCR technique based on specific molecular biological markers to detect CTC. The results were expressed as CTC-positive or CTC-negative samples. Patients underwent both spiral CT-scan and MRI to better define the size and number of metastases. CT-scan of the chest and whole-body 99mTc-MDP scintigraphy were also performed to exclude pulmonary and bone metastases, respectively. 18F-FDG-PET was used only in selected patients. Intraoperative ultrasound of the liver was performed in all patients. The chi-square test was used to analyze results.

Results: Nine patients showed CTC positivity, while three were CTC-negative. At 12-month follow-up, 9 patients developed relapse of the disease (CTC-positive = 8, CTC-negative = 1), and 3 were disease-free (CTC-positive = 1, CTC-negative = 2). A significant relationship between CTC-positivity and recurrence (chi-square = 3.7, p = 0.05) was found. The risk ratio (RR) was 2.66 (95%CI 0.53-13.43).

Conclusion: In patients with CRC and LMs who underwent surgery, CTC detection by RT-PCR represents a reliable tool for selecting those at risk of relapse, and should be suggested in all patients with advanced CRC. References: Lankiewicz S. et al. Circulating tumour cells as a predictive factor for response to systemic chemotherapy in patients with advanced colorectal cancer. Mol Oncol 2: 349-355, 2008.