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Case Report

Gastric mucinous carcinoma with micropapillary carcinoma component: Case report of tumor morphology not previously described in stomach

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ABSTRACT

Micropapillary (MP) carcinoma is an uncommon tumor with a distinct histologic pattern. Although micropapillary carcinoma has been reported in the stomach, the concurrence of mucinous carcinoma and micropapillary carcinoma has not been reported to-date. A 69-year-old gentleman who presented with anemia was found at endoscopy to have a 1.7 cm gastric ulcer which was biopsied and subsequently underwent a partial gastrectomy. There was an ulcerated moderately differentiated adenocarcinoma displaying a micropapillary component within a mucinous adenocarcinoma component and a metastatic MP carcinoma in 1 of 18 lymph nodes. The tumor was immunoreactive for EMA, MUC2, MUC5AC, MUC6, CDX2, and p53 in both mucinous and mucinous-MP carcinoma areas; and negative for CK7, CK20, CA-125, synaptophysin, chromogranin, PD-L1, MMR proteins, and EBV. To the best of our knowledge, this is the first reported case of MP gastric carcinoma in association with mucinous carcinoma.

1. Background

Micropapillary (MP) morphology refers to a distinct histologic pattern that has been described in carcinomas of several organ systems. This pattern is characterized by small epithelial nests residing in artifactual lacunar spaces and lacking fibrovascular cores, with nuclei polarized inversely towards the surface of these nests. Gastric carcinoma with MP architecture was reported in conjunction with tubular or papillary gastric carcinoma [1–3]. MP morphology in conventional carcinoma of the stomach is associated with poor prognosis and aggressive behavior, albeit the number of reported cases is small [1–3]. Mucinous carcinoma of the stomach is a distinct subtype defined in the WHO classification as a tumor with more than 50% mucinous carcinoma component that characteristically depicts chains or irregular tumor cell clusters floating within extracellular mucinous pools. The combination of mucinous and MP carcinoma has only been previously described in the breast and in the lung [4,5]. However, to our knowledge a MP component in a mucinous gastric carcinoma has not been previously reported. Herein, we describe a novel case of mucinous-MP gastric carcinoma.

2. Materials and Methods

2.1. Immunohistochemistry

Immunohistochemical studies for epithelial membrane antigen (EMA), human epidermal growth factor receptor 2 (Her2/neu), synaptophysin, chromogranin, cytokeratin 7 (CK7), cytokeratin 20 (CK20), carcinoembryonic antigen 125 (CA125), mismatch repair proteins (MLH1, MSH2, MSH6, and PMS2), mucin (MUC2, MUC5AC, and MUC6), programmed cell death ligand 1 (PD-L1), CDX2 protein, p53 protein, and Epstein-Barr Virus RNA (by in situ hybridization) were performed on 4 μm sections of a formalin-fixed, paraffin-embedded tissue block of the primary gastric tumor. Controls with adequate results were performed for each antibody. For a complete listing of antibody details, please see Table 1.

3. Case Presentation

3.1. Clinical presentation

A 69-year-old gentleman presented with anemia and a past medical history of hypertension, diabetes, chronic back pain, and hyperglycemia. Biopsies of a gastric ulcer found at endoscopy demonstrated a low grade (moderately differentiated) invasive adenocarcinoma. No

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Table 1
Summary of antibodies for immunohistochemistry.

Antibody	Clone	Vendor (platform)	Dilution	Control	Interpretation
EMA (MUC1)	E29	Ventana (Ventana/Roche ULTRA)	Prediluted, ready to use	Breast, Pancreas	Membranous cytoplasmic staining is considered positive
Her2/neu	4B5	Ventana (Ventana/Roche ULTRA)	Prediluted, ready to use	Her2 positive breast carcinoma	Membranous cytoplasmic staining is considered positive
Chromogranin	LK2H10	Ventana (Ventana/Roche ULTRA)	Prediluted, ready to use	Pancreas	Granular cytoplasmic staining is considered positive
Synaptophysin	SP11	Ventana (Ventana/Roche ULTRA)	Prediluted, ready to use	Pancreas	Granular cytoplasmic staining is considered positive
CK7	SP52	Ventana (Ventana/Roche ULTRA)	Prediluted, ready to use	Breast, Lung carcinoma	Membranous cytoplasmic staining is considered positive
CK20	SP33	Ventana (Ventana/Roche ULTRA)	Prediluted, ready to use	Colonic adenocarcinoma	Membranous cytoplasmic staining is considered positive
CA125	OC125	Ventana (Ventana/Roche ULTRA)	Prediluted, ready to use	Ovarian carcinoma	Membranous cytoplasmic staining is considered positive
MLH1	ES05	Leica (Leica Bond)	Prediluted, ready to use	Colon	Nuclear staining (tumor or normal) is considered positive
MSH2	FE11	Millipore (Leica Bond)	1:100	Colon	Nuclear staining (tumor or normal) is considered positive
MSH6	44	Leica (Leica Bond)	Prediluted, ready to use	Colon	Nuclear staining (tumor or normal) is considered positive
PMS2	MRQ-28	Leica (Leica Bond)	Prediluted, ready to use	Colon	Nuclear staining (tumor or normal) is considered positive
MUC2	MRQ-18	Cell Marque (Leica Bond III)	1:300	Colon	Cytoplasmic staining is considered positive
MUC5AC	CLH2	Dako (Leica Bond III)	1:50	Stomach	Cytoplasmic staining is considered positive
MUC6	MRQ-20	Cell Marque (Dako Omnis)	1:500	Stomach	Cytoplasmic staining is considered positive
PD-L1	SP142	Spring Biosciences (Lieca Bond)	1:1000	Lung, squamous cell carcinoma	Membranous staining (tumor or inflammation) is considered positive
CDX	EPR2764Y	Ventana (Ventana/Roche ULTRA)	Prediluted, ready to use	Colon	Nuclear staining is considered positive
P53	DO-7	Leica (Leica Bond)	1:100	Colon, adenocarcinoma	Nuclear staining is considered positive
EBV – ISH		Ventana (Ventana/Roche ULTRA)	Prediluted, ready to use	Lymph node, Hodgkin's lymphoma	Nuclear staining is considered positive

lymphadenopathy was seen on CT scan. The patient underwent a partial gastrectomy with gastrojejunostomy, and lymph node dissection. He then received an adjuvant sandwich regimen consisting of three months of chemotherapy with 5-FU and leucovorin followed by combined chemoradiotherapy. PET/CT scanning showed that he was disease-free 10 months postoperatively.

3.2. Pathologic and Immunohistologic features

The gastrectomy had a 1.7 cm exophytic tumor with a central depressed ulceration (Fig. 1a). The cut surface was gray-tan, and gelatinous (Fig. 1b) without hemorrhage or necrosis. The tumor grossly invaded into deep submucosa, without obvious invasion into the muscularis propria. Microscopically, the bulk of the tumor was confined to the submucosa but focal extension into the muscularis propria (pT2) was detected (Fig. 2a). No deep muscle proper or subserosal extension was seen. The tumor had both mucinous (60%) and nonmucinous (40%) carcinoma components. The non-mucinous component was composed of simple tubular malignant glands with occasional cribriform glands (low grade moderately differentiated intestinal-type adenocarcinoma). The mucinous component consisted of extracellular mucin pools with strips of tumor cells or incomplete glands floating freely within or partially lining the mucinous pools. Within several areas of mucinous carcinoma was the MP carcinoma component (20% of mucinous carcinoma component) composed of multiple slender small tight tumor cell nests with inverse nuclear polarization floating within the pools of extracellular mucin (Fig. 2b) (Fig. 3). No vascular or perineural invasion was seen. There was focal high-grade dysplasia of the gastric mucosa in areas immediately adjacent to the main invasive carcinoma component. Metastatic carcinoma was present in one of 18 lymph nodes examined. The nodal metastasis nearly completely replaced the entire node and displayed mucinous-MP features identical to those seen in the primary tumor (Fig. 2c). The AJCC tumor stage was thus pT2 pN1 M0, stage IIA. Focal complete intestinal metaplasia, proton-pump inhibitor (PPI) effect, and focal chronic active gastritis without associated Helicobacter pylori were present in the non-neoplastic portion of the stomach.

Immunohistochemical studies performed on the primary tumor demonstrated immunoreactivity for epithelial membrane antigen (EMA) in both mucinous and mucinous-MP carcinoma components of the tumor (Fig. 2d). Her2/neu, synaptophysin, chromogranin, cytokeratin 7, cytokeratin 20, and CA125 were negative in both mucinous and mucinous-MP carcinoma components. Staining for mismatch repair proteins (MLH1, MSH2, MSH6, and PMS2) was all positive (wild-type) in both tumor and normal tissue. MUC2, MUC5AC, MUC6, CDX-2, and p53 showed positive staining in MP, mucinous and conventional non-mucinous carcinoma components. PD-L1 immunostaining was negative (0% staining in both tumor and inflammatory cells), as was in-situ hybridization for Epstein-Barr Virus (EBV).

4. Discussion

Our case of combined mucinous and MP gastric carcinoma has unique morphology with this combination of histologic types not previously reported in the stomach. Our case shares features with other cases of MP gastric and MP carcinoma in other organs. Similar to MP carcinoma in other organs, gastric carcinomas with MP components have been reported to have an associated increased risk of regional lymph node metastases [2,3,6–8]. Our patient presented with a relatively "early" pT2 carcinoma but did have a nodal metastasis. The majority of reported cases of gastric MP carcinoma occurred as a secondary component of a more common type. The tumor in our patient also had a focal MP component. The immunohistochemical profile was similar to that found in a study of 32 MP gastric carcinoma cases, where 71.9%, 43.7%, 84.4% and 65.6% of the cases were negative for CK7, CK20, and Her2, and positive for CDX2, respectively. [9] EMA is often