Monitoring of circulating tumor cells in a patient with synchronous metastatic melanoma and colon carcinoma

**case report**

In July 2009, a 71-year-old woman was admitted to our department due to fatigue and dyspnea. Two years before, she was diagnosed with American Joint Committee on Cancer stage IIIIC melanoma. A computed tomography (CT) scan showed pulmonary, pleural and multiple hepatic metastases (Figure 1A). Radiological morphology of liver lesions was
judged suggestive of a malignancy other than melanoma. Blood tests showed increased transaminases and serum tumor markers carcinoembryonic antigen (CEA) and carbohydrate antigen 19.9 (CA 19.9) but not S100 protein. An ultrasound-guided fine-needle biopsy of a liver metastasis revealed an adenocarcinoma and a subsequent colonoscopy showed a 1.5-cm pedunculated polyp in the sigma. The histological examination confirmed the above diagnosis. The patient started treatment with 5-fluorouracil and oxaliplatin and, at the same time, was enrolled in a clinical investigation for the detection of circulating tumor cells (CTCs).

Twenty milliliters of peripheral blood was enriched for CTCs by CD45 depletion of the leukocyte fraction using a magnetic bead separation technique (EasySep®; Stem Cells Technologies, Inc., Vancouver, BC, Canada). Flow cytometry (FACSCanto II System; BD Biosciences, San Jose, CA, USA) detected seven epithelial CTCs per 10 ml of blood before chemotherapy started and zero cells 8 weeks later. CTCs of epithelial origin were defined as EpCam+ cytokeratin-7/8+ and CD45−. Dyspnea of the patient markedly increased. Further 20 ml of blood was therefore drawn for detection of circulating melanoma cells (CMCs), which were defined as MSCP (melanoma-associated chondroitin sulfate proteoglycan)+ and CD45−EpCam− and 551 CMCs per 10 ml of blood were detected (Figure 1B). A subsequent CT scan showed regression of some of the hepatic metastases, progression of intrathoracic disease, brain relapse and emerging of new liver metastases (Figure 1A). The patient did not wish further treatment, and her condition deteriorated and she died of respiratory failure several weeks later.

We based our initial strategy on the fact that the colorectal cancer seemed to be the more advanced tumor as (i) it presented d’embleée with liver metastases; (ii) the markers CEA and CA19.9 were elevated, whereas S100 was negative and (iii) intrathoracic involvement was therefore assumed to be potentially due to the epithelial malignancy in addition to the biopsy-proven hepatic metastasis. Disease progression might be due to the colon cancer or to melanoma. The absence of detectable epithelial CTCs at that time point did not exclude that colon carcinoma might have acquired resistance to chemotherapy, but the presence of CMCs at high numbers strongly suggested that disease progression was due to melanoma.

We did not draw blood for detection of CMCs before treatment started and we therefore do not know whether CTC detection would have been consistent with the negative S100 level at that time point and, moreover, whether detection of CMCs would have changed our treatment strategy. At the re-evaluation, CTCs and serum markers were in concordance, but CTC monitoring clearly displayed the switch when the colon carcinoma responded and the melanoma progressed. It is still not clear whether CTC monitoring may be a more specific and sensitive monitoring tool in comparison to traditional tumor markers. However, assessment of CTCs has been shown to be an earlier indication of disease status than current imaging methods [1–2].

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disclosure
None of the authors declare conflicts of interest.

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