CD44 and Helicobacter pylori-related colon oncogenesis

To the Editor

Basakran’s systematic review discussed CD44 as a diagnostic marker for specific cancer cells with an emphasis on breast and colon cancers.1 Regarding colorectal cancer (CRC), recent epidemiologic data indicate mainly a serologic association between the global Helicobacter pylori infection (Hp-I) and the risk of CRC, which warrants exploration of the underlying biologic mechanisms.2,3 Moreover, recent observations point to the possible involvement of Hp and stem cell cross-talk in gastrointestinal (GI) tumorigenesis.3

Experimental and preliminary data in humans suggest that Hp-I is implicated in gastric tumorigenesis through induction of chronic gastric inflammation that promotes the recruitment of bone marrow-derived stem cells (BMDSCs) from the circulation into the upper GI tract, which via intestinal metaplasia can contribute to gastric oncogenesis.3 Likewise, Hp-associated localization in the colon causing possible chronic inflammation, might also recruit BMDSCs in the intestinal epithelium that may contribute to CRC development and progression, similar to gastric cancer. In this respect, the cancer stem cell (CSC), which derives from transformation of normal stem cell has been considered to contribute to the onset and progression of cancer including CRC.3

Furthermore, the markers of CSCs are similar to those of stem cells of normal tissues, such as the transmembrane adhesion molecule CD44, mentioned by the author,3 which is also a marker of stem hematopoietic and tumor colon or gastric cells.3

It is important to note that Hp infection may be responsible directly or through inflammation for the increased expression of glycoprotein CD44 observed in gastric cancer wherein the BMDSCs appear to participate in its development.3 Furthermore, glycoproteins CD44, which are normally expressed only in the crypts of the intestinal epithelium are overexpressed in CRC and their overexpression is an early event in the sequence adenoma-CRC development.3 Of note, the serologic test does not discriminate between current and past infections; only current Hp-I induces humoral and cellular immune responses that induce, or perpetuate chronic inflammatory processes in the GI tract with oncogenic sequelae. Many cancers, including CRCs, arise at the sites of chronic inflammation and infection.3

Based on histologically documented active Hp-I, our studies in 50 CRC patients, 25 patients with colorectal adenomas (CRA) and 10 controls, showed significantly higher Hp-I presence in the CRA (68%) and CRC (84%) groups compared with controls (30%).3 Remarkably, Hp presence was documented by immunohistochemical stain in tissues.3,4 Presence of Hp-I with accompanying immunohistochemical expression of CD44 (CSCs and/or BMDSCs indicator) in biopsy specimens was found in 91% CRC patients, 81% CRA patients, and 33% controls;3 in particular, presence of Hp-I with CD44 expression 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%).3,4

Therefore, our results indicate that Hp-I might have an impact on colon oncogenesis by stimulating CSCs or recruiting BMDSCs, similar to Hp-I-associated chronic inflammation, hyperplasia, metaplasia, dysplasia, and BMDSC recruitment that may facilitate tumor formation and progression in animal models and humans; however, future studies are warranted to elucidate the proposed Hp-related oncogenic mechanism(s). As nearly 50% of the population is infected with Hp worldwide, and the prevalence of Hp-I is still high in the East Mediterranean countries including Saudi Arabia,5 it would be interesting to know if the author7 considered the involvement of Hp-I in the aforementioned oncogenic sequences by CD44-related CSC and/or BMDSCs.

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References


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