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CASE REPORT | STOMACH

Rapidly Growing Papillary Well-Differentiated Adenocarcinoma in a Patient With a *Helicobacter pylori*-Naive Gastric Mucosa

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ABSTRACT

Although undifferentiated adenocarcinomas and fundic gland-type carcinomas are known as *Helicobacter pylori*-naive gastric carcinomas, well-differentiated gastric phenotype adenocarcinomas with papillary growth are rare. We encountered a case of a rapidly growing pedunculated well-differentiated adenocarcinoma in a patient with a *H. pylori*-naive gastric mucosa. The tumor had characteristics of a gastric phenotype (pepsinogen I and H and K-adenosine triphosphatase staining negative; diffusely positive for both mucin-5AC [MUC-5AC] and MUC-6; and MUC-2, common acute lymphocytic leukemia antigen 10 [CD-10], and p53 negative) and treated with endoscopic mucosal resection. We report our case along with a relevant literature review.

INTRODUCTION

Although undifferentiated adenocarcinoma and fundic gland-type carcinomas are known as *Helicobacter pylori*-naive gastric carcinomas, differentiated adenocarcinoma with gastric phenotype and papillary growth is rare.[1] Papillary adenocarcinoma accounts for 1.5%–2% of all gastric cancers. Papillary adenocarcinomas have a poorer prognosis than other tubular adenocarcinomas, with more frequent vascular invasion and lymph node metastasis, which require surgical treatment.[2] We describe a case of a well-differentiated adenocarcinoma with a rapidly growing papillary in a patient with an *H. pylori*-naive gastric mucosa that was treated with endoscopic mucosal resection.

CASE REPORT

An 84-year-old woman with gastric tumor and no relevant medical history was referred to our hospital. Her palpebral conjunctivae appeared without anemia and with no tenderness in the epigastrium. The blood test did not reveal anemia (hemoglobin, 12.3 g/dL) and hypoproteinemia (total protein, 6.4 g/dL and albumin, 3.3 g/dL). The tumor marker was within the normal range (carcinoembryonic antigen, 2.4 ng/mL and carbohydrate antigen 19-9, 27.8 U/mL). Two years earlier, she underwent upper gastrointestinal endoscopy as part of a health checkup; no tumors in her stomach were noted (Figure 1). Furthermore, she has tested negative for *H. pylori* infection (had no eradication history, no mucosal atrophy in endoscopic and pathological findings, and negative rapid urease and serum antibody test results). This time, the patient presented with a tumor and was referred to our hospital for treatment. A biopsy, performed before presentation at our hospital, revealed adenoma (group 3). Conventional endoscopy revealed a mild, white-colored, clearly demarcated pedunculated tumor (50 mm in diameter) exhibiting a papillary development in the great curvature of the middle part of the stomach (Figure 2). Magnifying endoscopy revealed irregular microsurface and microvascular patterns (Figure 3). Computed tomography revealed the lesion to be a hyper vascular elevated lesion without any metastasis. Endoscopic ultrasonography revealed no evidence of tumor invasion to the submucosal layer (Figure 4).

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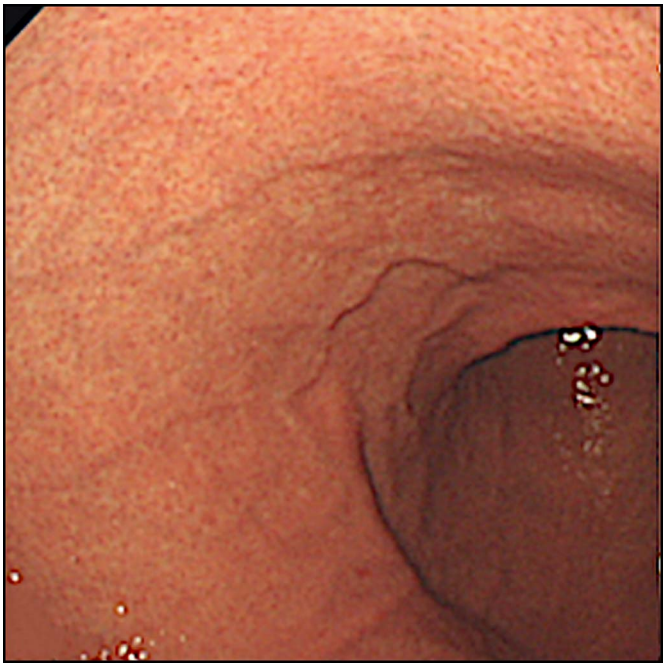

Figure 1. Upper endoscopic image from 2 years earlier.

Based on these findings, the tumor was considered early cancer. After injecting 0.4% sodium hyaluronate into the submucosal layer, endoscopic mucosal resection was performed using a double-channel type upper endoscope (GIF-2TQ260M; Olympus Corp., Tokyo, Japan) (Figure 5). For endoscopic mucosal resection, the tumor was lifted with forceps, the stalk was visualized and then snared the stalk of the tumor, and *en bloc* resection was achieved. After histopathological examination, the patient was diagnosed with a well-differentiated adenocarcinoma with papillary growth (pT1a, 0-I type according to the Paris classification, without venous or lymphatic invasions, and negative for horizontal and vertical margins with characteristics of a gastric phenotype (pepsinogen I and H and K-adenosine triphosphatase staining negative; diffusely positive for mucin-5AC [MUC-5AC] and MUC-6; negative for MUC-2, common acute lymphocytic leukemia antigen 10 [CD-10], and p53; and Ki-67 level of 78%) (Figure 6). Additional surgical resection was not needed, and no recurrence was observed at the 12-month follow-up.

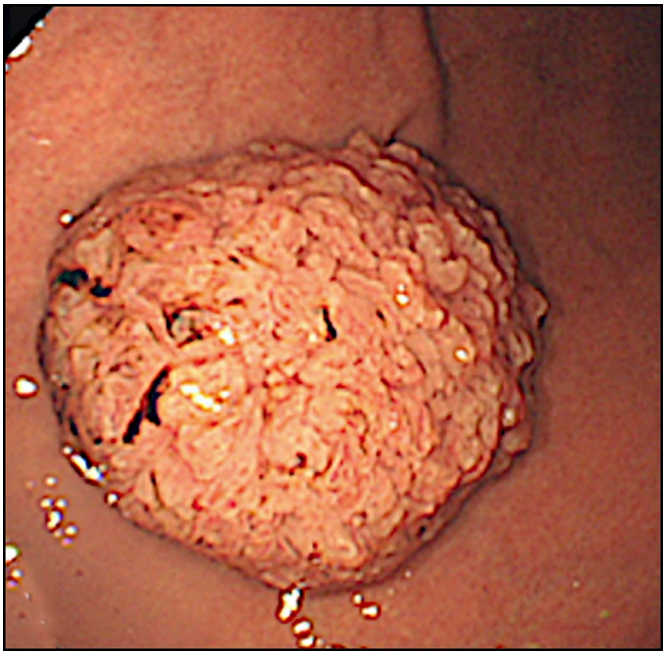

Figure 2. Upper endoscopy image showing a pedunculated tumor 50 mm in diameter in the middle part of the stomach.

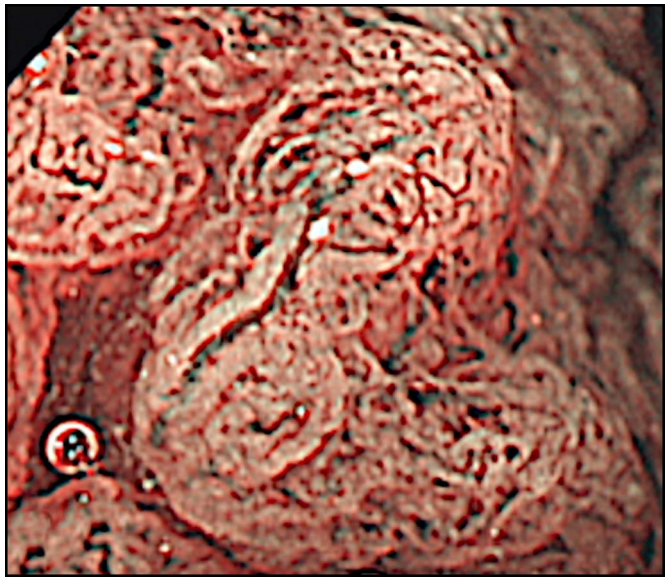

Figure 3. Magnified narrow-band image showing an irregular microsurface and a vascular pattern.

DISCUSSION

H. pylori-naive gastric cancers are rare, with an incidence of 2.5%, and mainly classified into 3 types as follows: pale

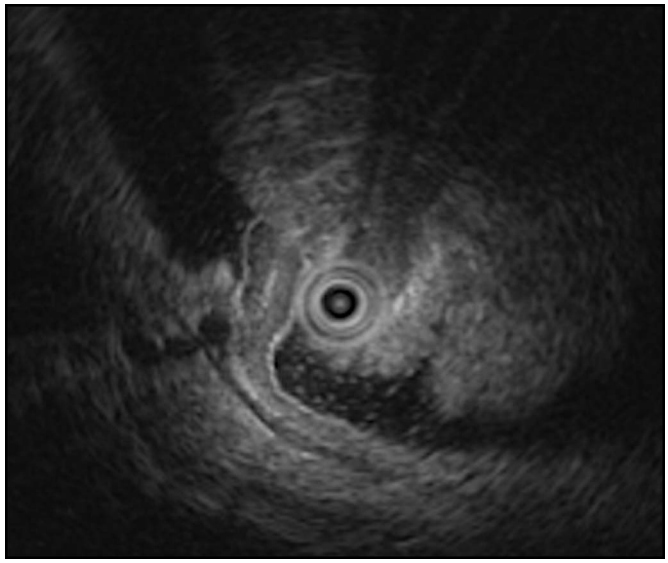

Figure 4. Endoscopic ultrasonographic image.

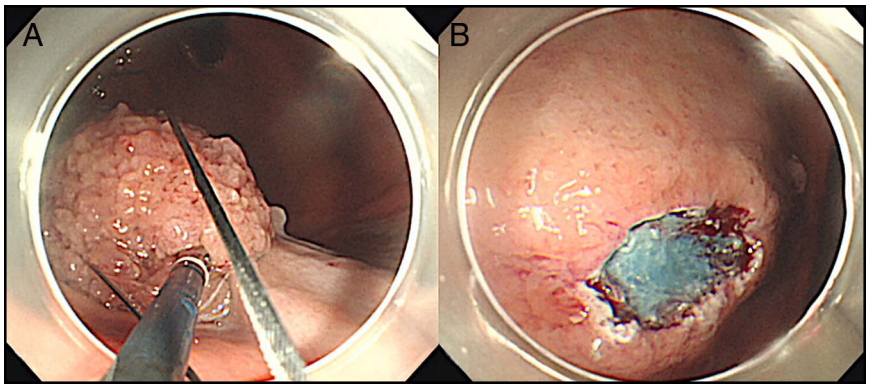

Figure 5. Procedural image of endoscopic mucosal resection showing (A) lifting the tumor with forceps and (B) the ulcer after endoscopic mucosal resection.

undifferentiated adenocarcinoma with a depression, lowly elevated fundic gland-type gastric carcinoma, and foveolar type gastric carcinoma with laterally spreading elevation.[3,4] Undifferentiated adenocarcinoma is relatively young and with high malignant potential. Standard treatment is surgery, but endoscopic resection is also considered for intramucosal tumors that are smaller than 20 mm in size. Other gastric cancers of a gastric phenotype are usually low atypia, and endoscopic resection is often possible.

We report a case of rapid papillary growth (within 2 years) of a gastric-phenotype well-differentiated adenocarcinoma in a patient with a *H. pylori*-naive mucosa. Macroscopically, the tumor was of the 0-I type according to the Paris classification and 5 cm in diameter, and endoscopic resection was feasible. The histological type was papillary-growing well-differentiated adenocarcinoma, and the mucinous traits were positive for MUC5AC and MUC6, which was considered of the gastric phenotype. No submucosal layer or lymphovascular invasion was observed.

Adenocarcinomas with rapid papillary growth of the gastric phenotype are rare. Previous reports tended to show biological malignancies with rapid growth and high lymphovascular invasion positivity in the case of adenocarcinoma with papillary growth rather than the usual tubular adenocarcinoma.[5,6] Papillary adenocarcinomas often have a gastric phenotype, and it has been reported that poorly differentiated adenocarcinomas are frequently mixed.[5] In addition, a case of a papillary well-differentiated adenocarcinoma with low-grade atypia but high malignancy has been reported, in which Ki-67, a protein induced by the mitosis karyorrhexis-index gene, was highly expressed.[5,7] The Cancer Genome Atlas project proposed that gastric cancers be classified as Epstein-Barr virus-positive tumors, microsatellite unstable tumors, genetically stable tumors, or tumors with chromosomal instability.[8] A high Ki-67 level may relate to microsatellite instability. Thus, before treatment, a detailed endoscopic evaluation and judgment about the indication of endoscopic treatment are important. Endoscopists must exercise caution when dealing with adenocarcinomas of the gastric phenotype that show papillary growth because of their potential for rapid growth and metastasis.

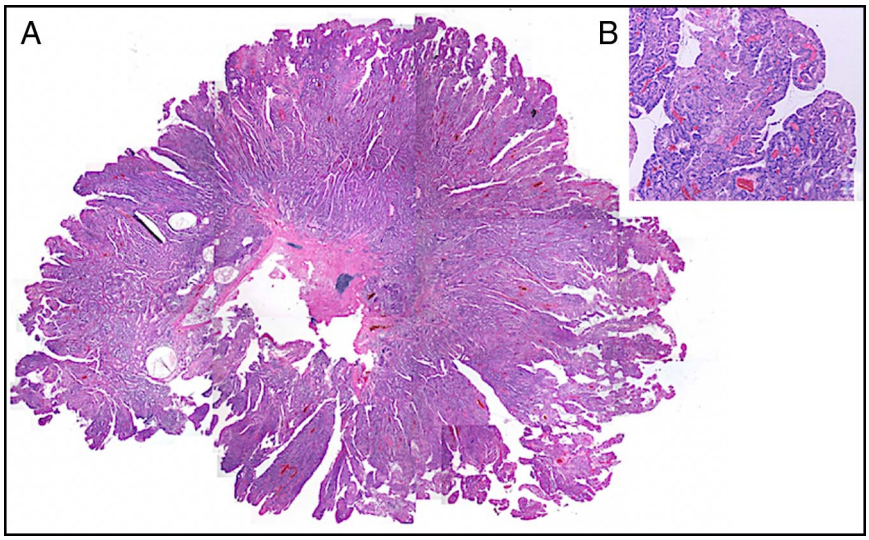

Figure 6. Microscopic view of (A) weak and (B) strong enlargement of the resected specimen (hematoxylin and eosin stain).

DISCLOSURES

Author contributions: Y. Shiratori drafted the manuscript, revised the manuscript for intellectual content, and is the article guarantor. T. Ikeya and K. Nakamura edited and revised the manuscript for intellectual content. K. Suzuki evaluated the pathology.

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Informed consent was obtained for this case report.

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