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Single Case

Early Colon Cancer Recurring as Liver Metastasis without Local Recurrence Three Years after Complete Endoscopic Mucosal Resection

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Keywords

Colorectal cancer · Early colon cancer · Endoscopic mucosal resection · Recurrence

Abstract

Early colon cancer is defined as colon cancer that invades mucosal or submucosal layer regardless of lymph node invasion. Endoscopic mucosal resection can effectively remove early colon cancer which has no lymph node metastasis. Especially, pedunculated polyp has higher complete resection rate and lower recurrence rate that rarely needs additional surgical treatment than sessile polyp. Hence, it is common to follow up without additional treatment after complete resection of pedunculated polyp. We report a case of early colon cancer recurring as liver metastasis 3 years after complete endoscopic mucosal resection.

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Introduction

Colorectal cancer (CRC) is the third most common cancer in men and the second most common cancer in women. In 2018, there were over 1.8 million new cases of CRC [1]. CRC has been recognized as a more common malignant tumor in industrialized western countries than that in eastern countries. However, the incidence of CRC has been increasing rapidly in Asian countries with progression of industrialization [2]. In South Korea, the incidence of CRC seems to increase drastically due to obesity and western pattern diet [3]. In 2018, Hungary had the highest incidence of CRC followed by South Korea [1].

Hence, early detection and treatment of CRC are important. Since 2004, screening for CRC has been included in the National Cancer Screening Program (NCSP) in South Korea. With generalization of screening endoscopy and the development of endoscopic devices and techniques, early CRC and precancerous lesions that can be treated only by endoscopy are rising.

Early colon cancer (ECC) is defined as colon cancer that invades within mucosa or submucosal layer regardless of lymph node invasion [4]. The goal of ECC treatment is to remove cancer cells as completely as possible from the patient. Endoscopic resection can effectively remove ECC which has no lymph node metastasis. After endoscopic resection, a complete cure can be expected through careful histological examination. Moreover, pedunculated polyp has a higher complete resection rate and lower recurrence rate than sessile polyp. Thus, pedunculated polyp rarely needs additional surgical treatment [5].

We report a case of ECC recurring as liver metastasis at 3 years after complete endoscopic mucosal resection (EMR). This patient had a malignant pedunculated colon polyp that was limited to within a head of the polyp without stalk invasion or lymphovascular invasion. However, 3 years later, a small metastatic lesion was found in the liver, and surgical resection was done. It was pathologically confirmed as metastasis of the ECC that was removed 3 years ago.

Case Report

A 47-year-old man visited our hospital because of colorectal polyps that were accidentally found on screening colonoscopy. There was no family history of the disease. Upon admission, vital signs were as follows: blood pressure, 126/82 mm Hg; pulse rate, 70 beats/min; respiratory rate, 20 beats/min; and body temperature, 36.5°C. Physical examination was normal. He was taking high blood pressure medications.

He had normal blood test results: white blood cell count, 6,890/ μ L (59.4% neutrophils); hemoglobin, 16.7 g/dL; and platelet, 232×10^3 μ L. He had mild elevations in levels of liver enzymes: aspartate transaminase, 58 U/L; alanine transaminase, 60 U/L; and total bilirubin, 1.15 mg/dL. An electrocardiogram showed atrial fibrillation with controlled ventricular response. He was unaware of atrial fibrillation and was referred to Cardiology Department. The chest X-ray was normal.

He underwent colonoscopy for EMR. A 20-mm-sized pedunculated polyp that was situated as far as 14 cm from the anal verge and a 5-mm-sized sessile polyp situated 8 cm far from anal verge were found. The endoscopist performed EMR for the 20-mm sized polyp (Fig. 1). The 5-mm-sized sessile polyp was removed by biopsy forceps. After the procedure, the patient was discharged without any complication.

On histologic examination, the 5-mm-sized sessile polyp showed tubular adenoma with low-grade dysplasia and the 20-mm-sized pedunculated polyp showed well-differentiated adenocarcinoma. Adenocarcinoma was partially present in the entire pedunculated polyp. It

invaded into the submucosa of the head, although stalk invasion was not visible. Hence, the adenocarcinoma was diagnosed as Haggitt level 1. The resection margin was clear. Lymphovascular invasion was not identified (Fig. 2a, b). Abdominal computed tomography (CT) was normal. There was no evidence of hypermetabolic local recurrence or distant metastasis in positron emission tomography-CT (PET-CT).

The patient underwent follow-up colonoscopy and abdominal CT every single year. There was no evidence of recurrence within 2 years after EMR. However, abdominal CT performed at 3 years after EMR showed a newly appeared 1.2-cm-sized mass on liver segment VIII (Fig. 3a).

Tumor marker results were alpha-fetoprotein 2.6 ng/mL and carcinoembryonic antigen 2.4 ng/mL. Liver MRI and PET-CT were performed to differentiate malignancy from benign mass. On PET-CT, there was no evidence of malignancy. However, liver MRI (Fig. 3b) showed high suspicion of malignancy. Liver biopsy was performed. No malignant tissue was found on histological examination. Nevertheless, we decided to perform surgery due to possibility of metastasis on liver MRI.

The patient underwent laparoscopic right hepatectomy. The tumor was located in segment VIII. There was no lymph node or vascular invasion. On histologic examination, the tumor was pathologically consistent with tissue of the pedunculated colon polyp removed 3 years ago (Fig. 2c). After chemotherapy, the patient is continuously receiving outpatient follow-up care.

Discussion

Recently, due to development of diagnostic technology with public interest in cancer and generalization of health screening, the proportion of ECC among CRC is gradually increasing [4]. Moreover, it is important to know indications for endoscopic resection because many ECC are resected by endoscopy. In the Japanese Society for Cancer of the Colon and Rectum (JSCCR) Guidelines for treatment of CRC, the indication for endoscopic resection was as follows [6]: (1) Intramucosal carcinoma or carcinoma with slight submucosal invasion; (2) Size does not matter; (3) Any macroscopic type. According to JSCCR, it was recommended to remove our patient's polyp by endoscopic resection.

In ECC, intramucosal carcinoma does not metastasize. Hence, if the lesion was resected completely by endoscopic resection, treatment is terminated. However, lymph node metastasis occurs in approximately 10% of cases of submucosal invasion of ECC [7, 8]. Careful examination of pathologic features of resected tissues can be used to more accurately estimate the likelihood of lymph node metastasis. It is very useful in determining whether additional surgical treatment is necessary. A recent systematic review and meta-analysis has been performed on histological factors influencing the risk of lymph node metastasis in ECC [9]. It has been concluded that a depth of submucosal invasion of more than 1 mm in the submucosa, the presence of lymphovascular invasion and tumor budding [10], and poorly differentiated cancer are significantly associated with lymph node metastasis.

Among these factors, JSCCR differently defined the criteria for the depth of invasion according to the presence of stalk [6]. In cases of sessile polyp, depth of submucosal invasion is measured from the lower border of the muscularis mucosae. When it is not possible to identify the location of the muscularis mucosae, depth of submucosal invasion is measured on the virtual line of the muscularis mucosae. However, for pedunculated polyp cases, depth of submucosal invasion is measured as the distance between the point of deepest invasion and the

baseline that is defined as the boundary between the tumor head and the stalk. Among them, an invasion confined to within head was defined as “head invasion” [6]. This case was also a “head invasion.” It could be called Haggitt level 1.

Haggitt et al. [11] have introduced a classification system for pedunculated polyps with levels of invasion ranging from 0 to 4. Level 0 indicates carcinoma confined to the mucosa. Level 1 is strictly limited to the head of the polyp. Invasion of the carcinoma into the neck of the polyp is level 2 invasion. Carcinoma invading the stalk of the polyp is considered as level 3 lesion. Level 4 is limited to the submucosa. The frequency of lymph node metastases increases with level 4 [11].

Kitajima et al. [12] have found that lymph node metastasis is 0% in case of invasion limited to within head and in stalk invasion cases when submucosal depth is less than 3,000 μm . In other words, malignant pedunculated colon polyps up to Haggitt level 2 have little possibility of lymph node metastasis.

A retrospective cohort study of 384 patients with pedunculated type of ECC has shown possibility of lymph node metastasis in stalk invasion [13]. Among 230 patients who underwent surgical resection, 101 patients had head invasion and 129 patients had stalk invasion. The incidence of metastasis to the lymph nodes was 0% (0/101) for lesions with head invasion and 6.2% (8/129) for stalk invasion. Thus, the probability of lymph node metastasis for head invasion was 0% in that study.

On the other hand, Kimura et al. [14] have stated that “head invasion” itself is not a metastasis-free condition. Of 76 patients who had a malignant pedunculated colorectal polyp, lymph node metastasis rate was 13.3% (4/30) for head invasion and 10.9% (5/46) for stalk invasion. There was no statistically significant difference in lymph node metastasis rate between head invasion and stalk invasion. Importantly, patients who had head invasion with lymph node metastasis had one or more of the following: lymphovascular infiltration, tumor budding, or a poor/moderately differentiated adenocarcinoma [15]. Therefore, metastasis occurring in a patient with head invasion without these factors is very rare.

In the present case, the patient’s polyp was confirmed as a well-differentiated adenocarcinoma invaded into the submucosa of the head (Haggitt level 1). The resection margin was clear. Lymphovascular invasion and tumor budding were not identified. Unlike the study of Kimura et al. [14], in the present case, invasion of the lesion was limited to within head without other histologic factors. However, this patient recurred as liver metastasis 3 years later without local recurrence.

It is regrettable that we did not perform additional surgical treatment after EMR. However, it is not easy to determine additional surgical treatment because it is not recommended in the guidelines. Also, the physician had to consider whether there were overtreatment and risk of complications from unnecessary surgical procedures. This single case cannot be said to be a problem with current guidelines. However, if additional cases similar to this case are reported, the current guidelines may be affected, and further studies may be needed.

Statement of Ethics

The authors have no ethical conflicts to disclose.

Disclosure Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Min Ho Jeon and Seok Bae Kim were involved in the literature review and creation of the manuscript. Sung Wook Jang was involved with editing the manuscript. Chang Min Lee was involved in the conception of the work.

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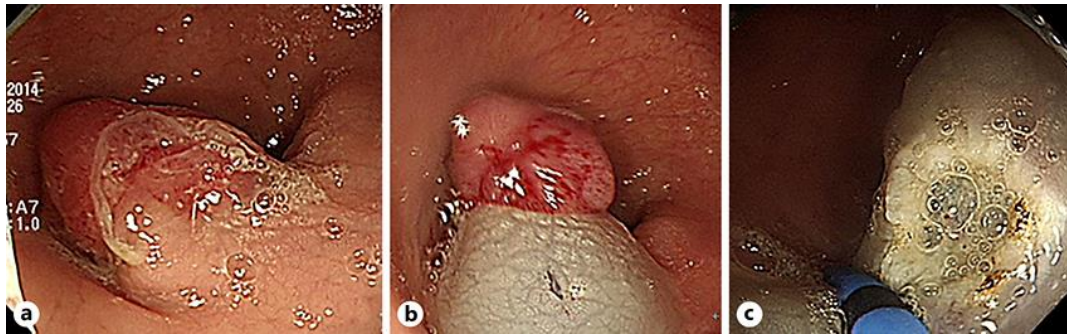


Fig. 1. Endoscopic findings. **a** A 20-mm-sized pedunculated polyp. **b** After injection of highly concentrated saline and epinephrine into the submucosal layer to make the area containing the lesion swollen. **c** The mucosa was lifted with forceps, strangulated by a snare, and then resected by electrocauterization.



Fig. 2. HE-stained tissue of the resected pedunculated polyp's head (**a**) and stalk (**b**). **a, b** Well-differentiated adenocarcinoma arising in tubulovillous adenoma invaded into the submucosa of only head, but not stalk. The tissue had a clear resection margin. Lymphovascular invasion or tumor budding was not identified. **c** HE-stained tissue of the resected liver. $\times 200$ magnification. Adenocarcinoma with mucinous change was consistent with the metastatic adenocarcinoma removed 3 years ago.

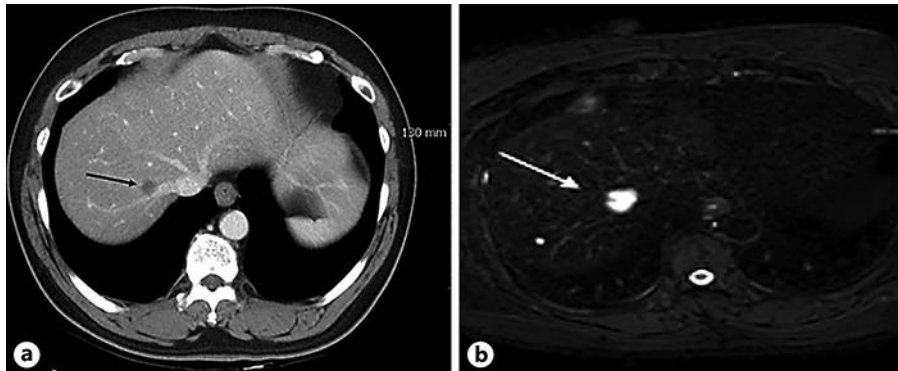


Fig. 3. Radiologic findings. **a** Abdominal CT findings. A newly appeared 1.2-cm-sized mass on liver S8 (black arrow) abutting right hepatic vein showed low attenuation with surrounding transient hyperemia. **b** MRI findings. On T2-weighted image, the mass had central bright high signal intensity but slightly peripheral intermediate signal intensity (white arrow).