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CASE REPORT

Repeatedly Recurrent Colon Cancer Involving the Appendiceal Orifice after Endoscopic Piecemeal Mucosal Resection: A Case Report

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Local recurrence after endoscopic piecemeal mucosal resection (EPMR) for colorectal tumors is a crucial issue. However, such recurrence is usually detected within one year and cured with additional endoscopic treatment, which makes EPMR acceptable. Herein, we report a rare case of repeatedly recurrent colon cancer involving the appendiceal orifice after EPMR, which was not cured with additional endoscopic treatments. A 67-year-old man was referred to us for endoscopic treatment of a 25 mm cecal tumor spreading to the appendiceal orifice in May 2002. The tumor was resected with EPMR, showing well differentiated intramucosal adenocarcinoma with a positive lateral cut margin of tubular adenoma. Endoscopic surveillance was conducted and the first local recurrence was detected in August 2006. Although we resected it endoscopically, the second local recurrence was found in September 2007 and we removed it with endoscopic resection again. However, the third local recurrence was detected in March 2008. Although endoscopic resection was performed also for the third recurrence, curative resection was not achieved. In February 2009, laparoscopic assisted colectomy was performed and histopathological examination showed well differentiated adenocarcinoma with deep submucosal invasion. This case is important in considering indication for endoscopic resection in colorectal tumors involving the appendiceal orifice. **(Korean J Gastroenterol 2013;61:286-289)**

Key Words: Appendiceal orifice; Endoscopic piecemeal mucosal resection; Endoscopic submucosal dissection; Laparoscopic assisted colectomy; Local recurrence

INTRODUCTION

Endoscopic piecemeal mucosal resection (EPMR) is widely performed for colorectal tumors, but the high frequency of local recurrence is a serious problem. The local recurrence rate after EPMR has been reported to be 10-23%,[1-4] much higher than that seen with endoscopic submucosal dissection (ESD) (0-3%).[5-8] However, previous studies have also reported that most cases of such recurrence can be detected within one year and cured with additional endoscopic treatment,[9] which makes EPMR acceptable. Herein, we report a rare case of repeatedly recurrent colon cancer involving the appendiceal orifice after EPMR, which could not be completely removed with additional endoscopic treatments.

CASE REPORT

The patient was a 67-year-old man. His medical history included appendicitis, treated with surgery. In May 2002, he was referred to our hospital (National Cancer Center Hospital, Tokyo, Japan) for endoscopic treatment of a cecal tumor. He had undergone total colonoscopy for a health check-up in a previous hospital one month before, which revealed a 0-Is tumor, 25 mm in size, spreading to the appendiceal orifice (Fig. 1A). Magnifying chromoendoscopy disclosed a non-invasive pattern (Fig. 1B).[10] We diagnosed the lesion as an in-

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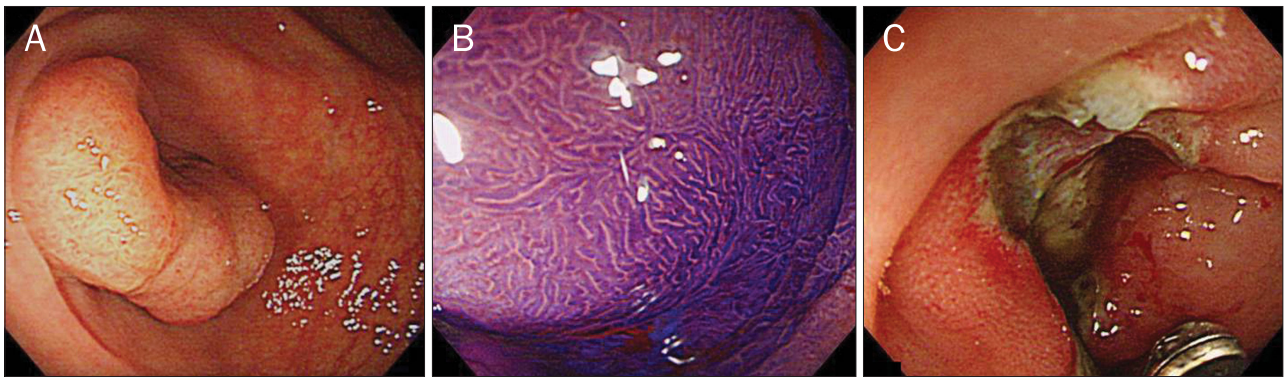

Fig. 1. (A) Conventional colonoscopy finding. A 25 mm cecal sessile tumor spreading to the appendiceal orifice was revealed. (B) Magnifying chromoendoscopy with crystal violet staining. A non-invasive pattern was disclosed. (C) Endoscopic finding after endoscopic piecemeal resection of the tumor showing macroscopically no residual tumor.

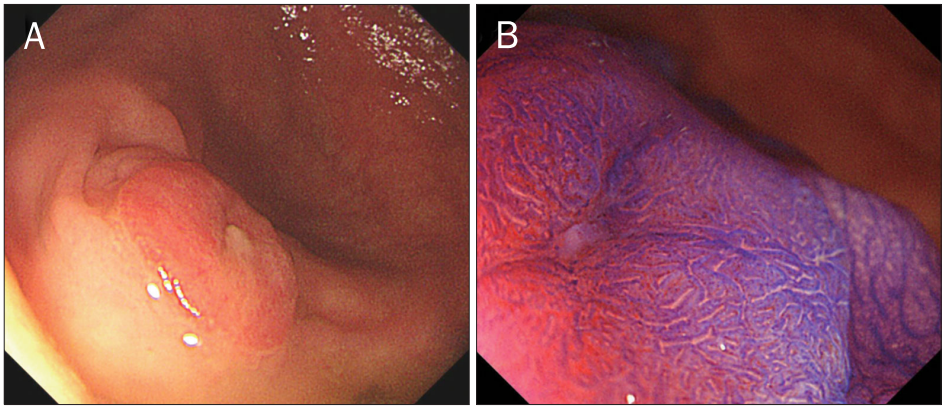

Fig. 2. (A) Follow-up colonoscopy finding. The third recurrent tumor, 10 mm in size, was detected at the site of the initial endoscopic piecemeal mucosal resection. (B) Magnifying chromoendoscopy with crystal violet staining. A non-invasive pattern was shown.

tramucosal or submucosal superficial (less than 1,000 μm from the muscularis mucosae) cancer, and tried to remove this lesion with *en bloc* endoscopic mucosal resection (EMR). However, the lesion was eventually removed with EPMR (2 pieces). Histopathological examination showed well differentiated intramucosal adenocarcinoma with a tubular adenoma component without lymphovascular invasion. Although no residual tumor was observed macroscopically in the post-EPMR ulcer site (Fig. 1C), and we presumed that endoscopic complete resection of the tumor was successful, the positive lateral cut margin of tubular adenoma was histopathologically revealed. Therefore, we conducted follow-up colonoscopies and took biopsies from the post-EPMR site 3 and 9 months after the initial treatment, which endoscopically and histopathologically revealed neither residual nor recurrent tumor. After that, endoscopic surveillance was continued at another hospital, and in August 2006, the first recurrent tumor, 0-IIa, 10 mm in size, was detected at the site of the initial EPMR. He was referred to our hospital again, and *en bloc* resection of the tumor with ESD was tried. However, *en bloc* resection was not achieved with ESD and hot biopsy was additionally performed. The tumor, histopathologically determined to be tubular adenoma showing low and high grade atypia, was detected both in the ESD and hot biopsy specimens, and a positive lateral cut margin and a negative vertical cut margin were revealed. No residual tumor was macroscopically seen after the endoscopic procedures and we considered that endoscopic resection of the tumor was successful, but histopathological evaluation showed a positive lateral cut margin and thus follow-up with close observation was continued. Three months after that, follow-up colonoscopy with biopsies from the post-treatment site did not show any findings of recurrence, but in September 2007, the second recurrent tumor, 0-IIa, 10 mm in size, was found. *En bloc* EMR was successfully performed, and histopathological examination showed well differentiated intramucosal adenocarcinoma without lymphovascular invasion. Although the positive lateral cut margin of an adenocarcinoma compo-

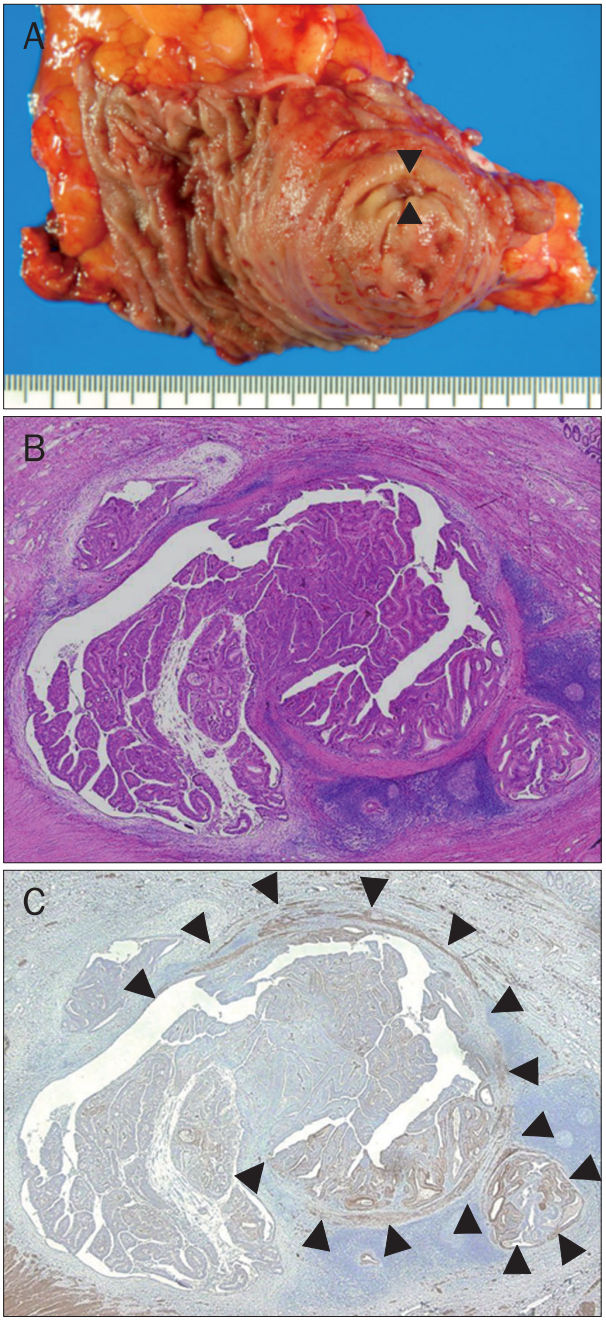

Fig. 3. (A) The surgically resected specimen. The recurrent tumor was seen in the appendiceal orifice (arrowheads). (B) Histopathological examination of surgically resected specimen. Well differentiated adenocarcinoma in the cecum and the appendix was revealed (H&E, ×40). (C) The assessment of muscularis mucosae with desmin staining (arrowheads). The disruption of the muscularis mucosae and the submucosal invasion of the tumor were demonstrated (Desmin staining, ×40).

nent was histopathologically revealed, the positivity was not extensive and close observation expecting a burn effect of the EMR was conducted. The third local recurrence, a 0-IIa tumor, 10 mm in size, was detected during the close follow-up with colonoscopy in March 2008 (Fig. 2A). Upon considering the clinical course of repeated recurrences after endoscopic resections, we proposed laparoscopic assisted colectomy (LAC), but the patient refused LAC at that time. After making sure that magnifying chromoendoscopy showed a non-invasive pattern[10] in the recurrent tumor (Fig. 2B) and that there was no mass in the cecum on computed tomography, endoscopic treatment was chosen again. *En bloc* resection was tried with ESD, but not achieved and additional hot biopsy was required. With these procedures, endoscopic resection macroscopically seemed successful, but histopathological findings of resected specimens including the hot biopsy specimen showed well differentiated intramucosal adenocarcinoma with a positive lateral cut margin. Because of the possibility of residual cecal cancer in the mucosa and/or submucosa, in February 2009, LAC was performed. According to guidelines for the treatment of colorectal cancer by Japanese Society for Cancer of the Colon and Rectum, ileocecal resection with D2 lymph node dissection was selected as an operative method. In the resected specimen, the recurrent tumor, 5 mm in size, was located in the appendiceal orifice (Fig. 3A). Histopathological examination revealed a well differentiated adenocarcinoma with deep submucosal invasion (Fig. 3B, C). Lymphovascular invasion and lymph node metastasis were not detected. After surgery, no recurrence has been detected for 40 months as of June 2012.

DISCUSSION

This is a case of recurrence after EPMR and is different from usual recurrent cases after EPMR in the following points: 1) it was a late recurrence detected 4 years after EPMR, and 2) could not be eliminated with repeated endoscopic treatments including ESD, necessitating LAC.[9] We speculate that this unusual clinical course was closely associated with the tumor location and the partially remaining appendix even after the appendectomy. The tumor spread to the appendiceal orifice, where endoscopic complete resection was difficult. The minute residual tumors after the endoscopic resections presumably invaded the submucosal layer in the remaining appendix.

Appropriate surveillance after EPMR and treatment for recurrent or residual tumors after endoscopic resection has

not yet been determined. In this situation, the present case is important in making us realize the following things: 1) recurrent or residual tumors involving the appendiceal orifice are difficult to cure completely with endoscopic resection even after appendectomy, and therefore LAC should be taken into account; and 2) such tumors may occur late, more than 1 year after EPMR, and longer surveillance may be necessary.

In addition, it is noteworthy that local recurrence occurred even after making sure that no residual was macroscopically seen in the post-EPMR site and biopsies from the post-EPMR scar performed in the follow-up colonoscopies were negative in this case. Previously, it was reported that after EPMR of large sessile adenomas, a normal macroscopic appearance of the EPMR site and negative scar biopsy specimens at the first follow-up are good predictors of long-term tumor eradication.[11] In this case, however, they were not predictive of the tumor eradication. This fact also may have been related with the tumor location.

Finally, we mention the initial treatment for a tumor involving the appendiceal orifice. Considering the risk of minute residual tumors after incomplete endoscopic resection as shown in this case, a treatment strategy enabling *en bloc* complete resection is necessary. Now that ESD for colorectal tumors has been widely accepted,[4-8] ESD can be one treatment option. However, *en bloc* complete resection for a tumor involving the appendiceal orifice with ESD is technically difficult and has a high risk of perforation. When ESD is considered unsafe and difficult, LAC should be chosen from the beginning.

In summary, we experienced a rare case of repeatedly recurrent colon cancer involving the appendiceal orifice after EPMR. This case is important in considering indication for endoscopic resection in colorectal tumors involving the appendiceal orifice and also informative about appropriate surveillance after EPMR and treatment for recurrent or residual tumors after endoscopic resection.

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