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Chronic myelogenous leukemia and colon cancer: A causal relationship or coincidence?

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Lately, there has been a lot of discussion on the likelihood of development of a non-hematological second malignancy in patients with chronic myelogenous leukemia (CML) receiving chemotherapy or other immunosuppressive drugs.

In 2005, Roy et al. referred to the occurrence of second malignancies in 6 among 189 CML patients treated with imatinib in the late chronic phase (CP) after interferon failure and expressed uncertainty whether the solid tumors were related to the drug. One of the cases was colon cancer [1]. In 2008, Frustaci et al. reported the occurrence of a colon adenocarcinoma in 2 out of 150 CML late CP patients treated with imatinib [2]. A surveillance analysis of clinical trials conducted until 2005, recorded 110 malignant neoplasias among 9,518 imatinib treated CML patients [3]. However, many CML patients were receiving hydrocycarbamide (hydroxyurea, HU) before the era of tyrocine kinase inhibitors. Few studies have been conducted on the development of secondary malignancies in patients receiving HU and those studies refer to bcr-abl negative myeloproliferative diseases. Most of them are anecdotal reports and the potential oncogenicity of HU remains a matter of debate [4,5,6].

In our department 21 patients have been diagnosed with CML. Only 2 of them had been treated with HU before starting tyrosine kinase inhibitors. One of the patients receiving HU, had also a diagnosis of colon adenocarcinoma. Nobody else has a positive history of other malignancy. This patient was a 63-year-old female diagnosed as having Ph+ CML in November 1999 and was treated with HU from diagnosis to December 2002, when imatinib was started at 400mg/day. The patient remained in chronic phase with complete cytogenic remission (CCR) and molecular response (CMR), until October 2009 when the disease entered an accelerated phase. Then imatinib at 800mg/day was started, and from June 2010 she is under treatment with 600mg/day with partial cytogenic response and major molecular response. From November 2010 the patient experienced episodes of diarrhea and persistent fever of unknown origin. Colonoscopy showed a mass of rectum and CT of abdomen revealed multiple lesions of the liver. The tumor markers CEA and CA 19.9 were both increased, 884.95 ng/mL and 784.9 U/mL respectively. A diagnosis of adenocarcinoma was made by histological examination (Dukes' stage D). At present the patient is being treated with chemotherapy consisting of oxaliplatin, capecitabine and bevacizumab, as well as with imatinib during the free internals of chemotherapy.

Solid tumors may occur in 3% of the patients with chronic myeloid leukemia (CML) [7]. It has also been reported that mainly elderly patients with hematologic malignancies, including CML, are likely to have multiple malignant neoplasms, mainly of the gastrointestinal tract [8]. However, single cases of CML in patients treated for other malignancies have been reported, three concerned colon adenocarcinoma after treatment with chemotherapeutic agents [7,9]. In our case a relationship between imatinib therapy or previous exposure to HU or cumulative effect of either exposures and development of colon adenocarcinoma cannot be completely excluded. However, an increased susceptibility of CML to secondary malignancies due to the malignant process of the disease itself cannot be ruled out. Only wider long term studies may clarify whether the concomitant occurrence of colon adenocarcinoma and CML is merely coincidental.

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