



A Case of Rectal Carcinoma Complicated with Adult T-cell Leukemia/Lymphoma Diagnosed by an Inguinal Lymph Node Biopsy

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Abstract: *Background:* Recently, double cancer is no longer uncommon. It is Particularly difficult to determine whether swollen lymph nodes (LNs) indicate malignant lymphoma or metastasis of other carcinoma. We experienced a case of rectal carcinoma complicated with adult T-cell leukemia/lymphoma (ATLL). *Case presentation:* We encountered a 77-year-old woman who had visited a previous hospital due to bloody stool. Colonoscopy revealed a 10-cm tumor in the lower rectum. Given its pit pattern and surface and vessel pattern, she was suspected of having adenocarcinoma *in situ*. However, enhanced computed tomography (CT) showed LN swelling around the rectum, and her bilateral inguinal LNs were palpable. Colonoscopy and a biopsy performed at our hospital showed adenoma (Group 3) with no malignant findings. We performed an inguinal LN biopsy and diagnosed her with ATLL. We suspected the rectal mass either be rectal carcinoma or ATLL invasion. We performed chemotherapy for ATLL. The inguinal LNs became no longer palpable, but the rectal mass did not shrink, so we performed operative resection for diagnostic treatment. Thereafter, we diagnosed her with double cancer of rectal adenocarcinoma and ATLL. *Conclusion:* It is difficult to determine whether swollen LNs indicate malignant lymphoma or metastasis of other carcinoma without performing an LN biopsy. However, a diagnosis of metastasis or non-metastasis does not influence either the staging of the carcinoma or the treatment plan.

Keywords: ATLL, Rectal Adenocarcinoma, Double Cancer, Inguinal Lymph Node Biopsy

1. Introduction

Recently, multiple cancer has become increasingly frequent with the aging of society and advances in diagnostic imaging, as well as prognostic improvement in cases of malignant tumor. It is particularly difficult to identify when gastrointestinal carcinoma is complicated with malignant lymphoma, due to the fact that it is difficult to determine whether the presence of swollen lymph nodes (LNs) indicate

the existence of malignant lymphoma or metastasis from some other carcinoma. We herein report a patient who was diagnosed with rectal carcinoma complicated with adult T-cell leukemia/lymphoma (ATLL).

2. Case Presentation

A 77-years-old woman with a complaint of bloody stool and epigastric pain visited her previous doctor, and colonoscopy

revealed a huge rectal mass that was determined to be lateral spreading tumor, granular type (LST-G). She was suspected of having adenocarcinoma *in situ* and referred to our department. However, enhanced computed tomography (CT) showed some swollen LNs around the rectum, and her bilateral inguinal LNs were palpable. Her history included laparoscopic appendectomy and adhesive ileus over 50 years earlier as well as hyperlipidemia, uterine fibroid, and chronic gastritis (after *Helicobacter pylori* eradication).

A blood test shows slight anemia with Hb 11.7 g/dl, while carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9 (CA19-9) levels were within the normal ranges (Table 1). Colonoscopy revealed a 10-cm LST-G in the lower rectum. The LST lesion showed a 1-cm mass at the oral side and 3-cm semicircular mass at the anal side, with a granular lesion surrounding (Figure 1A, B). The pit pattern was type IIIL and IV (Figure 1C), but only a part of the anal side mass was found to be type Vi (Figure 1D, E). In addition, narrow-band imaging (NBI) showed a nearly regular surface and vessel pattern (Figure 1F). A biopsy was performed at the anal side mass, which revealed tubulovillous adenoma (Group 3).

Enhanced CT showed that the mass occupied at the rectum of Ra to Rb (Figure 2A). We also noted swollen LNs (5 to 15 cm) around the rectum and common iliac artery (Figure 2B). The bilateral inguinal LNs had swollen to 12 cm (Figure 2C). A barium enema examination showed a granular and elevated lesion at the Rb of the rectum.

The patient was suspected of having adenocarcinoma *in situ* based on the colonoscopic findings, but it was an atypical case with inguinal LN swelling. We initially planned a surgical biopsy of the inguinal LNs. The intraoperative rapid diagnosis revealed a lot of atypical lymphocytes, and she was diagnosed with lymphoma (Figure 3). In addition, immunostaining showed positivity for CD3, 4, 5, 8, and 25, and her blood lymphocyte were not increased. She was diagnosed with ATLL, lymphoma type. Additional blood tests showed high levels of soluble interleukin-2 receptor (sIL-2R) and positivity for human T-cell leukemia virus type 1 (HTLV-1) antibody (Table 1). ¹⁸F-fluorodeoxy glucose-positron emission tomography (FDG-PET) showed the accumulation at the bilateral inguinal LNs (maximum standardized uptake value [SUV_{max}] 4.0 in 1 h, 4.7 in 2 h) and the rectum (SUV_{max} 12.3 in 1 h, 16.0 in 2 h).

A rectal mass biopsy was performed again but revealed no malignant findings. The differential diagnosis we suspected was ATLL with rectal infiltration. If that was the actual case, then chemotherapy for ATLL would be effective for the rectal mass. With such expectations, we prescribed two courses of THP-COP (Pirarubicin + Cyclophosphamide + Vincristine + Prednisolone) for ATLL therapy. The inguinal LNs became no longer palpable, and we judged the status to be a partial response (PR), but the rectal mass did not shrink.

Given the above, we suspected double cancer of ATLL and rectal carcinoma and performed laparoscopic-assisted low anterior resection and D2 dissection for diagnostic treatment. During the surgery, some mesenteric LNs were swollen, and the intraoperative rapid pathological diagnosis of the lower mesenteric trunk LNs showed not metastasis but lymphocyte

proliferation. The resected rectum had an LST lesion containing two elevated masses and a granular lesion along it (Figure 4A). The mass at the anal side had an ulcer.

The pathological findings of the resected rectum were 100×85 mm, Tub1>pap, pTisN0M0, surgical stump negative. There was an ulcer and vascular invasion at the anal side mass. Mapping observation showed that this part matched the lesion where the pit pattern diagnosis had been type Vi (Figure 4B). The dissected LN had atypical lymphocyte proliferation, and there was no normal structure. Immunostaining showed positivity for CD3, 4, 20, and 25 (Figure 4C-E).

She was discharged on postoperative day 8 and is scheduled to undergo chemotherapy for ATLL at department of hematology.

Table 1. Blood test.

CBC		Chemistry	
WBC	4400 /μl	TP	7.5 g/dl
Seg	51.0%	Alb	4.1 g/dl
Ly	43.0%	T-cho	218 mg/dl
Mo	4.1%	T-Bil	0.69 mg/dl
Eo	1.4%	AST	29 IU/L
Ba	0.5%	ALT	16 IU/L
RBC	397×10 ⁴ /μl	LDH	272 IU/L
Hb	11.7 mg/dl	ALP	248 IU/L
Ht	35.1%	γGTP	12 IU/L
MCV	88 fl	BUN	13.7 mg/dl
MCH	29.5 pg	Cre	0.84 mg/dl
MCHC	33.3%	Na	141 mEq/L
Plt	22.8×10 ⁴ /μl	K	4.2 mEq/L
		Cl	104 mEq/L
Coagulation		Serology	
PT	128.1%	CRP	0.01 mg/dl
PT-INR	0.89	HBsAg	(-)
APTT	34.4 sec	HCVAb	(-)
		CEA	2.4 ng/ml
		CA19-9	<2 U/ml

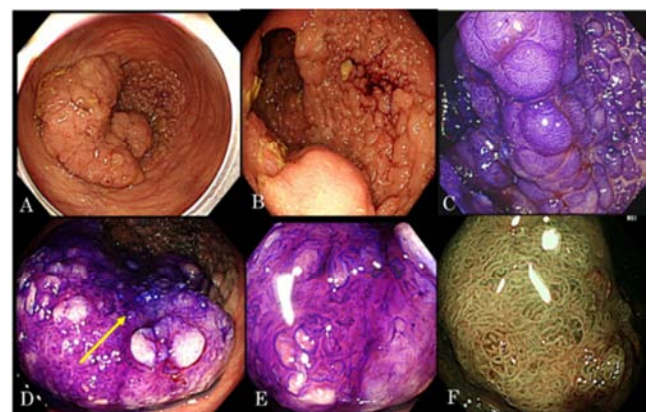


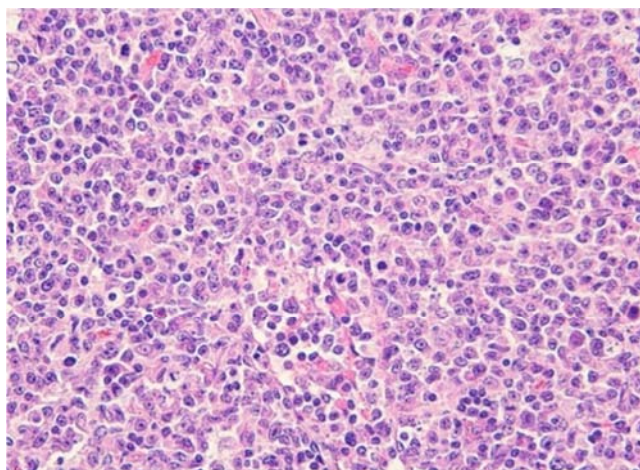
Figure 1. Colonoscopic findings.

(A) A 10cm LST lesion in the lower rectum. (B) A granular lesion adjacent to the mass. (C) A pit pattern shows type IIIL and IV disease. (D) A pit pattern type Vi is found in only a part of the anal side mass. (E) A magnifying pit pattern type Vi. (F) Narrow band imaging shows the surface and vessel pattern to have a rather regular pattern.



Figure 2. Enhanced CT scan.

(A) A mass was found to occupy the lower rectum Ra to Rb. (B) The LN around the rectum and common iliac artery were swollen. (C) Bilateral inguinal LN swelling.



There were numerous atypical lymphocytes.

Figure 3. Inguinal lymph node biopsy.

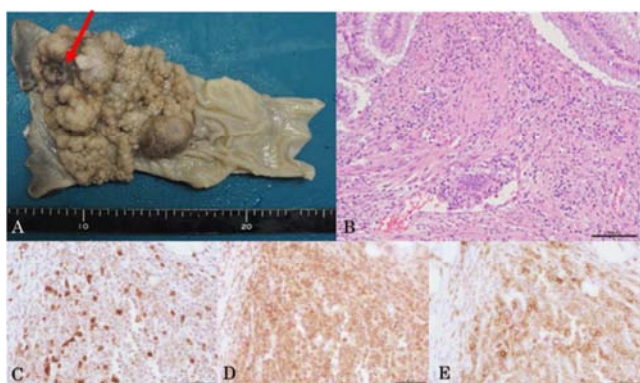


Figure 4. Resected rectum and pathological findings.

(A) The resected rectum. A small ulcer is observed on the mass (arrow indicated). (B) The arrow shows vascular invasion at the indicated spot. (C) Immunostaining, CD3 positive. (D) Immunostaining, CD4 positive. (E) Immunostaining, CD25 positive.

3. Discussion

ATLL is a T-cell malignancy resulting from infection by HTLV-1. HTLV-1 carriers are estimated to number over 30 million worldwide, with about 1 million carriers living in Japan. Infection with HTLV-1 is considered endemic in the southwestern part of Japan, but it has recently spread all over Japan through population migration [1, 2].

The rate of colorectal carcinoma complicated with other cancer is considered to be around 10%, while the rate of malignant lymphoma complicated with other cancer is 2.8% [3]. There have been 11 case in which malignant lymphoma was diagnosed in the perioperative period of colorectal carcinoma (Table 2), which we found when we searched the Japan Medical Abstracts Society using the key words “colorectal carcinoma”, “malignant lymphoma” and “complication”. Four were detected based on the pathological findings of dissected LNs after surgery for colorectal cancer, and another four were diagnosed from the results of preoperative examinations, while three cases were detected at an intraoperative rapid pathological diagnosis. There were only two complicated ATLL cases [4]. There have been some reports describing the rate of ATLL complicated with other cancer as being high 5.7% to 8.7% [12, 13]. Recently, progress has been made in the field of ATLL research, and the mechanisms underlying its carcinogenesis are being clarified. There are some factors associated with the development ATLL, such as the abnormal activation of nuclear factor- κ B signaling, which causes the abnormal proliferation of cancerous cells, and the inhibition of cell apoptosis by viral proteins [14, 15]. These mechanisms may support the opinion that ATLL tends to be complicated with other cancer.

In cases of double cancer with malignant lymphoma and colorectal carcinoma, there are mainly two problems. First, it is difficult to determine whether swollen LNs are lymphoma or metastasis. Diagnosing the presence of metastasis or non-metastasis is necessary for establishing the staging of the carcinoma and selecting the surgical strategy. Colorectal cancer usually metastasizes first to the regional LNs. It is atypical that other LNs are swollen without any swelling observed in the regional LNs.

Second, ATLL tends to invade to nearby organs, such as gastrointestinal organs. It is difficult to determine whether a colorectal mass is colorectal carcinoma or ATLL with colorectal invasion. Utsunomiya noted that 44% of ATLL autopsy cases showed invasion to the gastrointestinal tract, and 17.9% of them had invasion to the colon [16]. In addition, Yamaguchi found that 58.1% of colorectal invasive lesions resembled multiple elevated masses, as in the present case [17].

In our patient, treatment for rectal carcinoma as stage IV, after regarding the condition of the inguinal LNs as distant metastasis, would probably have involved excessively invasive treatment, such as preoperative chemotherapy or Mile's operation.

Table 2. The case reports that colorectal carcinoma complicated with malignant lymphoma.

Year	Age M/F	when diagnosed with lymphoma	Postoperative diagnosis
1990 [4]	57 F	after the Ope	sigmoid colon ca.(T1N0M0) +ATL
1998 [5]	88 M	after the Ope	dissending colon ca.(T3N0M0) +BLDCL
2005 [6]	70 M	after the Ope	sigmoid colon ca.(T3N0M0) +FL
2005 [6]	76 M	during the Ope	ascending colon ca. (T1N1M0) +AILD
2007 [7]	70 F	during the Ope	sigmoid colon ca.(T2N0M0) +HL
2008 [8]	61 F	after the Ope	sigmoid colon ca.(T3N1M0) +FL
2011 [9]	58M	before the Ope	sigmoid colon ca.(T3N2M0) +HL
2014 [3]	76M	during the Ope	sigmoid/rectal ca. (S: T3N0M0, Rb: T2N0M0) +DLBCL
2014 [10]	70 F	before the Ope	sigmoid colon ca.(T2N0M0) +DLBCL
2018 [11]	73M	before the Ope	cecal ca.(T3N3M0) +HL
2019※	77 F	before the Ope	rectal ca.(TisN0M0) +ATL

M/F: Male/Female.

Ope: Operation

Ca.: carcinoma

※Our case.

4. Conclusion

We experienced a case of rectal carcinoma complicated with ATLL that was diagnosed by an inguinal LN biopsy. Malignant lymphoma tends to be complicated with another cancer, especially ATLL. In addition, ATLL frequently invades the gastrointestinal tract. It is difficult to determine whether swollen LNs are malignant lymphoma or metastasis or whether a colorectal mass is colorectal carcinoma or an invasive lesion of malignant lymphoma. It is important to consider the differential diagnosis when abnormally swollen LNs are found, and we should not hesitate to biopsy them.

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