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Submucosal Invasive Micropapillary Carcinoma of the Colon with Massive Lymph Node Metastases: A Case Report

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Key Words

Lymph node metastases · Micropapillary carcinoma · Submucosal colonic cancer

Abstract

Micropapillary carcinoma was originally reported to be an aggressive variant of breast carcinoma, and it is associated with frequent lymphovascular invasion and a dismal clinical outcome. It has subsequently been found in other organs; however, at present, only a limited number of cases of colorectal micropapillary carcinoma have been reported. We present a case of early colon cancer with extensive nodal metastases in a Japanese patient. An 82-year-old man was found by colonoscopy to have a 20-mm pedunculated polyp in his sigmoid colon. Endoscopic resection of the sigmoid colon tumor was performed, and pathological examination of the resected specimen revealed a poorly differentiated adenocarcinoma component and a micropapillary component. Despite the tumor being confined within the submucosa, massive lymphatic invasion was noted. Thereafter, the patient underwent laparoscopic sigmoidectomy with lymph node dissection, and multiple lymph node metastases were observed. Our case suggests that when a micropapillary component is identified in a pre-operative biopsy specimen, even for early colorectal cancer, surgical resection with adequate lymph node dissection would be required because of the high potential for nodal metastases.

Background

Invasive micropapillary carcinoma (IMPC), originally described as a distinctive type of invasive carcinoma of the breast [1], is characterized by small neoplastic cell clusters surrounded by peculiar stromal spaces and is known to exhibit an aggressive behavior with a high incidence of lymph node metastases and a poor clinical outcome [1–4].

IMPC has been reported in various organs, including the breast [1], lung [2], parotid gland [3], ovary [5], pancreas [6], gallbladder [7], and stomach [8]; however, reports of colorectal micropapillary carcinoma, especially in early stages, are rare.

In this study, we present a case of early, submucosal sigmoid colon cancer that had a micropapillary component and multiple nodal metastases.

Case Report

An 82-year-old Japanese man was admitted to Hiroshima University Hospital because of hematochezia. A pedunculated polyp with a diameter of 20 mm was detected in his sigmoid colon by colonoscopy (fig. 1). Blood test results and the levels of serum carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9 (CA19-9) were within the normal ranges.

Initially, the patient underwent diagnostic endoscopic mucosal resection for his sigmoid colon tumor because the small size of the tumor made regional mesenteric nodal metastases unlikely.

Macroscopically, the tumor was a 20-mm pedunculated polyp. Microscopically, massive submucosal invasion to the depth of 2,000 μm from the muscular layer of the mucosa (fig. 2a) and extensive lymphatic invasion were observed. The tumor was mainly composed of atypical cells arranged in micropapillary structures, and tumor cell clusters were observed to float in clear spaces (fig. 2b). Immunohistochemically, MUC1 expression was not observed in a luminal staining pattern, as in typical adenocarcinoma foci, but at the stromal edges of tumor clusters, as in micropapillary structures. The latter staining represented the characteristic ‘inside-out’ pattern of the micropapillary component, and we diagnosed the tumor as IMPC (fig. 2c). The micropapillary structures comprised 70% of the tumor, and the remaining 30% was poorly differentiated tubular adenocarcinoma.

A diagnosis of submucosal IMPC of the colon was made on the basis of the results of the histological analysis of the endoscopic mucosal resection specimen, and thereafter computed tomography (CT) scans taken for staging diagnosis revealed intramesenteric lymph node swelling, which was suspected to represent lymph node metastasis (fig. 3a). The swollen lymph node exhibited increased accumulation of 18F-fluorodeoxyglucose in CT/positron emission tomography (PET) scans (fig. 3b). The clinical diagnosis was sigmoid colon cancer with lymph node metastasis. Therefore, we performed laparoscopy-assisted sigmoidectomy with regional lymph node resection.

Upon examination of the resected specimen, there was no residual cancer lesion in the colonic wall; however, metastasis of the micropapillary component was observed in 5 of the 12 resected lymph nodes.

After an uneventful postoperative course, the patient was discharged on the ninth postoperative day. The patient received adjuvant chemotherapy consisting of 6 cycles of modified FOLFOX6, and he is currently in good condition with no evidence of recurrence 12 months after surgery.

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Discussion

In 1993, Siriaunkgul and Tavassoli [1] reported that IMPC was a rare variant of invasive breast cancer. IMPC has been reported to exhibit an aggressive behavior with a higher incidence of lymph node metastases and worse prognosis than conventional adenocarcinomas [4]. A similar histological type of IMPC has been reported in other organs; however, reports of IMPC of the colorectum are rare.

IMPC has distinctive histological features characterized by small, tight, round-to-oval clusters of neoplastic cells surrounded by clear spaces and a lack of fibrovascular cores. The pathological and diagnostic feature of IMPC is its characteristic ‘inside-out’ immunostaining pattern with EMA or MUC1, which is indicative of the inversion of cell polarization; the outer surface of the tumor cell cluster is immunopositive for EMA or MUC1 [9].

IMPC is usually associated with conventional adenocarcinoma; however, it is rarely the predominant component in an otherwise conventional adenocarcinoma. The micropapillary component proportion required for the diagnosis of IMPC has not been established. There were 4 previous reviews of IMPC of the colorectum [10–13], and in general, IMPC is defined as a tumor in which the micropapillary component comprises at least 5% of the tumor volume [11–13]. The micropapillary component in IMPC of the colorectum varies from 5 to 95% of the tumor volume; however, in most of the reported cases, the micropapillary component comprised <30% of the tumor volume. The micropapillary component in colorectal carcinoma is usually a minor component of the entire tumor. Thus, cases like ours, which show a predominant micropapillary component, are very rare, especially in early-stage tumors, and only 1 similar case has been reported thus far [14].

A summary of previous reports is shown in [table 1](#). The incidence of IMPC in the literature ranges from 9 to 19% of colorectal cancers. In these reports, in comparison with conventional adenocarcinoma of the colorectum, IMPC of the colorectum has consistently been associated with lymphovascular invasion, lymph node metastasis, distant metastases, and a higher tumor stage.

The association of prognosis with the micropapillary component proportion is controversial. Kim et al. [11] reported that the presence of a micropapillary component in the primary tumor but not its proportion affected the histopathological parameters or overall tumor stage. Conversely, Haupt et al. [10] reported that the micropapillary component proportion might be an important factor for nodal metastases, although no statistical difference was observed because of the small sample size.

We agree with Haupt et al. [10], as in the previously reported series, the cases of IMPC in which the micropapillary component comprised >10% of the entire tumor had a higher rate of positive lymph node metastases (table 1). Verdu et al. [12] reported that only 3 (5%) cases had a substantial IMPC component (>30%), and all 3 cases had lymph node metastases. Haupt et al. [10] also reported that only 9 (30%) cases had an IMPC component of >10% of the tumor volume, and all 9 cases had lymph node metastases.

There was a clear trend that the frequency of lymph node metastases was associated with a larger micropapillary component. Larger sample sizes will be necessary to verify the importance of the micropapillary component proportion.

In the present case, the pedunculated polyp of early sigmoid colon cancer with a micropapillary component was associated with extensive lymphovascular invasion and multiple lymph node metastases, although pedunculated polyps are generally considered to exhibit few lymph node metastases [15].

We administered modified FOLFOX6 chemotherapy to prevent recurrence in the presented case; the optimal chemotherapy for IMPC has not yet been established. Further study is needed to elucidate the chemosensitivity and optimal chemotherapy regimen of this unique morphologic subtype.

Conclusion

If there is a micropapillary component, particularly in biopsy specimens, then the pathologist should inform the treating physician that there is a high probability of nodal metastasis, and this should be taken into account by the physician when considering the treatment strategy and the extent of surgical resection.

Disclosure Statement

The authors declare that they have no competing interests.

Table 1. Clinicocharacteristics of micropapillary carcinoma of the colorectum in previously published review series

Authors	Kim et al. [11]	Haupt et al. [10]	Xu et al. [13]	Verdu et al. [12]
Reported year	2006	2007	2009	2011
Review cases	585	178	221	379
Cases of IMPC	55	34	30	60
Proportion of IMPC	9.4%	19.1%	13.6%	16%
Ratio of IMPC component	5–80%	5–60%	5–75%	5–95%
Additional information	87.7% of cases had <30% of IMPC component	70% of cases had <10% of IMPC component	ND	95% of cases had <30% of IMPC component
Proportion of nodal metastases	74.5%	73.5%	63%	80%
Proportion of nodal metastases especially in cases having >10% of IMPC component	ND	100%	ND	94%
Lymphovascular invasion	45.5%	41.2%	33%	30.0%
T1/T2	10.9%	23.5%	17%	8.3%
T3/T4	90.1%	76.5%	83%	91.7%
Distant metastases	23.6%	11.7%	3%	16.7%

ND = Not defined.

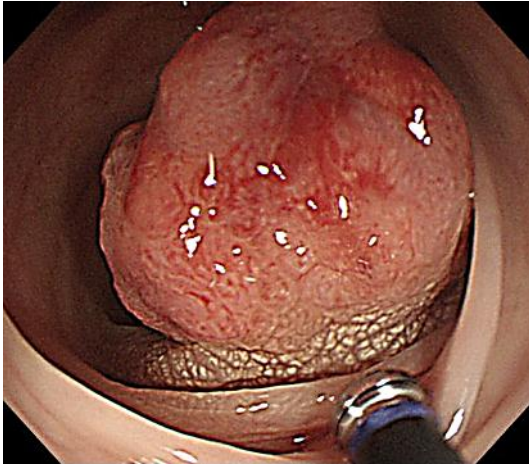


Fig. 1. A pedunculated polyp of 20 mm in diameter was detected in the sigmoid colon by colonoscopy.

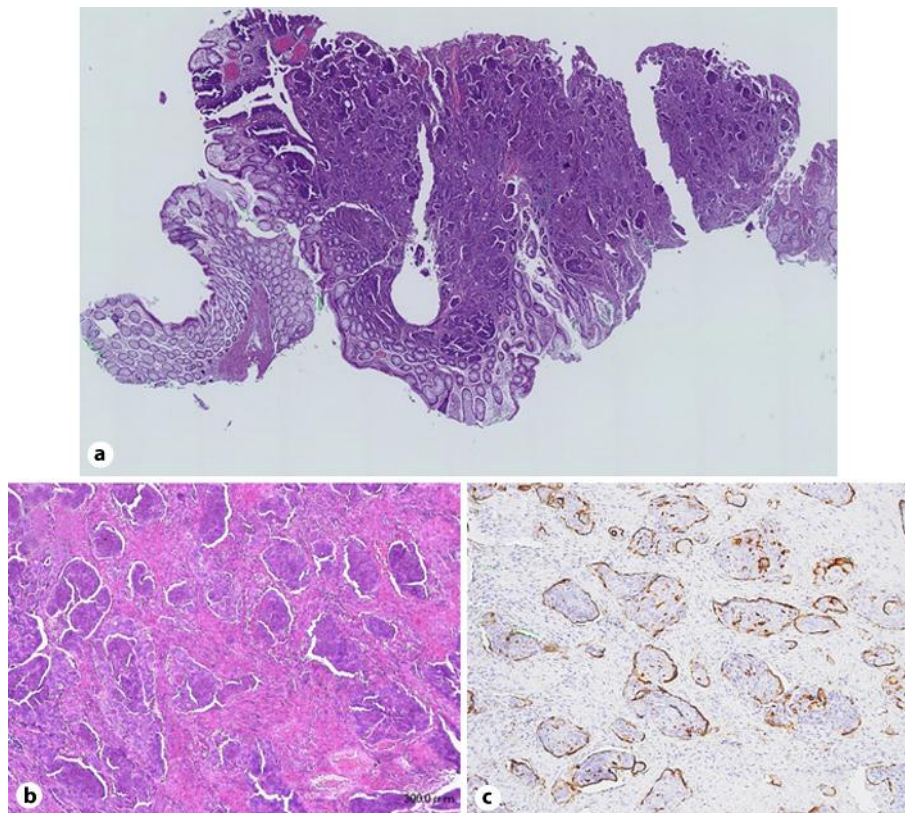


Fig. 2. **a** A loupe image shows massive submucosal invasion of 2,000 μm from the muscular layer of the mucosa. **b** Microscopic findings of the colon tumor. Proliferation of atypical glandular cells was observed and the cribriform proliferating pattern was also identified. A tumor consists of neoplastic cells forming alveolar configuration with glandular cavity. Tumor clusters are surrounded by clear empty spaces. Spaces reminiscent of vascular lumens were seen between micropapillary carcinoma cells and the stroma. **c** Immunohistochemical staining for MUC1 reveals extensive lymphatic invasion. MUC1 expression was observed in a luminal staining pattern in typical adenocarcinoma foci, but at the stromal edges of tumor clusters in the micropapillary structures. The latter staining represented the characteristic 'inside-out' pattern of IMPC.

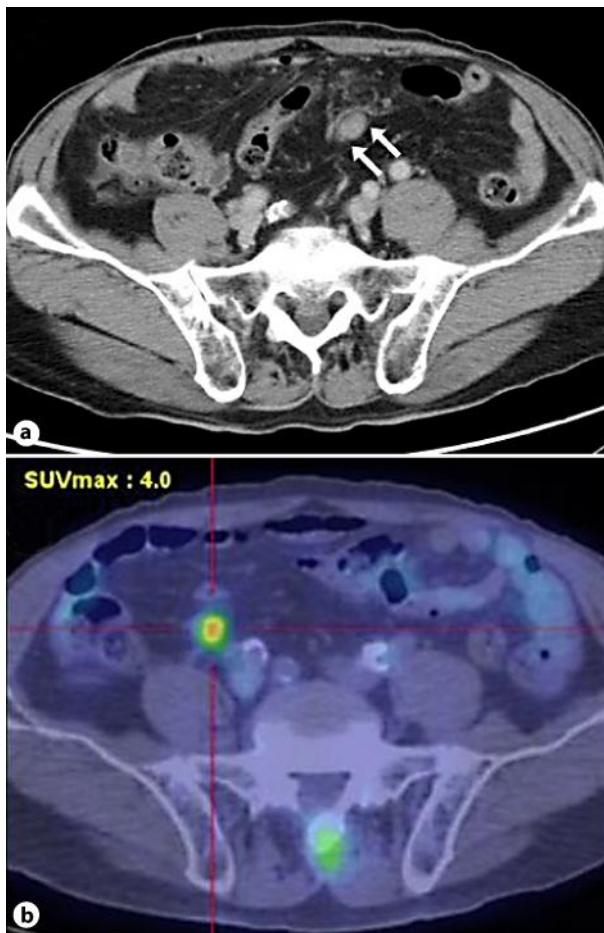


Fig. 3. a Abdominal CT scan showed swollen regional mesenteric lymph node (arrows). b PET/CT scan showed increased FDG accumulation along with swollen mesenteric lymph node.

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