Metachronous ileal cancer after surgery for ascending colon cancer in a patient with Lynch syndrome: A case report

Yuichi Tachikawa,a, Hiroaki Nozawa, Keisuke Hata, Hiroyuki Abe,b Tetsuo Ushiku,b Soichiro Ishihara,a

a Department of Surgical Oncology, Graduate School of Medicine, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo, Japan
b Department of Pathology, Graduate School of Medicine, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo, Japan

1. Introduction

Lynch syndrome is an autosomal dominant disorder caused by mutations in the DNA mismatch repair genes such as MLH1, MSH2, MSH6 and PMS2, and EPCAM [1]. It is clinically characterized by an early age of cancer onset and a high lifetime risk of colorectal cancer (CRC), but also of cancers of the endometrium, stomach, ovary, urinary tract, biliary tract, pancreas, brain, skin, and small bowel [2,3].

Small bowel cancer is rare, accounting for less than 5% of gastrointestinal cancers [4]. However, the life-time risk of developing small bowel cancer is estimated to be 1–4% for Lynch syndrome patients, which is 100-times higher than that for the general population [5]. The mean age at diagnosis of small bowel cancer in Lynch syndrome was 49 years, about 10–15 years younger than in sporadic small bowel cancer [6]. Although few guidelines recommend routine surveillance of small bowel cancer in Lynch syndrome [6,7], its efficacy is not supported by most guidelines [8–12]. Even in the two guidelines that recommended routine surveillance, the optimal surveillance modalities, intervals, and starting age differ [6,7].

We report a Lynch syndrome patient with metachronous ileal cancer diagnosed by the first follow-up endoscopy after surgery for ascending colon cancer and discuss how to survey the small bowel in Lynch syndrome patients.

The work has been reported in line with the SCARE 2020 criteria [13].

2. Presentation of case

A 47-year-old man visited our hospital for a check-up for positive fecal occult blood. Computed tomography (CT) (Fig. 1a) and colonoscopy (Fig. 1b) revealed a circumferential tumor in the ascending colon, which was diagnosed as adenocarcinoma by biopsy. His father developed colon cancer at age 53 and his sister was diagnosed with endometrial cancer at age 45, as shown in the family tree (Fig. 2). His family history fulfilled the Amsterdam criteria II of Lynch syndrome. The ascending colon cancer demonstrated high-frequency microsatellite instability (MSI-H) by analysis using the Bethesda markers (Fig. 3, middle panel). Therefore, he was diagnosed with Lynch syndrome clinically according to the guidelines.
Fig. 1. a Axial image of computed tomography before the first surgery. Ascending colon cancer was indicated by an arrow. b Colonoscopy revealed a circumferential cancer of the ascending colon. c Macroscopic appearance of the ascending colon cancer (arrows).

Fig. 2. Family tree of the patient. The patient fulfilled the Amsterdam criteria II.

Fig. 3. Molecular testing for microsatellite instability. The electropherograms of the polymerase chain reaction products of five markers are shown. The results of the normal mucosa, ascending colon cancer, and ileal cancer are presented in the upper, middle, and lower panels, respectively.
for hereditary CRC [8]. Laboratory findings demonstrated that serum carcinoembryonic antigen level was elevated (11.9 ng/mL). He smoked half a pack of cigarettes per day for 27 years and drank socially.

He underwent laparoscopy-assisted right hemicolectomy with D3 lymphadenectomy [14]. After resecting the tumor-bearing specimen extracorporeally, the lumen of the remaining ileum was manually washed out using cotton balls impregnated with povidone iodine. We confirmed no particular lesion up to 4 cm proximal to the stump, and inserted an anvil of a circular stapler (ECS25A, Johnson & Johnson, New Jersey, USA) into the end. After the colonic lumen was similarly washed out, the circular stapler was inserted through the stoma to perform side-to-end anastomosis. The colonic stump was closed using a linear stapler (Endo GIA, purple, 60 mm, Medtronic, Dublin, Ireland). The resected specimen contained a 3-cm-long segment of the terminal ileum (Fig. 1c), with oral and anal margins being histologically free of cancer. The ascending colon tumor was CK7-positive and CK20-positive by histochemical study. No metastasis was found in 44 lymph nodes retrieved. The final diagnosis was moderately differentiated adenocarcinoma of T4N0M0, stage IIIB according to the UICC TNM classification [15].

Follow-up CT (Fig. 4a) and colonoscopy (Fig. 4b) detected ileal cancer just above the anastomosis the next year after the initial surgery. Biopsy of the lesion demonstrated adenocarcinoma. Serum carcinoembryonic antigen level was elevated (12.5 ng/mL). We performed laparoscopic resection of the ileal cancer together with the previous anastomosis. Four harvested lymph nodes had no metastasis. The distal edge of the tumor was located 10 mm proximal to the anastomosis in the resected specimen (Fig. 5a). The histology of the resected specimen comprised a mixture of mucinous, well differentiated, and moderately differentiated adenocarcinomas (Fig. 5b, c). The ileal tumor was CK7-positive and CK20-positive by histochemical study. In addition, we observed normal mucosa

Fig. 4. a Axial image of follow-up computed tomography. An ileal cancer was indicated by an arrow. b Follow-up colonoscopy after colon surgery revealed ileal cancer (arrows) near the anastomosis (arrowheads).

Fig. 5. a Macroscopic appearance of the resected specimen in the second surgery. The ileal cancer (arrows) did not involve the anastomosis (arrowheads). b Histological appearance of a section near the distal edge of the ileal cancer (indicated by a bar in a). The asterisk indicates the distal border of the ileal cancer and the dagger indicates the ileocolic anastomosis. The normal mucosa of the small bowel consisting of intestinal villi and prominent lymphoid follicles was observed between the ileal cancer and colonic mucosa. Hematoxylin and eosin staining, original magnification 12.5×. c Magnified appearance of the border (indicated by a dashed square in b) between the normal mucosa and ileal cancer. Hematoxylin and eosin staining, original magnification 40×.
of the small bowel, consisting of intestinal villi and prominent lymphoid follicles between the ileal cancer and initial anastomosis (Fig. 3b). Therefore, the tumor was considered primary ileal cancer of T4N0M0, stage IIB according to the UICC TNM classification [15]. The ileal cancer also exhibited MSI-H (Fig. 3, lower panel), but its patterns of replication errors in the Bethesda panel differed from those of the ascending colon cancer (Fig. 3, middle panel).

The patient was followed basically by serum carcinoembryonic antigen level every three months, CT every six months, and annual ileocolonoscopy. Currently, he is free from recurrent disease for five years after the second surgical treatment.

3. Discussion

Lynch syndrome is characterized by an increased risk of cancers in multiple organs [6,7]. More than 60% of small bowel cancer in Lynch syndrome had synchronous or metachronous CRC [16]. The present Lynch syndrome patient developed metachronous ileal cancer shortly after surgery for ascending colon cancer.

Surveillance by colonoscopy in patients with Lynch syndrome reduces the mortality of CRC [17]. Several guidelines recommend that Lynch syndrome patients be followed up using colonoscopy every one to two years after colectomy [8–12]. As for small bowel cancer, routine surveillance is not recommended because of a high rate of false-positive findings and its low cost effectiveness in many guidelines [8–12]. On the other hand, the European Consortium “Care for CMMR-D” proposed annual video capsule endoscopy for the small bowel for patients with constitutional mismatch repair-deficiency from the age of 10 years [6]. The guidelines by a group of European experts (the Mallorca group) uniquely suggest inspection of the distal duodenum during upper gastrointestinal endoscopy and the ileum during colonoscopy, as small bowel cancer is frequently located in these segments [7]. Indeed, metachronous ileal cancer of stage IIB was diagnosed by the first follow-up colonoscopy after surgery for ascending colon cancer in our patient. He has been disease-free for five years after the second surgery.

A high percentage of patients with small bowel cancer were diagnosed at advanced stages due to non-specific abdominal symptoms such as dull or cramping pain, distention, and obstruction [16,18]. Jun et al. reported that the frequency of pT4 small bowel cancer was 59% for sporadic cases and 50% for Lynch syndrome [16]. Regarding the prognosis, the 5-year overall survival (OS) rate was reportedly 14–33% for all small bowel cancer patients in a review by Aparicio et al. [4]. On the other hand, the guidelines proposed by the Mallorca group stated that Lynch syndrome patients with small bowel cancer had a 5-year OS rate of 30–35% [7]. Therefore, small bowel cancer has a poor prognosis independently of Lynch syndrome [16]. Previous studies reported several prognostic factors for small bowel adenocarcinoma, including old age, pT4, poor differentiation, lymph node metastasis, and distant metastasis [4,19]. However, lymph node metastasis is considered the main prognostic factor after R0 resection of localized cancer [20]. Consistently, the ileal cancer did not metastasize to regional lymph nodes in our long-surviving patient.

4. Conclusion

We presented a Lynch syndrome patient who developed primary colon and ileal cancers within a short period. In colon cancer patients with Lynch syndrome, the small bowel should be carefully examined during surgery. This case supports the recommendation that the ileum in addition to the anastomosis be checked during colonoscopy.

Declaration of Competing Interest

The authors report no declarations of interest.

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Ethical approval

Our institution does not require ethics approval for case reports.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author contribution

Yuichi Tachikawa, Hiroaki Nozawa, Keisuke Hata and Soichiro Ishihara performed the operation. Hiroaki Nozawa and Keisuke Hata made substantial contributions to conception and design. Keisuke Hata performed the MSI analysis. Hiroyuki Abe and Tet-suo Ushiku made the pathological diagnoses. Yuichi Tachikawa has made the draft of this manuscript and Hiroaki Nozawa and Soichiro Ishihara substantively revised it by critical reading. All authors read and approved the final manuscript.

Registration of research studies

This is not a 'First in Man' study, and thus we did not register this case report.

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