Intestinal-type poorly differentiated gastric adenocarcinoma with microsatellite instability and defective DNA mismatch repair proteins expression

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INTRODUCTION

DNA mismatch repair genes hMLH1, hPMS2, hMSH2 and hMSH6 are one of the multiple mechanisms human cells use to avoid defects in the cell cycle. Impaired function of these proteins via mutations or promoter hypermethylation leads to microsatellite instability (MSI).

CASE REPORT

We report a case of an 80-year-old female patient with a chronic anemia at study. A ulcerated mass in the pyloric antrum was endoscopically visualized (Fig. 1 A and B). In the resected specimen, this lesion measured 5 x 4 cm. Histologically it was composed of a variable mixture of infiltrative nests and cords of atypical cells that reached the muscularis propria. There were occasionally poorly-formed glands with their lumen occupied by apoptotic cells or necrotic debris. A marked intraepithelial lymphocytosis was characteristically identified (Fig. 2A) and a peripheral inflammatory Crohn’s-like response with prominent lymphoid aggregates formation (Fig. 2B). The immunohistochemical study revealed a strong expression of AE1/AE3 and CAM 5.2 cytokeratins (Fig. 2C) and focal positive staining for nuclear transcription factor CDX2 (Fig. 2D). Interestingly, expression of hMLH1 (Fig. 3A) and hPMS2 (Fig. 3B) DNA mismatch repair proteins were...
completely lost in tumor cells. In contrast, such cells demonstrated preserved hMSH2 (Fig. 3C) and hMSH6 (Fig. 3D) protein-expression. There were no metastases in regional lymph nodes. According to these features, the neoplasm was diagnosed as intestinal-type poorly differentiated gastric adenocarcinoma with associated MSI.

DISCUSSION

DNA mismatch repair proteins hMLH1, hPMS2, hMSH2 and hMSH6 are one of the multiple mechanisms used by human cells to avoid defects in the cell cycle. Impaired function of these proteins via mutations or promoter hypermethylation leads to microsatellite instability (MSI). This alteration has been largely studied in colorectal cancer where high levels of MSI (MSI-H) have been associated with a proximal tumor location, female gender, lower stage and a better survival stage-for-stage (1). According to this, different investigators have reported dissimilar results due to a possible survival benefit of MSI-H status in gastric adenocarcinoma (2,3). Recent studies relate such data with a more aggressive behavior on MSI-H intestinal-type gastric adenocarcinoma (4). Besides, clinical parameters like an older age, increased tumor size, distal location and lower incidence of lymph node metastasis (3), as well as histological features such as intraepithelial lymphocytes, intestinal-type, poor differentiation and tumor necrosis are likely linked with MSI-H phenotype (4). Furthermore, MSI-H gastric cancer seems to be related with the development of synchronous and multiple gastric tumors (5). In summary, further studies should be undertaken to reveal the prognostic significance of MSI-H status patients with gastric cancer.

Fig. 2. Characteristically there were observed plenty intraepithelial lymphocytes [arrows] (H&E, magnification x400 [A]). At the periphery of the lesion there was an intense inflammatory Crohn’s-like response (H&E, magnification x40 [B]). Neoplastic cells showed strong immunoexpression for cytokeratins (CAM 5.2, magnification x100 [C]) and focally for nuclear transcription factor CDX2 (CDX2, magnification x400 [D]).
We report here a case of an 80-year-old-female with an intestinal-type poorly differentiated gastric adenocarcinoma with associated MSI with loss of hMLH1 and hPMS2 immunohistochemical expression.

REFERENCES