Mucinous Carcinoma of the Duodenum Associated with Hereditary Nonpolyposis Colorectal Cancer: Report of a Case

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Abstract
We herein report a rare case of primary mucinous carcinoma of the duodenum associated with hereditary nonpolyposis colorectal cancer (HNPCC). A 50-year-old man known to have HNPCC based on the Amsterdam criteria I was admitted because of the presence of a duodenal tumor. Duodenoscopy revealed an ulcerated tumor in the posterior wall of the second portion of the duodenum and the malignancy was confirmed by a biopsy. He underwent a pylorus-preserving pancreaticoduodenectomy with a regional lymph node dissection. The histological diagnosis was mucinous carcinoma of the duodenum with lymph node metastasis. High-frequency microsatellite instability (MSI-H) was identified in both the colon and a duodenal specimen based on a microsatellite assay. A germline mutation in the hMSH2 gene was also identified. Even though extracolonic malignancies are associated with HNPCC, duodenal cancer is nevertheless very rare, and only two cases have been reported over the past 20 years. We herein report the third case of an HNPCC patient who demonstrated carcinoma of the duodenum. The clinicopathological characteristics of duodenal carcinoma associated with HNPCC are examined based on a review of the literature.

Key words Primary duodenal carcinoma · Colorectal cancer · Hereditary nonpolyposis colorectal cancer · Multiple primary cancers

Introduction
As extracolonic malignancies associated with hereditary nonpolyposis colorectal cancer (HNPCC), the majority of cases are endometrial, and gastric carcinomas.1,2 Duodenal cancer is also a recognized component of HNPCC, owing due to its rarity,1–7 there have so far been few reports of this condition. Only two cases have been reported over the past 20 years. We herein report the third case of an HNPCC patient who demonstrated carcinoma of the duodenum. The clinicopathological characteristics of duodenal carcinoma associated with HNPCC are examined based on a review of the literature.

Case Report
A 50-year-old man, who had HNPCC based on the classic ICG-HNPCC Amsterdam criteria (Amsterdam criteria I), was referred to our hospital to undergo gastroendoscopy. He had been in a surveillance program of yearly gastroendoscopy and colonoscopy after a resection of transverse colon cancer at 48 years of age. We found an ulcerated tumor, measuring about 2.5 × 2.0 cm in size, in the posterior wall of the second portion of the duodenum (Fig. 1a). Signet ring cell carcinoma was confirmed based on a biopsy. Endoscopic ultrasonography showed a hypoechoic mass including a cystic area (Fig. 1b). Laboratory investigations did not show any abnormalities, including tumor markers such as carcinoembryonic antigen and carbohydrate antigen 19-9. A laparotomy was performed which revealed a soft mass at the second portion of the duodenum without any extramural invasion. Neither metastatic lesions of the liver nor any peritoneal implants were evident. The patient underwent a pylorus-preserving pancreaticoduodenectomy with a regional lymph node dissection. The histological diagnosis was mucinous carcinoma of the duodenum with lymph node metastasis. The clinicopathological characteristics of duodenal carcinoma associated with HNPCC are examined based on a review of the literature.
dissection. An examination of the resected specimen revealed the advanced duodenal cancer in the posterior of the second portion to be an ulcerated tumor measuring 2.3 × 2.2 cm in size (Fig. 2a). The histological diagnosis was mucinous carcinoma of the duodenum with peripancreatic head lymph node metastasis. The depth of invasion was the subserosa, with remarkable mucinous nodules in both the submucosal and subserosal layers (Figs. 2b and 3). After obtaining the informed consent of the patient, we extracted DNA from formalin-fixed, paraffin-embedded tissue specimens resected during the past two operations and analyzed the specimens for microsatellite instability (MSI) using six fluorescence-labeled microsatellite markers (D2S123, D5S346, D17S250, BAT25, BAT26, BAT40).8

High-frequency microsatellite instability (MSI-H) was thus identified in both the colon and duodenal specimens (D2S123, D5S346, and BAT40 exhibiting instability length changes). In addition, a germline mutation of hMSH2 at codon 496 substituting TTA (Leu) to TGA (stop) was also identified. The patient’s postoperative course was uneventful and he was discharged on the 33rd postoperative day. He is currently alive and doing well without any evidence of recurrence, 30 months after the operation.

Discussion

Heredity in colorectal cancer was first referred to by Alfred Warthin in 1895.9 Owing to progress of the molecular genetic science, the hereditary colonic cancer syndrome presenting early onset without colonic polyposis, with or without extracolonic malignancies such as endometrium, stomach, and urinary tract, has since been revealed to be a syndrome caused by inherited defects of mismatch repair genes. This disease is now referred to as hereditary nonpolyposis colorectal cancer (HNPCC) syndrome,10 which is estimated to account for 5%–10% of all cases of colorectal cancer.11-13 As