Onset of segmental colitis associated with diverticulosis after treatment with bevacizumab for metastatic colorectal carcinoma

Dear Sir,

A 48-year-old male underwent to colonoscopy due to an 8-month history of abdominal pain, iron-deficiency anemia and weight loss. Erythro-sedimentation rate and C-reactive protein were increased, and searching for fecal occult blood test was positive. Colonoscopy showed a stenosing neoplastic lesion involving the ascending colon (Fig. 1a); at the same time, diffuse diverticulosis was found in descending and sigmoid colon (Fig. 1b). The patient underwent to surgical treatment of the colorectal cancer (CRC) followed by six courses of chemotherapy (5-fluorouracil, folinic acid, and oxaliplatin) associated with biologic treatment with bevacizumab due to metastases located in the right liver. Six weeks after the last infusion of bevacizumab (and therefore 8 months after the surgical remove of the CRC), he experienced recurrent rectal bleeding associated to abdominal pain. Inflammatory indexes were normal. Colonoscopy showed normal appearance of ileo-colonic anastomosis (Fig. 1c); on the contrary, hyperaemic areas were found in the sigmoid and in the distal descending colon, not involving the diverticula orifices (Fig. 1d). No other lesions were found in the remaining colon. Endoscopic diagnosis of segmental colitis associated with diverticulosis (SCAD) was made. Histological assessment confirmed the endoscopic diagnosis, and the patient was successfully treated with mesalazine.

Bevacizumab is a monoclonal antibody (~ 93% human and 7% murine protein sequence) blocking vascular endothelial growth factor (VEGF). We know that angiogenesis is viewed as a fundamental component of IBD pathogenesis, and that

Figure 1 Neoplastic lesion, detected at the ascending colon (panel a). Uncomplicated diverticulosis, detected in the sigmoid region (panel b). Colonic appearance 8 months later: normal endoscopic aspect of the ileo-colonic anastomosis (panel c). Colonic appearance 8 months later: diffuse hyperaemic areas with diverticular sparing, according to a type A SCAD, detected in the sigmoid colon (panel d).
VEGF is significantly released by inflamed intestinal mucosa.\(^2\) We know also that SCAD share a lot of immune characteristic with IBD, for example increased tumour necrosis factor (TNF-\(\alpha\)) levels.\(^3\) Thus, it is therefore hypothesized that treatment with bevacizumab may cause an unstable equilibrium between the different angiogenetic factors involved in the pathogenesis of IBD: blockade of VEGF may cause increased release of intercellular adhesion molecule (ICAM)-1, integrin \(\alpha(v)\beta_3\), tissue factor (TF), and fractalkine (FKN),\(^2\) with rapid and increasing release of other proinflammatory cytokines (TNF-\(\alpha\) included). In genetically, predisposed subjects it is probably that a Th2 predominant pattern may suddenly occur and favour the onset of UC, a typical Th2-related disease. This hypothesis comes also from literature, in whom only cases of new UC under treatment with biologics are described. Since SCAD shows most frequently endoscopic and histological damage similar to that of UC than Crohn’s disease,\(^4\) it is hypothesized that similar pathogenetic events may occur in genetically, predisposed subjects affected by diverticulosis. Whatever the immune mechanism elicited may be, this case shows that bevacizumab therapy in patients suffer from metastatic CRC may have more significant effects on immunity than expected, and that in genetically predisposed it subjects may be able in inducing the onset of other colonic inflammatory diseases.

References


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1 May 2012