H. pylori and colorectal cancer risk - Letter -

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Dear Editor,

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

Remarkably, the serological 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 *Hp* 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).

Based on histology for documentation of current *Hp*-I, our series in 50 CRC patients, 25 patients with colorectal adenomas (CRA) and 10 controls, showed significantly higher *Hp*-I presence in CRA (68%) and CRC (84%) groups than controls (30%) (4). Remarkably, *Hp* presence was documented by immunohistochemical stain in CRA and CRC tissues (4,5).

Presence of *Hp*-I with accompanying immunohistochemical expression of CD44 [indicator of cancer stem cells (CSCs) and/or bone marrow-derived stem cells (BMDSCs)] in biopsy specimens was found in a high proportion of CRA patients accompanied with moderate/severe dysplasia (88%) and CRC patients with moderate/severe degree of malignancy (91%). Comparable pictures were also obtained for proliferation marker Ki-67, anti-apoptotic Bcl-2 and CD45 (assessing mainly T and B lymphocytes locally) immunohistochemical expressions (4,5); these mediators might also serve as risk *Hp* biomarkers involved in the sequence: normal colon epithelium-CRA-CRC development/progression.

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

Finally, the following concept regarding the VacA antibody association with R-CCs observed by the authors (1) might be considered: since R-CCs have higher distant metastases than left-sided CCs, circulation of activated monocytes (possibly infected with \( Hp \) due to defective autophagy) might lead to potential \( Hp \)-related metastatic disease (6); VacA promotes \( Hp \) intracellular survival and modulates host immune responses.

References


