

Letter to the Editor

Helicobacter pylori and Colorectal Cancer Risk—Letter

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Epplein and colleagues (1) reported that the overall *Helicobacter pylori* (*H. pylori*) seropositivity was not associated with colorectal cancer risk, and seropositivity to specific *H. pylori* proteins, particularly the toxin VacA antibodies, may be associated with a higher risk of colorectal cancer and right-sided colon cancers.

Remarkably, the serologic test does not discriminate between current and past infections and, apart from past infections that may even be more relevant for oncogenesis, such a distinction is essential because only current *H. pylori* infection (*Hp-I*) induces humoral and cellular immune responses that produce or perpetuate chronic inflammatory processes in gastrointestinal tract with potential oncogenic sequelae; many neoplasms including colorectal neoplasms arise at the sites of chronic inflammation and infection (2, 3).

On the basis of histology for documentation of current *Hp-I*, our series in 50 patients with colorectal cancer, 25 patients with colorectal adenomas, and 10 controls showed significantly higher *Hp-I* presence in colorectal adenomas (68%) and colorectal cancer (84%) groups than controls (30%; ref. 4). Remarkably, *H. pylori* presence was documented by immunohistochemical stain in colorectal adenomas and colorectal cancer tissues (4, 5).

Presence of *Hp-I* with accompanying immunohistochemical expression of CD44 [indicator of cancer stem cells (CSC) and/or bone marrow-derived stem cells (BMDSC)] in biopsy specimens was found in a high proportion of

patients with colorectal adenomas accompanied with moderate/severe dysplasia (88%) and patients with colorectal cancer with moderate/severe degree of malignancy (91%). Comparable pictures were also obtained for proliferation marker Ki-67, antiapoptotic Bcl-2, and CD45 (assessing mainly T and B lymphocytes locally) immunohistochemical expressions (4, 5); these mediators might also serve as a risk *H. pylori* biomarkers involved in the sequence: normal colon epithelium–colorectal adenomas–colorectal cancer development/progression.

Considering the mechanisms underlying the *Hp-I* involvement in the aforementioned sequence, apart from the left colon–limited oncogenic actions of *Hp*-induced gastrin, also mentioned by Epplein and colleagues (1), our studies indicate that *Hp-I* may be involved in colon carcinogenesis by: (i) inducing a possible chronic inflammatory mucosal damage, comparable with upper gastrointestinal tract (UGT); (ii) stimulating CSCs or recruiting BMDSCs, similar to UGT *Hp-I*-associated chronic inflammation, metaplasia, dysplasia, and BMDSCs recruitment that may facilitate tumor formation/progression in animal models and humans; (iii) and affecting oncogenes and immune surveillance processes (4, 5).

Finally, the following concept about the VacA antibody association with right-sided colon cancers observed by Epplein and colleagues (1) might be considered: (i) as right-sided colon cancers have higher distant metastases than left-sided colon cancers, circulation of activated monocytes (possibly infected with *H. pylori* due to defective autophagy) might lead to potential *H. pylori*-related metastatic disease (6); and (ii) VacA promotes *H. pylori* intracellular survival and modulates host immune responses.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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