



## A Case Report of Primary Jejunal T-Lymphoblastic Lymphoma and a Review of the Literature

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### Abstract

We report a 29-year-old male who developed primary jejunal T-Lymphoblastic Lymphoma (T-LBL). The patient was admitted to our hospital due to epigastralgia and back pain. An abdominal contrast-enhanced Computed Tomography (CT) showed thickness of jejunal wall and enlargement of peri-jejunal lymph nodes. A gastrointestinal endoscopy showed an ulcerative tumor with bleeding at proximal end of jejunum beyond the Treitz ligament. A 18F-Fluorodeoxyglucose (FDG) -positron emission tomography/CT showed abnormal FDG uptake in jejunum, peri-jejunum lymph nodes, and left supraclavicular fossa lymph node as well as mediastinal and para-aortic lymph nodes. The tumor biopsy revealed middle to large sized abnormal lymphoblasts' proliferation which were positive for CD3, CD5, CD10, CD79a, BCL2, and TdT, and negative for CD4, CD8, and CD20. We diagnosed him with T-LBL (Lugano stage IV). After administration of three courses of alternating hyper-CVAD with high-dose methotrexate and cytarabine he underwent umbilical cord blood transplantation at 1<sup>st</sup> Complete Remission (CR) and has maintained CR for more than 33 months. Intestinal T-LBL is very rare and has poor prognosis. To understand this disease, accumulating each case precisely and further investigation are very important.

### OPEN ACCESS

**Keywords:** T-lymphoblastic lymphoma; Jejunum; Umbilical cord blood transplantation

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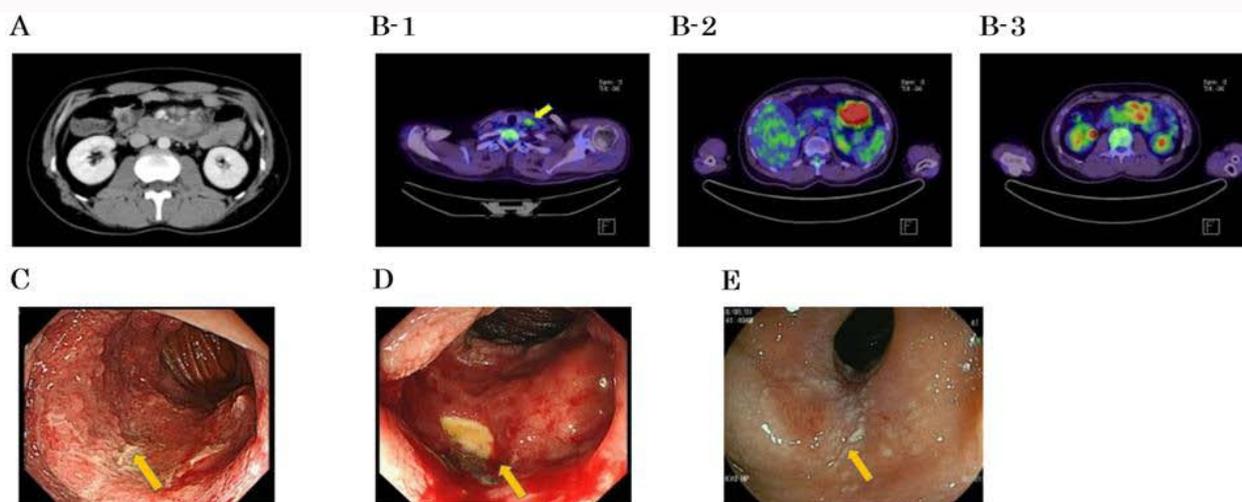
### Introduction

Lymphoblastic Lymphoma (LBL) is a highly aggressive form of Non-Hodgkin's Lymphoma (NHL), comprising approximately 2% of all adult NHL cases [1]. The World Health Organization classification of lymphoid neoplasms has unified these entities as precursor T-cell or B-cell lymphoblastic leukemia/lymphoma [2]. T-LBL is more common than B-LBL; 85% to 90% of all cases of LBL are of T-LBL [3]. T-LBL is typically seen in adolescents and young adults, predominantly in males, and presents as a mediastinal mass in 60% to 70% of cases often accompanied by compression of the superior vena cava or pericardial and/or pleural effusion [4]. Extranodal lesions of T-LBL occur mostly in bone marrow, skin, testis, and bone. Also, a 5% to 10% incidence of central nervous system involvement at presentation has been reported. On the other hand, there are few reports that T-LBL has intraperitoneal lesion or digestive tract involvement [5,6].

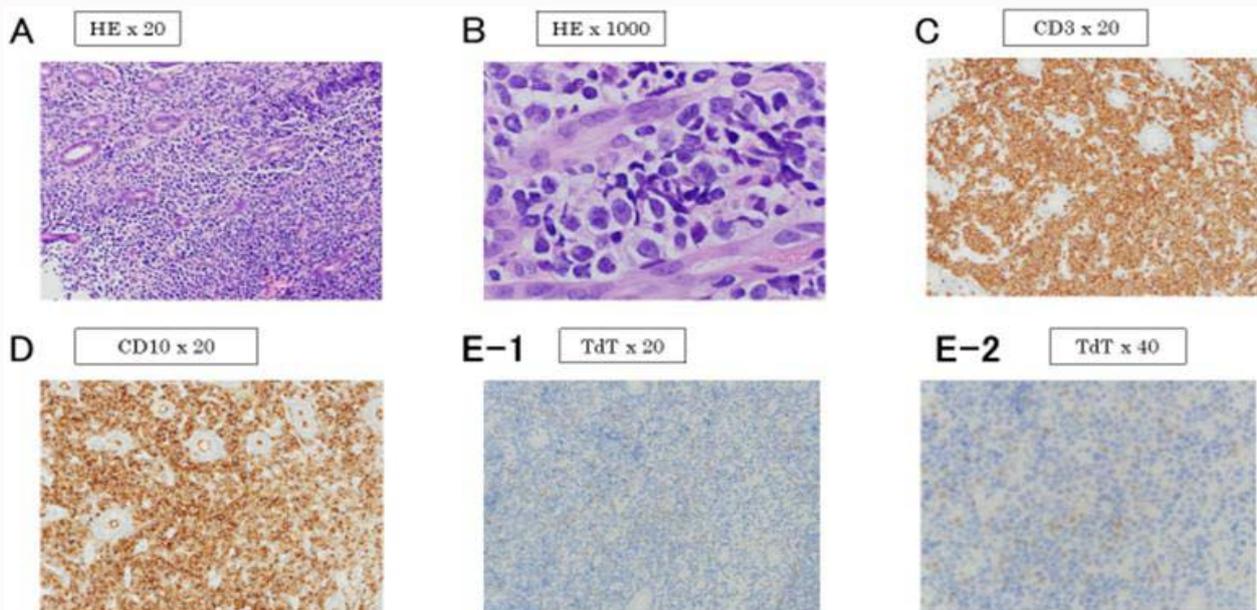
We report here a young male who developed primary jejunal T-LBL. After administration of Acute Lymphocytic Leukemia (ALL) -type intensive chemotherapy he achieved Complete Remission (CR). Then he underwent allogeneic Umbilical Cord Blood Transplantation (UCBT) and has maintained CR for more than 33 months.

### Case Presentation

A 29-year-old male was admitted to our hospital due to intermittent epigastralgia and back pain for two weeks. He had no B symptoms. Body surface lymph nodes were not palpable. No abnormal cardio-pulmonary signs were found. Neither liver nor spleen was palpable. He felt tenderness at epigastric area without rebound tenderness. Abdomen was soft and flat with normal bowel sound. His hemoglobin level was 13.6 g/dL (16.8 g/dL: Data from 6 months ago). Serum LD level was 288 U/L (normal range: 124 to 222), CRP: 2.39 mg/dL (0.00 to 0.14), soluble interleukin 2 receptor: 517 U/mL (122 to 496). An abdominal contrast-enhanced Computed Tomography (CT) showed



**Figure 1:** A) Abdominal CT shows thickness and fluid collection in jejunum. Around jejunum there are increased CT value of panniculitis and lymphadenopathies. B1-3) 18F-FDG PET/CT shows abnormal accumulations in the abdomen and left supra-clavicular lymph node (yellow arrow). C) Esophagogastroduodenoscopy (EGD) shows circumferential ulcerative tumor in jejunum adjacent to Treitz' ligament (yellow arrow). D) After the first hyper - CVAD, EGD shows the reduced tumor size with ulcer (yellow arrow). E) After the alternating high dose MA, EGD shows the lesion is scarred (yellow arrow).



**Figure 2:** Histopathological finding. A, B) Hematoxylin-eosin (HE) staining. Diffuse proliferation and infiltration of the medium to large sized lymphoblasts to lamina propria and granulation tissue of the ulcer bottom (x20). B) High magnification (x1000). Nucleolus is apparent observed in lymphoblasts. C-E) Immunohistochemical staining. The cells are positive for CD3, CD10 and partially positive for TdT. C). D). E1) x20 and E2) x40.

thickness of jejunal wall with fluid collection, increased density of CT value in peri-jejunal fatty tissue, enlargement of peri-jejunal lymph nodes, and mild ascites (Figure 1A). An Esophagogastroduodenoscopy (EGD) showed an ulcerative tumor with bleeding at proximal end of jejunum beyond the Treitz ligament (Figure 1C). The biopsy histopathology from the tumor revealed middle to large sized abnormal lymphoblasts with apparent nucleolus were proliferated into lamina propria and granulation tissue of ulcer bottom (Figure 2A and 2B). Immunohistochemical staining revealed that lymphoblasts were positive for CD3, CD5, CD10, CD79a, BCL2, and negative for CD4, CD8, and CD20 (Figure 2C and 2D, and data not shown) with MIB1 index (Ki-67) of 70%. Terminal deoxynucleotidyl Transferase (TdT) staining was partially positive (Figure 2E1 and 2E2). A

18F-Fluorodeoxyglucose (FDG)-Positron Emission Tomography (PET)/CT showed abnormal FDG uptake from the duodenum to jejunum (maximum standard unit value (SUV max): 9.07), peri-jejunal lymph nodes, and left supraclavicular fossa lymph node (Figure 1B1-1B3). Abnormal FDG uptake was also observed at many enlarged mediastinal lymph nodes and para-aortic lymph nodes. A bone marrow biopsy did not show abnormal lymphoblasts' infiltration. His cerebrospinal fluid test was also negative for lymphoblasts. We diagnosed him with T-LBL (Lugano stage IV).

He received one course of hyper-CVAD (cyclophosphamide, vincristine, doxorubicin, dexamethasone). After the first course of chemotherapy, EGD revealed the tumor was reduced in size (Figure 1D). After alternating high-dose methotrexate and cytarabine (MA

**Table 1:** The cases of T-LBL in primary small intestine.

	Age/ Sex	Symptom	Onset Site	Macroscopic	Other involvements	Stage*	Tx	Survival
Chinu [15]	29 M	Abdominal pain edema BW loss (protein-losing enteropathy)	Multiple	Tumor ulcer	LN (both supra -clavicular fossae, left axilla, both groins, retrocrual and para- aortic areas)	IV	CTx	2M Deceased (intestinal he morrhage)
Tsutsumi [16]	68 M	Edema BW loss (protein- losing enteropathy)	Multiple	Ulcer	Ascites	II E	U	2M Deceased (intestinal he morrhage)
Katoh [14]	36 M	Abdominal pain	Jejunum	Tumor	-	I	Ope CTx	10M Alive
Present Case	29 M	Abdominal pain	Jejunum	Tumor	LN (both supra -clavicular fossae, multiple mediastinal and abdominal areas)	IV	CTx UCBT	33M Alive

BW: Body Weight; LN: Lymph Node; CTx: Chemotherapy; Ope: Operation; UCBT: Umbilical Cord Blood Transplantation; M: Months; U: Unavailable

\*Lugano Classifications

therapy EGD showed the tumor was scarred and slight stenosis was observed (Figure 1E). Biopsy specimen was negative for lymphoblasts. An abdominal contrast-enhanced CT showed the shrinking of enlarged lymph nodes. This chemotherapy regimen was effective, and total 3 courses of alternating hyper-CVAD with high-dose MA were administered to him and he achieved Complete Remission (CR) confirmed by contrast-enhanced CT and gastrointestinal endoscopy. Then, we planned upfront umbilical cord blood transplantation at 1<sup>st</sup> CR. Conditioning was 12 Gray of total body irradiation (6 fractionations), etoposide 30 mg/kg, and cyclophosphamide 120 mg/kg. Total nuclear cell number of the transplant cord blood graft was  $2.24 \times 10^8$ /kg (CD34-positive cells:  $0.42 \times 10^5$ /kg) and the graft was from HLA 1 locus-mismatched female. Immunosuppressive agents consisted of tacrolimus 0.03 mg/kg with short term methotrexate (15 mg/m<sup>2</sup> on day 1, 10 mg/m<sup>2</sup> on day 3, and 6 he was discharged on day 65 and has been in CR.). Engraftment was observed: Neutrophils were on day 27, erythroid on day 31, and platelet on day 36. No serious complications were found including sepsis, sinusoidal obstruction syndrome, and thrombotic microangiopathy. On day 45 stage 3 skin graft-versus-host diseases was observed, which was recovered with the administration of prednisolone. Cytomegalovirus antigenemia was also observed, that was treated with ganciclovir. He was discharged on day 65 and has been in CR for more than 33 months.

## Discussion

The diagnosis of T-LBL is, essentially, a presence of immature lymphoblast, and further relies on immunophenotypic demonstration of T-cell lineage with CD3, the most specific T-cell marker [7]. T-LBL is a highly heterogeneous disease, and CD4, and 8 double negative T-LBL as well as double positive are reported. Interestingly, many CD10 positive T-LBL cases have been reported [8]. A rare T-LBL case was reported that TdT, an enzyme expressed in immature cells, was negative [9]. In our case CD3, 5, 10, 79a, and BCL2 positive, double negative, TdT partially positive lymphoblasts were proliferated, and T-LBL diagnosis was made histopathologically. The definition of primary malignant lymphoma of the gastrointestinal tract is applied by Lewin's criteria in which "if the main lesion is in the gastrointestinal tract, the gastrointestinal tract is regarded as the primary organ regardless of the stage" [10]. Our patient had epigastralgia and back pain at his disease onset, and imaging study also revealed proximal jejunum was the main lesion of disease. Thus, we made diagnosis of his disease as primary jejunal T-LBL. Also, according to Lugano staging system for gastrointestinal lymphomas his clinical stage was IV [11].

In general, gastrointestinal lymphoma accounts for 5% to 20% of NHL and 30% to 50% of extranodal lymphomas, with the stomach being the most primary site (60% to 80%), and then the small intestine (20% to 30%) and the large intestine (5% to 10%)

[12]. Histopathologically diffuse large B-cell lymphoma is the most common, and T-cell lymphoma is reported to be 11% to 13% [13]. Histology of most gastrointestinal T-cell lymphoma is peripheral T-cell lymphoma not otherwise specified, and gastrointestinal T-LBL is precisely reported only as a case [14-16]. Table 1 shows 4 case reports including our case in which two cases were dead with multiple ulcer-formation and protein-losing gastroenteropathy, and one localized stage patient is alive with surgical resection and chemotherapy. Gastrointestinal T-cell lymphoma shows poor prognosis with 5-year survival of 28% compared with B-cell lymphoma with 71%, because many intestinal complications are reported such as perforation, bleeding, and intestinal obstruction [17]. It is not well understood why T-LBL has more serious complications than B-LBL. Our case also had a high risk for perforation and bleeding because tumor was ulcerative and bleeding was observed. Thus, gastrointestinal T-LBL is very rare and has high risk for sudden fatal deterioration and very poor prognosis.

LBL is highly progressive like ALL and specific research on LBL treatment has been conducted. Conventional NHL treatment protocols yielded low rates of CR, low rates of disease free survival, high relapse rates, and finally low rates of overall survival. Although intensive protocols for aggressive NHL have increased the CR rate, overall survival remained poor [17]. Improvements in long-term outcome have been achieved with ALL-type regimens for LBL. With the alternating hyper-CVAD with high-dose MA regimen followed by maintenance therapy CR was reportedly 91%, and 3-year progression-free and overall survival was 66% and 70%, respectively [18]. However, gastrointestinal T-LBL is very rare and shows worse prognosis, and the established treatment strategy has not been reported. A retrospective analysis of 48 Partial Remission (PR)/CR T-LBL cases indicates that allogeneic Hematopoietic Stem/progenitor Cell Transplantation (HSCT) is superior to only chemotherapy after alternative hyper CVAD/MA in which 3-year overall survival is 72.8% in HSCT group and 17.5% in chemotherapy group, respectively [19]. Recently it was reported that 21 T-LBL patients including 2 cases with gastrointestinal extranodal lesions underwent upfront HSCT and 5-year overall survival rate of 79.5% in standard disease (1st CR or 1st PR) [20]. Although the number of patients was small it is promising to achieve upfront allogeneic HSCT to T-LBL patients in standard disease.

We report here that jejunal T-LBL was successfully treated with ALL-type chemotherapy followed by upfront allogeneic HSCT. To understand this disease, accumulating each case precisely and further investigation are very important.

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