

Superficial Depressed Type (IIC) Early Cancer of the Colon : Report of Two Cases

Michiko IWAMOTO¹⁾, Kazuya MAKIYAMA²⁾, Fuminao TAKESHIMA²⁾, Yohei MIZUTA¹⁾, Katsuhisa OMAGARI¹⁾, Masaki YAMAKAWA³⁾, Ikuo MURATA⁴⁾, Shiro FUNATSU⁵⁾, Masuho HARAGUCHI⁶⁾, Minoru ITSUNO⁷⁾, Masumi IFUKU⁸⁾, Hidehiko FUKUDA⁸⁾, Shigeru KOHNO¹⁾

1) Second Department of Internal Medicine, Nagasaki University

2) Department of Endoscopy, Nagasaki University

3) Nagasaki Prefectural Shimabara Onsen Hospital

4) Third Department of Internal Medicine, University of Occupational and Environmental Health

5) Goto Central Hospital

6) Sasebo Municipal General Hospital

7) Itsuno Internal Medicine Clinic

8) Fukuda Internal Medicine Clinic

Two cases of superficial depressed type (IIC) early cancer of the colon are reported. Case 1 was a 65-year-old male and case 2 a 69-year old male. The lesion was located in the descending colon in both cases, and was removed by strip biopsy endoscopically in the former and surgically in the latter. The size of the lesion after resection was 6 mm in case 1 and 5 mm in case 2. Histopathologically, both cases were well differentiated adenocarcinoma without adenomatous components, and carcinoma developed de novo by submucosal (sm) invasion. As to the immunohistochemical staining of the cancer tissue by tumor associated antigen, case 1 showed a strong expression of carcinoembryonic antigen (CEA) and partial expression of sialyl Lewisx, and case 2 showed expressions of both CEA and sialyl Lewisx. The nuclear DNA content by flow cytometry was aneuploid only in case 1. Thus, although the two cases were morphologically the same IIC type cancer, the process of carcinogenesis and secondary phenomena varied.

Key words : IIC type early colorectal carcinoma, Tumor associated antigen, Nuclear DNA content

Introduction

The occurrence of colorectal carcinoma is generally thought to be subsequent to adenoma adenoma-carcinoma sequence theory^{1,2)}. This theory has been proposed and supported since most adenomas and early cancers are morphologically polypoid, develop to focal carcinoma as they grow, and the area shared with adenomatous components diminishes at the stage of submucosal invasion carcinoma (sm cancer). Consequently, depressed type adenomas and early cancers were infrequently observed. Recently, however, superficial depressed type (IIC type)

lesions are being found more frequently^{3,6)}, and serve as a basis for the so-called de novo carcinogenesis theory⁷⁻¹⁰⁾. Thus, the process of morphological development from early cancer to advanced cancer is being clarified. Thorough analysis of the pathophysiology of IIC type colorectal early cancer is required in order to elucidate the progress of colorectal carcinoma from the histological occurrence to growth and advancement.

The authors experienced two cases of IIC type colorectal early cancer, and stained the cancer tissue immunohistochemically using carcinoembryonic antigen (CEA) antibody and CSLEA1 monoclonal antibody to identify sialyl Lewisx, and CSLEX1 monoclonal antibody to identify sialyl Lewisx, and also performed the flow cytometric analysis of nuclear DNA content.

Cases

Case 1. 65-year old male

The patient had a history of upper lobectomy of the right lung for pulmonary tuberculosis at age 38. He underwent cholecystectomy for gallstone in August 1989, and subsequently received treatment for pulmonary hypofunction and prostatic hypertrophy at the outpatient clinic. On January 29, 1990, he was admitted for influenza-like symptoms and jaundice due to inflammation of the bile duct. At admission, he complained of frequent bloody stool. Barium enema demonstrated findings suggestive of polypoid lesions in the sigmoid colon, and fiberoptic examination of the large intestine was performed. Hematological and biochemical examinations revealed

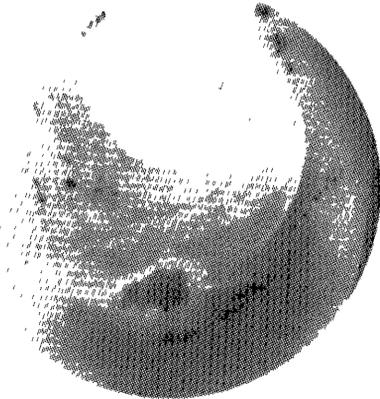


Fig. 1. Colonoscopic picture of the IIC type lesion in Case 1. It was a depressed lesion of approximately 10 mm in size located in the descending colon. The depressed portion was covered with whitish exudate, and the periphery was somewhat protruded and reddened, showing a typical morphology of IIC type.

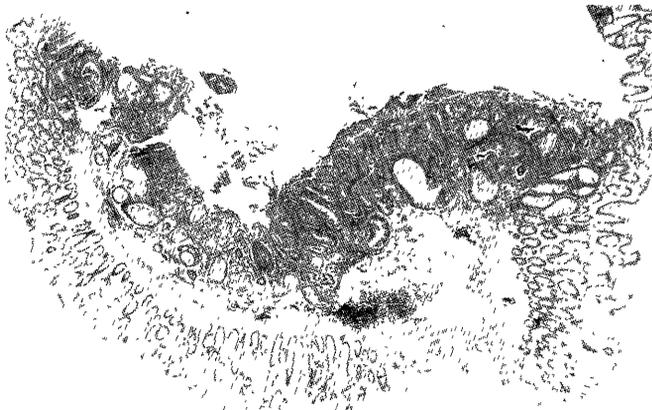


Fig. 2. Histopathological picture of the specimen resected by endoscopic strip biopsy from Case 1. The polyp after resection was 6 mm in size; histologically, it was well differentiated adenocarcinoma without adenomatous components. The carcinoma was mostly localized within the lamina propria of the mucosa and partially invaded the lower layer of the mucosa.

only an increase of bile duct enzymes and no findings of anemia. Barium enema : A pedunculated polyp measuring 16×12 mm was observed in the sigmoid colon and another measuring 18×13 mm was observed in the descending colon. The test was otherwise normal.

Colonoscopy : The polyps demonstrated by the barium enema were resected by endoscopic polypectomy. Histologically, these were adenoma with moderate atypia. A depressed lesion of approximately 10 mm in size was found in the descending colon although it was not detected by the enema. The depressed portion was covered with whitish exudate, the edge was irregular and the periphery was somewhat protruded and reddened (Fig. 1). The lesion was resected by endoscopic strip biopsy. The polyp after the

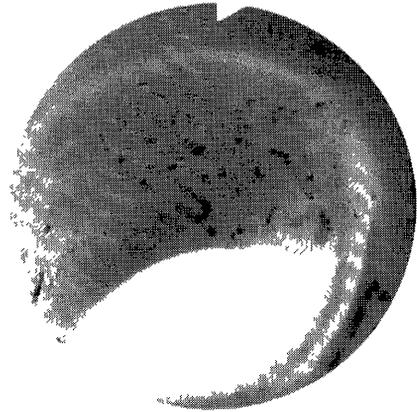


Fig. 3. Colonoscopic picture of the IIC type lesion in Case 2. A small depressed lesion with reddening was observed on the meniscus fold of the descending colon.

resection was 6 mm in size; histologically, it was well differentiated adenocarcinoma without adenomatous components. The carcinoma was mostly localized within the lamina propria of the mucosa and partially invaded the lower layer of the mucosa (Fig. 2).

Immunohistochemical staining : CEA was stained strongly only at the cancer tissue, and sialyl Lewis_x appeared in a minor part. The staining of Lewis_x was not specific to cancer tissue. The nuclear DNA content analysis revealed an aneuploid pattern.

Case 2. 69-year-old male

In early March 1990, the patient visited a neighboring physician for persisting diarrhea. Colonoscopy revealed a depressed lesion of approximately 10 mm in the descending colon. He was admitted for thorough examination and treatment.

On admission, there was no abnormal finding in physical examination or hematological and biochemical examinations.

Barium enema : A light shadow filling defect of 9×6 mm suggestive of a low polypoid lesion was observed on the meniscus fold of the descending colon.

Colonoscopy : A small depressed lesion with reddening was observed on the meniscus fold of the descending colon (Fig. 3). The histological diagnosis of forceps biopsy was well differentiated adenocarcinoma. The lesion was surgically removed since resection by strip biopsy was considered difficult due to poor demarcation of the lesion. Histopathological findings of the resected specimen : The lesion was 5 mm in size, and the cancer was well differentiated adenocarcinoma without adenomatous components. Small focal invasion was revealed beneath the mucosa, and histiocytic colonies and giant cells were located in the adjacent areas (Fig. 4). Metastasis to lymph nodes was



Fig. 4. Histopathological picture of the specimen surgically resected from Case 2. The lesion was 5 mm in size and the cancer was well differentiated adenocarcinoma without adenomatous components. Small focal invasion was revealed beneath the mucosa.

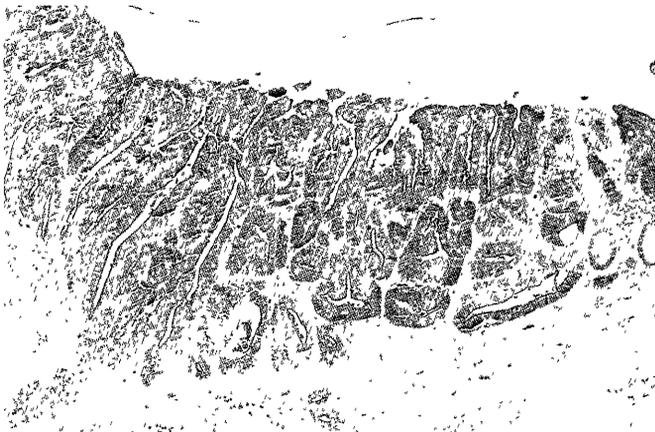


Fig. 5. In the immunohistochemical staining of cancer tissue of Case 2, sialyl Lewisx stained strongly only at the cancer tissue.

not observed. Sialyl Lewisx and CEA stained strongly only at the cancer tissue (Fig. 5); sialyl Lewisa was not specific for cancer tissue. The DNA content analysis revealed a diploid pattern.

Discussion

It is not easy to verify the number of reported cases of IIC type early cancer of the colon, which is frequently observed as IIA with polypoid periphery and occasionally with indistinct protrusion when the air volume is large, because of the difficulty in determining whether or not a IIA element is also present. Nevertheless, 44 reported cases of IIC lesions without a IIA element were identified in the literature in reference to the macroscopic, microscopic and histological findings of formalin-fixed specimens^{6,11,12}. Among these, sm cancer was observed in 16 cases (36%). In

terms of size, 24 lesions were less than 5 mm, including 7 lesions (29%) with sm cancer; and 20 lesions were 5 mm or more, including 9 lesions (45%) with sm cancer, showing a higher rate of sm cancer with the increase in size. Even among the small lesions less than 5 mm, the IIC type showed a high rate of sm cancer 29%, and in most cases was de novo carcinoma without adenomatous components⁶. This is highly significant, and will provide an important insight in the study of the occurrence, growth and progress of the cancer, as well as in the aspect of clinical diagnosis and therapy¹³. The two cases reported here were detected due to polyps and diarrhea that were not directly associated with the lesion. The fact that chance played such a major role in their discovery suggests the risk of overlooking IIC type lesions in the clinical setting.

The colon cancer cells revealed CEA which is a glycoprotein, and sialyl Lewisa and sialyl Lewisx which are carbohydrate antigens probably because they are associated with the mechanism of carcinogenesis, or they appeared as concomitant phenomena^{14,15}. The nuclear DNA content of tumor cells is different from that of normal cells and the distribution pattern is often aneuploid¹⁶. It is particularly important in IIC type early cancer of the colon which is considered de novo developed carcinoma to examine the immunohistochemical staining and staining pattern of antigens such as CEA, sialyl Lewisa and sialyl Lewisx. The response of CEA was stronger in case 1, being sufficiently stained only in the cancer tissue which was completely distinguished from the negative portion of the normal gland. In contrast, sialyl Lewisx appeared strongly only in the cancer tissue in case 2, but partially in case 1. The staining of sialyl Lewisa was observed in both cases but was not specific for cancer (Table 1).

The pattern of the tumor cell nuclear DNA content was aneuploid in case 1, but not in case 2. It is essential to recognize that cases of early cancer that is classified as IIC type in terms of macroscopic morphology may be considerably different regarding the nature of the process of carcinogenesis or the secondary concomitant phenomena.

Small IIC type lesions can be resected endoscopically, and specimens for complete pathological examination are made available providing much histopathological information; however the but information leading to a determination of lymphatic metastasis is poor. If cancer associated antigens such as CEA and sialyl Lewisx are indices of clinical malignancy, and the results of nuclear DNA content analysis are closely associated with the clinical behaviour of cancer, the difference in the nature of cancer cells in our cases is anticipated to be useful for determining the treatment of patients after endoscopic resection. It is desirable in the future that the nature and function of cancer cells, in addition to pathomorphological findings, be assessed by molecular biological analysis and applied clinically.

Conclusion

Two cases of IIc type early cancer of the colon were studied. The resected cancers, measuring 6 mm and 5 mm respectively, were well differentiated adenocarcinoma without adenomatous components and de novo developed carcinoma with submucosal invasion.

The two cases differed in immunostainability by tumor associated antigens and in nuclear DNA content. It was considered that IIc type early cancer of the colon may not be uniform as to the process of carcinogenesis or concomitant phenomena despite identical macroscopic morphology.

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