A liver angioma colonized by colon cancer cells in a patient with two primitive localizations by colon adenocarcinoma: biologic, diagnostic and therapeutic implications

In January 2001, after the appearance of abdominal pain in an apparently healthy 64-year-old female patient, colonoscopy revealed the presence of two different tumors in the ascendant and descendent colon, respectively. No laboratory abnormalities were found and tumor markers were all negative. An abdomen CT scan during pre-operative staging found an angioma at the VII liver segment. The patient was subjected to right emicolectomy and left colon resection, which demonstrated at pathological examination a pT3N0 moderately differentiated adenocarcinoma and a pT1Nx mucinous adenocarcinoma at the right and left colon, respectively. After 1 month from intervention the patient was subjected to a second laparotomy for peritonitis. The peritoneal infection was completely resolved in April 2001 when no adjuvant treatment could be performed during the long interval from the initial intervention. Figure 1(A, B)

Figure 1. (A) Pre-contrast-enhanced and (B) contrast-enhanced CT scan of the liver at diagnosis. Arrows show liver angioma. Total body PET with 18F deoxyglucose at diagnosis (C) and at progression (D). Arrows show specific liver hyperaccumulation.
shows the lesion in pre-contrast-enhanced and contrast-enhanced CT imaging. A total body PET did not demonstrate metabolic liver hyperaccumulations, but only non-specific accumulation in abdomen compatible with peritonitis remnants (see Figure 1C). Colon cancer markers were negative and remained unchanged until July 2004 when CEA levels increased to 97.1 U/ml and a total body PET with $^{18}$F deoxyglucose demonstrated the presence of a pathologic metabolic hyperaccumulations at the VII liver segment (Fig. 1D, arrow).

In December 2004 the patient was subjected to transarterial chemoembolization (TAE), equally active at both the angioma and metastatic site, and after 30 days from the first TAE sitting an approximate two-fold reduction of CEA levels was recorded. Several clinical and instrumental findings suggest that the liver lesion was initially an angioma. In fact, both serum CEA levels and the CT and PET imaging remained unchanged for almost 4 years without evidence of the tumor spreading.

It has recently been demonstrated that circulating tumor cells can still be detected in the peripheral blood of patients 7–22 years after mastectomy [1]. Moreover, the activation of oncogenes can cause active proliferation of dormant tumor cell tissues [2]. In colon cancer, genetic instability is a frequent finding [3]. The reported patients had a double neoplasm at diagnosis and a genetic instability as the basis of cancer development can, therefore, be hypothesized. In these conditions the activation of an awaking oncogene during 4 years can be supposed. In our case the metastases localized in a highly vascularized lesion and the persistence of dormant tumour cells in a highly vascularized tissue can favouer cancer progression. In fact, some tumor cell lines do not form visible tumors when inoculated into immuno-suppressed mice [4]. However, transfecting the cells with either vascular endothelial growth factor (VEGF165) or activated c-Ha-ras induced loss of dormancy [4] suggesting a switch to an angiogenic phenotype in our case.

These data support the hypothesis of dormant colon cancer cells in a liver angioma where the balance between apoptosis and cell proliferation was lost for both the genetic instability of the primitive neoplasm and for the vascular features of the colonized tissue.

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