Acta Med. Nagasaki 47 : 75−78

Case Report

Spontaneous Regression of Colonic Lesions in Adult T-cell Leukemia

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A 74-year-old man was admitted to our hospital because of diarrhea. Serum anti-HTLV-1 antibody was positive without abnormal lymphocytes. Colonoscopy demonstrated a edematous and congested mucosa with erosions, and ulcers in the region extending from the cecum to rectum. Biopsy specimens showed diffuse infiltration of abnormal lymphocytes positive for T-cell markers in the lamina propria. Conservative therapy was provided but no chemotherapy because of improvement of diarrhea within two weeks. A repeat colonoscopy 6 months later revealed scars without erosions or ulcers. Eight months after first admission, the patient was readmitted to our hospital because of acute ATL crisis, and died of hepatic involvement 7 days later. Colonic lesions associated with ATLS may show spontaneous regression and recurrence.

ACTA MEDICA NAGASAKIENSIA 47 : 75−78, 2002

Key Words: ATL, spontaneous regression, colonic involvement

Introduction

Adult T-cell leukemia (ATL) is an aggressive T-cell malignancy caused by human T-lymphotropic virus type I (HTLV-l) (1). ATL is characterized by infiltration of leukemic cells into various organs including the liver, spleen, skin and gastrointestinal tract. We have previously reported the clinical and pathological features of gastrointestinal lesions in patients with ATL (2-4). In autopsy series, gastrointestinal involvement is frequently seen in patients with ATL (5). However, colonic involvement diagnosed by colonoscopy is relatively rare (6,7).

Spontaneous regression has been reported in ATL, however, the pathogenesis of the remission is not clear (8,9). We report here a rare case of spontaneous regression of colonic involvement in a patient with ATL.

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Case report

A 74-year-old man was admitted to our hospital because of a 2-week history of diarrhea. He was known hypertensive and taking an anti-hypertensive drug. Past history revealed amebiasis 54 years earlier and ischemic colitis 14 year earlier. The family history was unremarkable.

Physical examination on admission showed tenderness in the lower abdomen, but no hepatosplenomegaly or superficial lymphadenopathy. Hematogram on admission showed a leukocyte count of 11,180/mm^3 with a normal differential count and no abnormal lymphocytes, and CRP was 8.4 mg/dl (Table 1). Serum LDH level was normal, but, serum anti-HTLV-1 antibody was positive. No pathogenic bacteria was isolated for

Table 1. Laboratory Data

	1999/09/04 (first admission)		2000/05/25 (second admission)	
WBC	11800	/mm^3	2870	/mm^3
Ab-Ly	0	%	17	%
RBC	3.93	$\times 10^6$	3.53	$\times 10^6$
Hb	3.3	g/dl	12.4	g/dl
Plt	23.4	$\times 10^4$	2.1	$\times 10^4$
CRP	8.4	mg/dl	5.4	mg/dl
T-bil	0.72	mg/dl	2.85	mg/dl
GOT	32	IU/ml	905	IU/ml
GPT	18	IU/ml	265	IU/ml
LDH	355	IU/ml	1790	IU/ml

stool. PCR of stool for tuberculosis was negative. Endoscopic examination of the colon demonstrated an edematous and congested mucosa with erosions, and ulcers in the area from the cecum to the rectum (Fig. l-A). Biopsy specimens taken from the descending colon showed diffuse infiltration of abnormal lymphocytes with morphological characteristics of ATL cells in the lamina propria (Fig 1-B). Immunohistochemical analysis revealed that these abnormal cells were negative for B-cell but positive for T-cell markers (UCHL-1) (Fig. 1-C). Based on these findings, the diagnosis was established as ATL of lymphoma subtype with colonic involvement. The patient was treated conservatively without chemotherapy because of improvement of diarrhea within two weeks, and inflammatory reaction improved (CRP: 0.76 mg/dl).

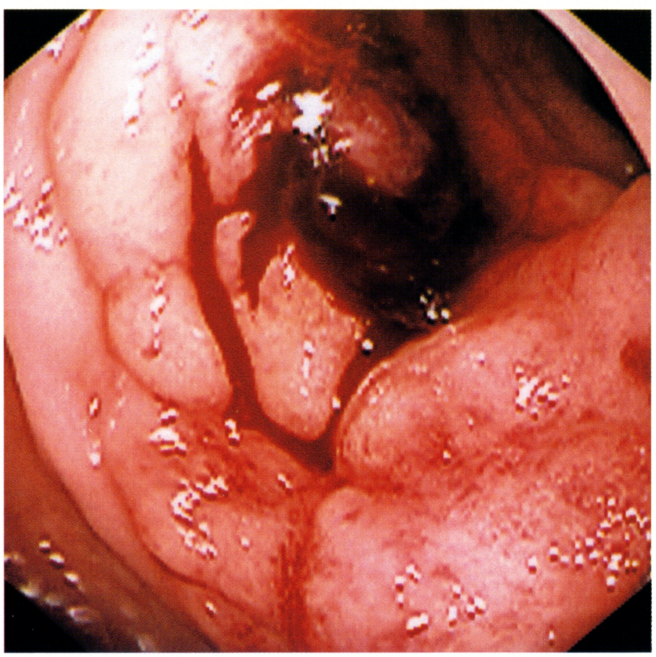

Figure 1-A. Colonoscopy performed on admission demonstrating edematous and congested mucosa with erosions and ulcers in the transverse colon.

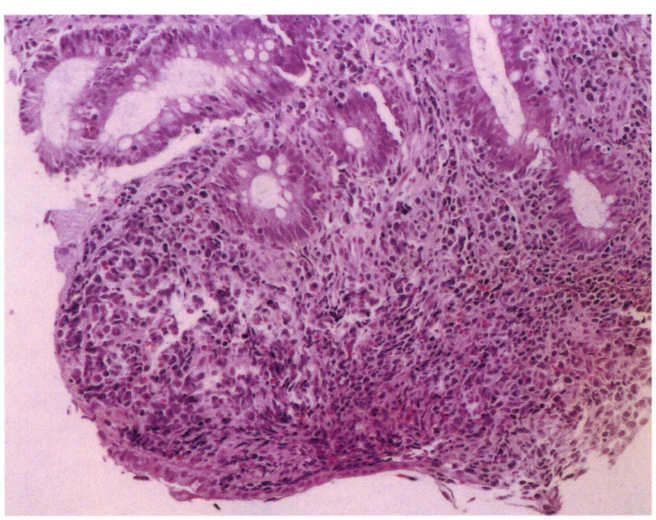

Figure 1-B. A biopsy specimen of the transverse colon showing a dense cellular infiltration of abnormal lymphocytes (H & E stain, x100).

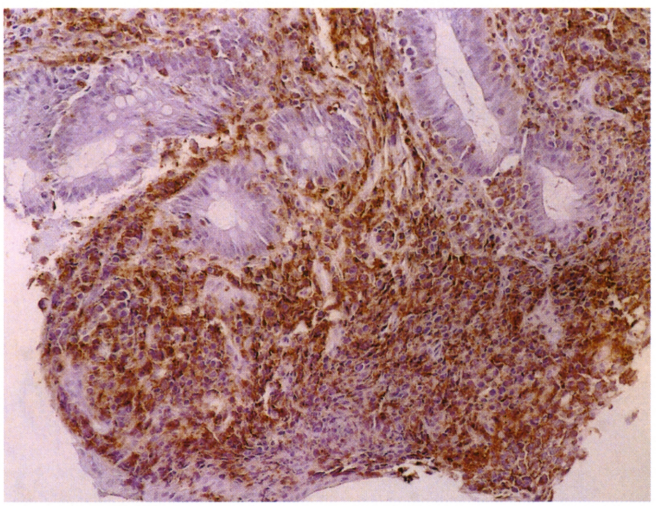

Figure 1-C. Most of the proliferating cells were positive for T-cell markers (UCHL-antibody immunostaining, x100).

Colonoscopy after 6 months revealed scars without erosions but no ulcers (Fig. 2-A). Biopsy specimens taken from the scar lesions in the cecum showed focal infiltration of abnormal lymphocytes with morphological characteristics of ATL cells (Fig. 2-B). Eight months after the first admission, he was readmitted to our

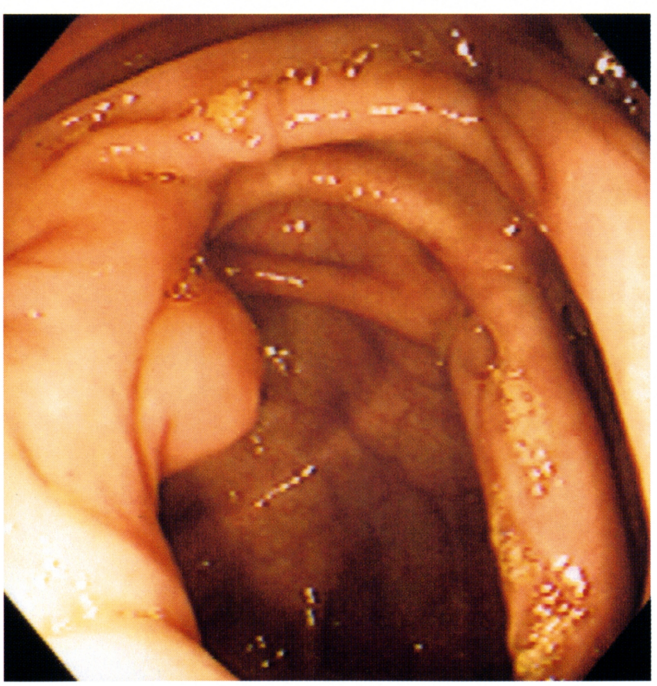

Figure 2-A. A repeat colonoscopy six months after first admission showing scars without erosions or ulcers.

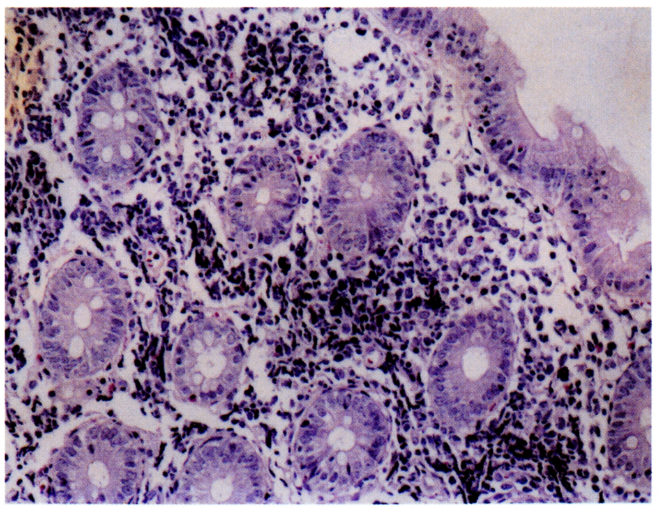

Figure 2-B. A biopsy specimen of the scar caecal lesions showing focal infiltration of abnormal lymphocytes with morphological characteristics of ATL cells (H & E stain, x100).

hospital because of low-grade fever (37.5°C) and anorexia. Hematogram on second admission showed a leukocyte count of 2,870/mm^3 with 17% abnormal lymphocytes; mainly CD4 positive lymphocytes (Table 1, 2). Combination chemotherapy consisting of vincristine, cyclophosphamide and adriamycin was administered, but the condition worsened suddenly, and the patient died of hepatic failure by hepatic infiltration of ATL 7 days after commencement of chemotherapy. The postmortem examination was not performed.

Table 2. Surface markers of lymphocytes on second admission

	(2000/05/25)
CD2	95.0%
CD3	92.8%
CD4	78.9%
CD5	93.7%
CD8	17.0%
CD19	6.6%
CD20	63%
CD25	25.4%

Discussion

Nagasaki prefecture is located in the southwestern part of Japan and is known to be an endemic area of for HTLV-1 (10). Patients with ATL suffer from various gastrointestinal symptoms including abdominal pain, melena, and diarrhea (11, 12). Leukemic cell infiltration and infection with strongyloides, Isospora belli and cytomegalovirus infection of the gastrointestinal tract often cause diarrhea in patients with ATL (13-15). However, refractory diarrhea is frequently noted, which is caused by severe and extensive leukemic infiltration (16,17).

In autopsied cases, leukemic infiltration into the gastrointestinal tract are common (18), Sato et al. (18) reported a high percentage of gastrointestinal tract involvement (stomach in 29.2%, intestine in 25.0%). On the other hand, only a few endoscopic studies have described colonic lesions in patients with ATL (5-7, 19, 20). One reason is that when patients with such complications are suspected of having lower intestinal lesions, based on clinical features and blood/fecal examinations, they are often in poor general condition with pancytopenia or infectious complications, and are unfit to undergo colonoscopy (6, 7). Indeed in our case, we could not examine the colonic lesions when our patient was readmitted to our hospital because of poor condition.

Colonoscopic findings in patients with leukemia and lymphoma include mucosal edema, erosions, ulceration, petechial hemorrhages, diffuse bleeding, granular appearance, submucosal tumor formation and multiple polypoid lesions (6, 7, 19, 20). Utsunomiya and Hanada (21) studied the colorectal lesions of ATL patients endoscopically and classified these lesions into edematous and granular lesions (21). In this regard, Matsushita et al (22) reported that the colonoscopy of patients with early stage leukemia showed minute erosions. In our patient, colonoscopic findings in included edematous and congested mucosa with erosions, and ulcers.

Spontaneous regression without chemotherapy has been reported in patients with ATL in Japan, but in none of the cases there was a spontaneous persistent regression over several years (8, 23). The underlying mechanism responsible for the spontaneous regression of ATL is thought to be related to the preceding infections or surgical biopsies (23-25). Arima et al. (26) reported that antigen stimulation may induce secretion of interleukin-2 and subsequent clonal expansion of T-cells including ATL cells. The present case indicates that colonic involvement in patients with ATL can occur as erosion with spontaneous regression, followed by systemic acute crisis. Colonoscopic biopsies were performed. Although no bacteria were detected in stool specimens, we could not completely rule out colonic infection or exclude the role of such factors in the regression of colonic lesions.

In conclusion, we reported here a case of ATL with colonic involvement and spontaneous regression followed by recurrence. Colonic involvement may be important event in the clinical course of ATL.

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