Early Stage of Colonic Adenocarcinoma Associated with Traditional Serrated Adenoma

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Abstract

We describe a 68-year-old woman diagnosed as having a colonic adenocarcinoma associated with traditional serrated adenoma (SA) with submucosal invasion of the sigmoid colon. Colonoscopy revealed a 0-IIa+IIc colon cancer with a SA component, about 12 mm in diameter, in the sigmoid colon. She underwent laparoscopy-assisted resection of the sigmoid colon. In the resected specimen, colon cancer with mucin pools was adjacent to the SA. Cases of colonic adenocarcinoma associated with traditional SA with submucosal invasion are relatively rare. This case suggests that SA may play a role in the development of colorectal cancer.

Key words: serrated adenoma-carcinoma sequence, serrated pathway, colonoscopy, sigmoid colon cancer, laparoscopy-assisted sigmoidectomy

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Introduction

Serrated adenoma (SA) is a morphological subtype of colorectal adenoma, as proposed by Longacre and Fenoglio-Preiser in 1990 (1). It combines the histological features of hyperplastic and adenomatous epithelium, showing serrated glandular structure reminiscent of hyperplastic polyps (HP) and neoplastic cytological features. It has malignant potential (1) and is thought to play a role in the development of colorectal cancer (CRC) (2-4). In Japan, most reported cases of carcinoma in SA (Ca in SA) were mucosal cancers (5-7). Herein we report a relatively rare case of colonic adenocarcinoma associated with traditional SA with submucosal invasion.

Case Report

The patient was a 68-year-old woman, 148 cm tall and weighing 49.0 kg. She visited our hospital for the further evaluation of fecal occult blood in a yearly physical checkup. She had been in good health and no specific family, past medical, or drug history was identified. Her body temperature was 36.8°C, blood pressure was 104/66 mmHg, and radial pulse rate was 72 beats/min and regular. She had neither anemia nor jaundice. A neurological examination revealed no abnormal findings and there was no lymphadenopathy. Physical examinations revealed no abnormalities. Routine hematological examination and biochemical tests were within normal limits. Serological studies for hepatitis B and C viruses were negative and some tumor markers such as carcinoembryonic antigen and carbohydrate antigen 19-9 were also negative.

A colonoscopic examination revealed a 0-IIa+IIc lesion with mucosal convergence, about 12 mm in diameter in the sigmoid colon (Fig. 1A). Endoscopic findings of the end of the lesion showed a pinecone-like part with branch-like pits and the center of the lesion revealed a red amorphous area with irregular branched capillaries (Fig. 1B). Thus, this lesion was thought to have both benign and malignant components. Histological examination of the biopsy specimens obtained from the center of the lesion revealed moderately differentiated adenocarcinoma. The biopsy specimen obtained from the end of the lesion was diagnosed with SA. Examination by computed tomography (CT) revealed no abnormalities in the abdomen. The patient underwent laparoscopy-assisted resection of the sigmoid colon with regional lymph node dissection.

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The resected tumor with central depression, 11×10 mm in size, was hard. The SA component was seen in one slice of resected specimens cut into 3 mm slices (Fig. 2). The colon cancer with submucosal invasion was seen in the remained 2 slices (Fig. 2). The malignant tumor cells involved lamina propria to the deep submucosa, just short of the muscularis propria (Fig. 3A) with mucin pools (Fig. 3B). Histological examination of the resected tumor identified moderately differentiated adenocarcinoma with the presence of mucin. The end of the lesion revealed histological findings of branching of the serrated glands, thus this lesion was diagnosed with SA (Fig. 4). The SA component was assumed to account for 10-20% of this tumor on the basis of superficial area and endoscopic findings because the SA component was seen in only one slice in the resected specimen. Immunohistological studies were carried out on the resected specimen, and the cancerous lesion showed a negative immunohistochemical reaction for MUC5AC, MUC2 and CD10. The lesion with SA showed a positive immunohistochemical reaction for MUC5AC but it was negative for MUC2 and CD10. The resected tumor was diagnosed as colonic adenocarcinoma as-
associated with traditional SA with submucosal invasion of the sigmoid colon. Lymph node metastasis was not seen in resected regional lymph nodes. The postoperative course was uneventful. She has been under close periodic observation, and there has been no evidence of disease for 40 months after surgery.

Discussion

SAs are characterized by serrated glandular patterns similar to those seen in hyperplastic polyps (1, 8). Recent molecular investigations have demonstrated that the genetic background of SA may differ from that of traditional adenoma. Hiyama et al (9) claimed that mutation of the p53 gene was the most characteristic genetic alteration in SAs, a relatively early event in the multistep carcinogenic pathway of SA, because they confirmed that 9 of 19 (47%) SAs and 5 of 10 (50%) adenocarcinomas in/with SAs harboured p53 gene mutations. In SA, APC and K-ras mutations were reported to be infrequent, while microsatellite instability (MSI) was observed more frequently than in traditional colorectal adenoma (10).

Yao et al supposed that CRCs originating from SA account for 2.5-5% of all Japanese CRCs (11). SAs are potentially malignant lesions reported to comprise 3.3-20% of colonoscopic examinations and in endoscopic mucosal resection (EMR) specimens; they are predominant in man and distal colon (14). On the other hand, Mäkinen et al (15) proposed the clinical entity of serrated carcinoma (SC) that included CRCs with serrated adenoma and CRCs with serrated structure (4). SC is a recently described, distinct variant of colorectal cancer, accounting for about 7.5% of all CRCs and up to 17.5% of most proximal colon cancers (4, 15), although almost SC are advanced cancer. There is frequent MSI in SCs (11). Histological characteristics of SC were as follows: 1) a serrated structure of carcinomatous glands, 2) infiltrative growth, 3) presence of mucin pools, 4) tendency to de-differentiate at the invasive front, 5) rare necrotic foci, and 6) tendency to express a gastric phenotype (11). O’Brien et al also reported that invasive carcinomas arisen from SA had a tendency of frequent possession of mucinous component (16). In the report described by Yao et al (11), all 12 of their Japanese patients (15 lesions) with SC were advanced cancer, with 73.3% having lesions in the proximal colon, and the man to woman ratio was 4:8 (predominant in women). There is a discrepancy in the clinical characteristics between Ca in SA and SC.

Colorectal serrated polyps form a group of related lesions that include aberrant crypt foci (ACF), conventional hyperplastic polyps, mixed (admixed) polyps, serrated adenomas and sessile serrated adenomas/polyps (SSA/SSPs) (15, 16). SSA/SSP reveals the histological findings of glandular branching, asymmetrical proliferation zone, and mitoses in the upper portions of the crypts, which reflect the abnormal proliferation (17). SSA/SSPs are flat lesions predominant in the proximal colon with a tendency of rapid progression, and are thought to be precursors of the SCs (14). Thus, it is speculated that there are differences in the genesis between SC and Ca in SA.

In the present case, the cancer did not fulfill the following pathological characteristics of SC: 1) a serrated structure of carcinomatous glands, 2) infiltrative growth and 3) tendency to de-differentiate at the invasive front. Thus, we speculated that the present case showed histological findings of colonic cancer associated with traditional SA with submucosal invasion. Although there is no direct evidence at present, the present case may indicate that SA is involved in the etiology of cancer, because cancer was adjacent to SA and revealed the histological finding of mucin pools.

Yamauchi et al (18) reported a case of SA developing to advanced colon cancer in 2 years, but in their report, the resected tumor was replaced with poorly differentiated adenocarcinoma and included no adenomatous component, thus their case was thought to be SA developing to SC without an adenomatous component. If the tumor is replaced with carcinoma and includes no adenomatous component as in their case, it cannot be judged whether or not CRC originated from SA. We should analyze cases of adenocarcinoma associated with SA component as in the present case to clarify the tumor growth mechanism and malignancy of CRC originating from SA. Thus, it is important to observe CRCs carefully by endoscopy whether SA component is coexisting or not.

We should be aware that SA may develop to CRC, and there are several kinds of pathways from SA to CRC. To clarify the pathogenesis and tumor growth mechanism of CRC originating from SA, we should practice the following: 1) to locate the SSA/SSP in the colon and follow-up with careful observation in the colonoscopic examination, and 2) accumulation and analysis of many cases of early CRCs associated with SA.

In conclusion, we reported a case of colonic adenocarcinoma associated with traditional SA with submucosal invasion of the sigmoid colon. This case suggests that SA may play a role in the development of CRC. Further studies of CRC originating from SA and genetic analysis of the SA-carcinoma sequence are certainly required in the future.

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