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Case Report

Rare Case of Gut-associated Lymphoid Tissue Carcinoma in the Sigmoid Colon of a Very Elderly Patient: A Case Report

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Abstract

Colorectal cancer with gut-associated lymphoid tissue (GALT) carcinoma histopathology is particularly rare in very elderly patients. GALT is characterized by submucosal localization and prominent lymphoid infiltration with germinal center formation within tumor-infiltrating lymphocytes. This study aims to report a case of colorectal cancer with GALT carcinoma histopathology in a very elderly patient and to provide a comprehensive literature review. In this case, a 90-year-old female presented with an irregularly elevated tumor in the sigmoid colon, diagnosed via colonoscopy. Computed tomography revealed no lymph node or distant metastases. The patient underwent laparoscopy-assisted sigmoid colon resection with D3 dissection. Histopathological examination revealed well-differentiated adenocarcinoma in the submucosal layer with partial invasion into the muscle layer. Lymphocytes, along with lymph follicles, proliferated compressively in the stroma surrounding the tumor glands. Immunohistochemical analysis showed lost expression of mismatch repair proteins, MLH1 and PMS2, consistent with the tumor immunohistochemistry profile. B cells (CD20- and CD79a-positive) were generally distributed in and around the lymph follicles, while T cells (CD3-positive) were primarily located between the lymph follicles. This case highlights the rare histopathology of GALT carcinoma in colorectal cancer and underscores the importance of considering such diagnoses in elderly patients with colorectal tumors.

Keywords

gut-associated lymphoid tissue carcinoma, dome-type carcinoma, colon cancer

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Introduction

Colorectal cancer with gut-associated lymphoid tissue (GALT) carcinoma histopathology is extremely rare, with only a few cases reported in the literature. In 1999, de Petris et al. reported the first case of GALT carcinoma in the absence of ulcerative colitis[1]. Histopathologically, GALT carcinoma is characterized by the proliferation of columnar epithelial cells with well-differentiated eosinophilic cytoplasm, set against a background of stromal infiltration by lymphocytes with germinal center formation, primarily in the submucosal layer. Due to the rarity of this condition, the understanding of its clinical behavior, optimal management, and prognosis remains limited. Previous studies have focused primarily on younger patients or those with ulcerative colitis, leaving a gap in knowledge regarding the presentation and outcomes in very elderly patients. This case is particularly significant as it addresses this gap and provides insights into the histopathological features and prognosis of GALT carcinoma in an elderly population. This study aims

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to report a case of colorectal cancer with GALT carcinoma histopathology in a very elderly patient and to provide a comprehensive literature review. Including our case, a total of 19 cases have been reported, and we discuss their histopathological features and prognosis[1-3].

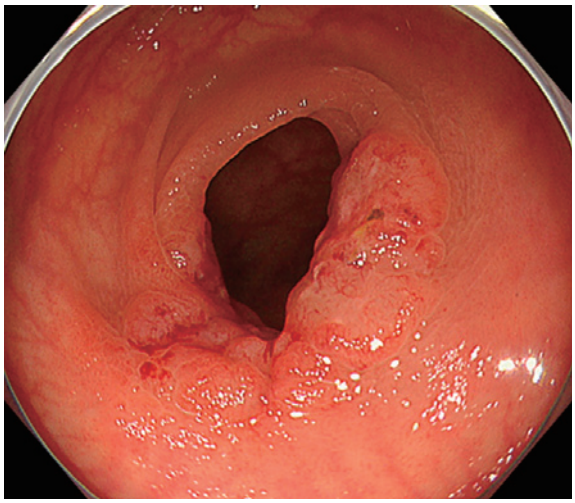

Figure 1. Colonoscopy revealing an irregularly elevated tumor in the sigmoid colon, located 30 cm from the anal verge.

Case Report

A 90-year-old female presented with constipation and underwent a colonoscopy. The colonoscopy revealed an irregularly elevated tumor in the sigmoid colon, located 30 cm from the anal verge (Figure 1). A biopsy revealed a well-differentiated carcinoma. Blood examination results were normal, with carcinoembryonic antigen [CEA] at 2.1 ng/mL and carbohydrate antigen 19-9 [CA19-9] at 19.8 U/mL. Contrast-enhanced computed tomography revealed irregular wall thickening of the sigmoid colon with a contrast effect, but no lymph node or distant metastases were found. Laparoscopy-assisted sigmoid colon resection with D3 dissection was performed. The excised specimen showed a gently elevated 13 × 7 mm lesion. Histopathology identified a well-differentiated adenocarcinoma in the submucosal layer with partial muscle layer invasion. Lymphocytes with lymph follicles proliferated in the stroma surrounding the tumor glands (Figure 2a, b). Some glands were cystically dilated and contained eosinophilic debris in their lumina (Figure 2 c). Eosinophilic cytoplasm and pseudostratification of nuclei were present in the constituent cells of the tumor (Figure 2 d). In addition, eosinophilic debris in the lumina were periodic acid-Schiff diastase (D-PAS)-positive (Figure 2e, f). Immunohistochemical analysis showed B cells (CD20- and CD79a-positive) generally distributed in and around the lymph follicles (Figure 3a, b), while T cells (CD3-positive)

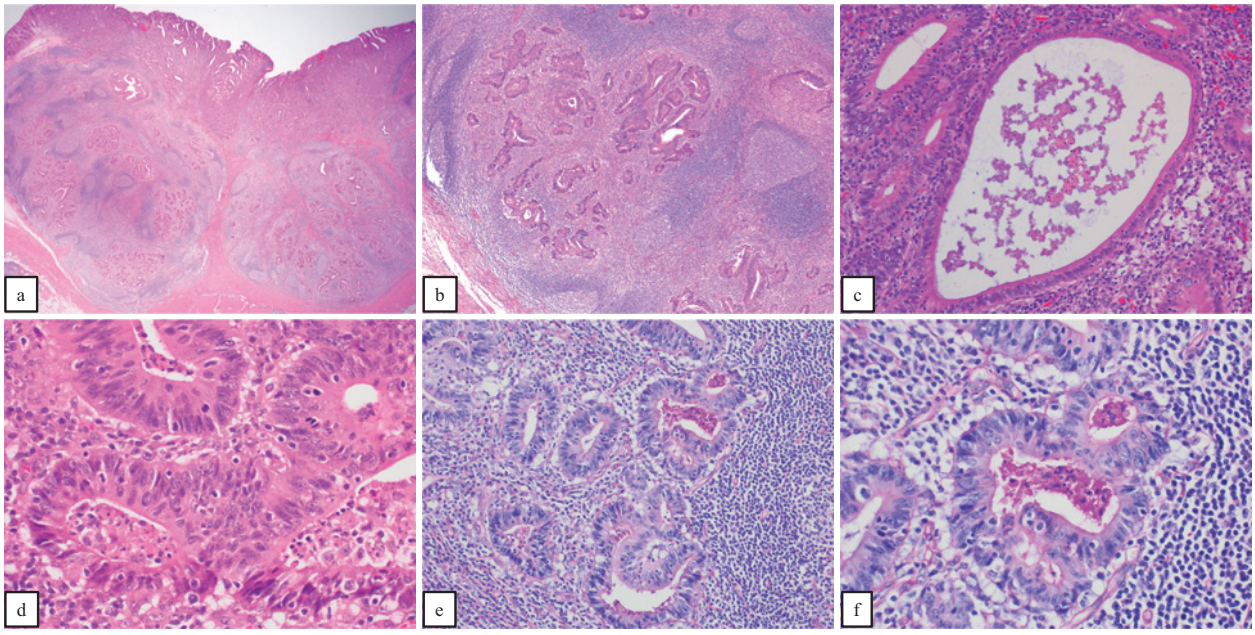

Figure 2. Histopathological analysis of the tumor.
a) A well-differentiated adenocarcinoma is present in the submucosal layer with partial muscle layer invasion (H&E stain, 2×). b) Lymphocytes proliferated with lymph follicles in the stroma surrounding the tumor glands (H&E stain, 4×). c) Some glands are cystically dilated and filled with eosinophilic debris (H&E stain, 20×). d) Eosinophilic cytoplasm and pseudostratification of nuclei are present in the constituent cells of the tumor (H&E stain, 20×). Eosinophilic debris in the lumina of the glands are D-PAS positive (D-PAS, e: 10×, f: 20×).

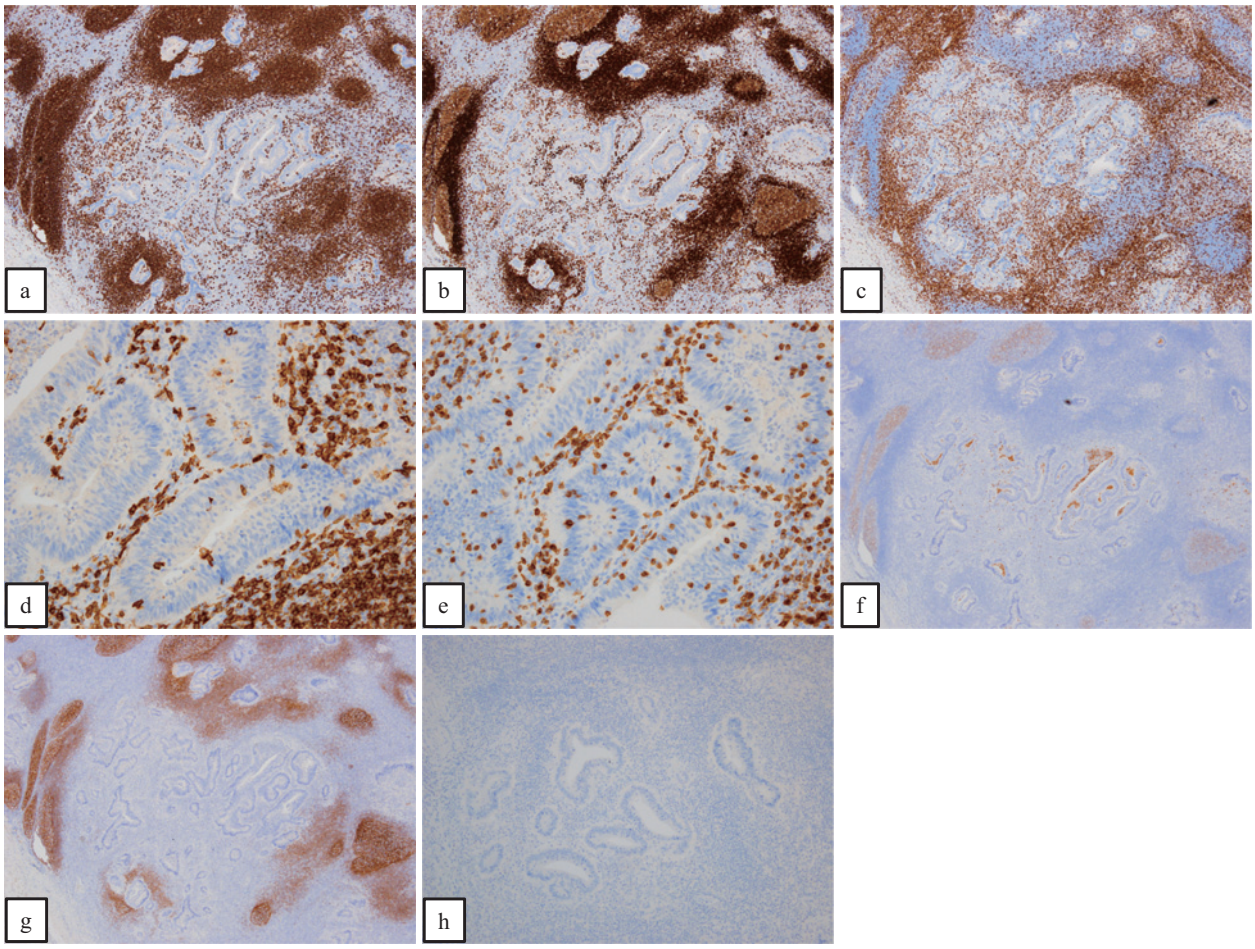

Figure 3. Immunohistochemical analysis of the tumor.
B cells (CD20- and CD79a-positive) are generally distributed in and around the lymph follicles (a: CD20, 4×; b: CD79a, 4×), while T cells (CD3-positive) are primarily located between the lymph (c: CD3, 4×). B and T cells are also present in the adenocarcinoma (d: CD20, 10×; e: CD3, 4×). CD10-positive cells (f: CD10, 4×) and CD21-positive follicular dendritic cells (FDCs) (g: CD21, 4×) are observed in the germinal center region. In addition, MUC2 expression is absent, indicating the lack of goblet cells (h: MUC2, 4×).

were primarily located between the lymph follicles (Figure 3 c). B and T cells were also present in the adenocarcinoma epithelium (Figure 3d, e). CD10-positive cells (Figure 3f) and CD21-positive follicular dendritic cells (FDCs) (Figure 3g) were observed in the germinal center region. In addition, MUC2 expression was absent, indicating the lack of goblet cells (Figure 3h). Among mismatch repair proteins, MSH2 and MSH6 were expressed, but MLH1 (Figure 4a) and PMS 2 (Figure 4b) were not consistent with the tumor's profile. In situ hybridization for Epstein-Barr virus (EBV)-encoded small RNA-1 was negative. Based on these findings, the patient was diagnosed with GALT carcinoma. No metastases were detected in the 15 dissected lymph nodes. No adjuvant chemotherapy was administered, and no recurrence was observed 12 months after resection.

Discussion

In 1984, Rubio et al.[4] first described "GALT carcinoma" as a type of colorectal cancer originating from the lymphocyte-associated mucosa in a patient with ulcerative colitis. In 1999, de Petris et al.[1] reported "dome-type carcinoma (DC carcinoma)" as synonymous with GALT carcinoma due to the dome-shaped elevation of the mucosal surface observed grossly. To date, 19 cases of GALT or DC carcinoma have been reported in the English literature[1-3], including our case (Table 1). The ages of the patients ranged from 44 to 90 years, with 9 males and 10 females. The primary lesion was located in the right colon in 11 patients, the left colon in 5 patients, and the rectum in 3 patients. There were no sex-related differences, and the right colon was more frequently involved.

Histopathology reveals several characteristic features[5]:

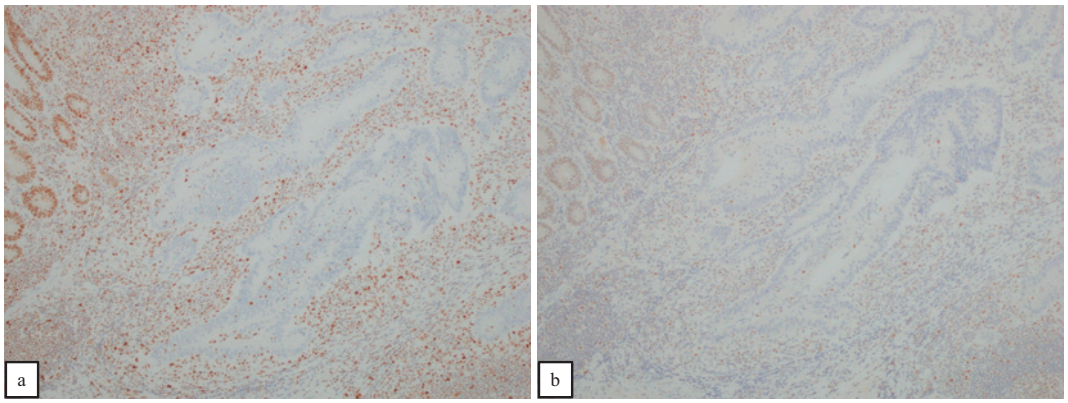

Figure 4. Immunohistochemical analysis of mismatch repair proteins. MSH2 and MSH6 are expressed, but MLH1 (a: MLH1, 4×) and PMS2 (b: PMS2, 4×) are not consistent with the tumor's profile.

Table 1. Clinico-pathological Characteristics of GALT Carcinoma and Dome-type Carcinoma of the Colon.

Case	Author/year	Age	Sex	Symptoms	Bowel-associated lesion	Location	Size (mm)	TNM	MSI status
1	De Petris/1999	44	M	Abdomen pain, Weight loss	Lynch syndrome	Ascending	9	pT1N0	None
2	Jass/2000	56	M	No symptoms	FAP	Ascending	30	pT1N0	Stable (PCR)
3	Clouston/2000	63	F	None	None	Sigmoid	None	pT1N0	None
4	Clouston/2000	56	M	None	None	Sigmoid	14	pT1N0	None
5	Rubio/2002	53	F	Diarrhea	UC	Ascending	None	pT1N0	None
6	Stewart/2008	70	M	No symptoms	UC	Ascending	5	pT1N0	Stable (IHC)
7	Stewart/2008	63	F	Diverticulitis	No	Transverse	17	pT1N0	Stable (IHC)
8	Asmussen/2008	76	F	Bowel bleeding	No	Sigmoid	20	pT1N0	Stable (IHC)
9	Asmussen/2008	86	F	Bowel bleeding	No	Rectum	24	pT2N0	Stable (IHC)
10	Rubio/2010	53	F	No symptoms	Family history CRC	Ascending	8	pT1N0	Instable (IHC): MLH1
11	Coyne/2011	76	M	No symptoms	Family history CRC	Cecum	23	pT1N0	Stable (IHC)
12	Puppa/2012	56	M	Constipation	No	Right flexure	8	pT1N0	Stable (IHC)
13	Yamada/2012	77	M	Abdomen discomfort	No	Transverse	30	pT3N0	Stable (IHC)
14	Rubio/2013	68	F	No symptoms	No	Transverse	None	pT1N0	None
15	Yamada/2013	76	F	No symptoms	No	Rectum	10	pT1N0	Stable (IHC)
16	Zhou/2015	47	M	Bowel bleeding	CRC	Descending	8	pT1N0	Stable (IHC)
17	Kannuna/2015	57	F	Abdomen pain	No	Cecum	30	pT1N0	Stable (IHC)
18	Noh/2022	58	M	No symptoms	No	Rectum	16	pT1N0	Stable (IHC)
19	Our case	90	F	Constipation	No	Sigmoid	13	pT2N0	Instable (IHC): MLH1, PMS2

(1) well-differentiated adenocarcinoma composed of columnar epithelial cells with eosinophilic cytoplasm, proliferating against a background of lymphoid aggregations with germinal center formation; (2) an infiltrate lacking desmoplasia and instead showing a compact and compressible proliferation of carcinoma components and GALT-like lymphocytes; (3) a lesion lacking goblet cells and showing an absence of MUC2 expression; (4) secretory luminal material that is periodic acid-Schiff diastase (D-PAS) positive; and (5) most tumor glands cystically dilated and containing an abundance of necrotic to eosinophilic debris (D-PAS positive) in their lumina. The histopathology results of the present case showed characteristic features of GALT carcinoma, including features (1)-(3), and (5), but not (4). In addition, eosinophilic cytoplasm and pseudostratification of nuclei were present in the constituent cells of the tumor. Furthermore, most cases of GALT carcinoma show intra-epithelial lymphocytes (IELs) within the glands, with both B lymphocytes and T lymphocytes observed[6]. These features, as observed in the present case, are thought to result from the differentiation of

the dome epithelium (follicle-associated epithelium) accompanied by GALT[6].

In cases of colorectal cancer with lymphocytic infiltration around the tumor, it is crucial to differentiate between GALT carcinoma, EBV-associated colorectal cancer, and Lynch syndrome-associated carcinoma, which is a type of microsatellite stability (MSI)-high colorectal cancer. To distinguish EBV-associated colorectal cancer, we performed Epstein-Barr encoding region in situ hybridization [ERER-ISH], which was negative in our case. Diagnosis of MSI-high CRC typically involves testing for microsatellite stability using polymerase chain reaction (PCR) or assessing mismatch repair protein expression by immunohistochemistry. In our case, immunohistochemistry revealed the absence of MLH1 and PMS2 expression. There was no evidence of Lynch syndrome, which we inferred to be due to methylation of the *MLH1* promoter region. One reported case did include a patient with Lynch syndrome[7], indicating that caution is necessary when differentiating MSI-high colorectal cancer from GALT carcinoma. Nonetheless, the diagnosis of GALT carcinoma in our patient was justified based on the characteristic histopathological findings.

Endoscopic findings of GALT carcinoma typically reveal soft "plaque-like" tumors with gentle ridges. This carcinoma retains an intramucosal component in all cases and grows in the submucosa with a compressible lymphocytic stroma, often presenting with submucosal tumor-like gross features, such as bridging folds. Regarding the origin of the dome-type carcinoma, some reports suggest that DC carcinoma, synonymous with GALT carcinoma, is identified by the endoscopic finding of a "dome-shaped elevation"[1]. However, the histopathologic finding of "dome epithelium" is considered the more accurate origin[6].

All cases of GALT/dome-type carcinoma have been diagnosed via polypectomy or large bowel resection. There have been no reports of additional surgery or adjuvant therapies such as radiation or chemotherapy. In terms of tumor depth, three cases, including ours, extended beyond the submucosal layer[8,9]. No cases of lymph node or distant metastases have been observed, resulting in favorable prognosis with no reported recurrences or cancer-related deaths.

Our patient, a 90-year-old female, was diagnosed with GALT carcinoma through radical colorectal resection. Histopathological examination showed tumor cells and lymphocytes co-existing in the submucosal tissue, along with germinal center formation. The diagnosis of GALT carcinoma was based on these characteristic histopathological features, despite the decreased expression of mismatch-repair proteins. Given the generally favorable prognosis of GALT carcinoma, we plan to continue long-term follow-up for this patient. Our study has the limitations of being a single case report and having a relatively short follow-up period. Additionally, the diagnostic process may have benefitted from more extensive genetic testing to further rule out hereditary cancer syndromes.

Conclusions

Here, we present a case of GALT carcinoma exhibiting rare histopathology in a very elderly patient with colorectal cancer. Given the small number of cases reported to date, further accumulation of similar cases is essential to better understand the clinical behavior, optimal management, and long-term prognosis of GALT carcinoma. Future studies should focus on detailed genetic and molecular analyses to differentiate GALT carcinoma from other lymphocyte-rich colorectal cancers, such as EBV-associated colorectal cancer and Lynch syndrome-associated carcinoma. Long-term follow-up and larger case series are necessary to confirm the prognosis and inform treatment strategies for this rare entity.

Conflicts of Interest

There are no conflicts of interest.

Author Contributions

KK and KY prepared the manuscript. YaF and TS provided the pathological data. YI, SY, MHo, MHi, TO, SE, YoF, and TU edited the manuscript. All the authors have read and approved the final version of the manuscript.

Approval by Institutional Review Board (IRB)

Not applicable.

Informed Consent

Written informed consent was obtained from the patient and her family.

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