CASE REPORT

Gut and Liver, Vol. 6, No. 4, October 2012, pp. 516-519

A Case of Enteropathy-Type T-Cell Lymphoma Diagnosed by Small Bowel Enteroscopy: A Perspective on Imaging-Enhanced Endoscopy

Jun Yong Bae*, Bong Min Ko*, Seul Ki Min*, Jong Chan Lee*, Gun Wha Lee*, La Young Yoon*, Su Jin Hong*, Moon Sung Lee*, and Hee Kyung Kim†

*Departments of *Internal Medicine and †Pathology, Soonchunhyang University Bucheon Hospital, Soonchunhyang University College of Medicine, Bucheon, Korea*

Enteropathy-type T-cell lymphoma (ETL) or enteropathy-associated T-cell lymphoma is a very rare malignant intestinal tumor. ETL is usually diagnosed by surgery. Endoscopic findings of ETL are not well known, and there are few reports of findings from endoscopy that has been performed only using white light. Additionally, there are no definite treatment guidelines for ETL. Therefore, we report a case of ETL diagnosed by enteroscopy with imaging-enhanced endoscopy and also review recently developed treatment options. **(Gut Liver 2012;6:516-519)**

Key Words: Enteropathy-type T-cell lymphoma; Imaging enhanced endoscopy; Narrow band image

INTRODUCTION

Enteropathy-type T-cell lymphoma (ETL) is primary extranodal T-cell lymphoma arising in the intestine originating from intraepitheial T-cells.[1] ETL is very rare and accounts for fewer than 5% of all gastrointestinal tract lymphomas. The clinical course of ETL is very aggressive. Five-year survival rate is 20% to 25%.[2-6] The treatment options are chemotherapy with or without radiotherapy and surgery. Currently, there are no definite treatment guidelines for ETL. Diagnosis of ETL was very difficult and usually made by surgery because of complications of ETL at presenting time, such as intestinal perforation or obstruction, or lack of endoscopic experiences. There were few articles about endoscopic findings of ETL with only white light and capsule endoscopy.[7-12]

CASE REPORT

A 70-year-old malnourished male patient visited because of anemia and hematochezia. Hemoglobin was 8.9 g/dL and albumin was 2.9 g/dL. There was no definite bleeding focus found on gastroscopy and colonoscopy. Relatively long segmental wall thickening of jejunum with mild dilatation, fluid collection and suspicious mesenteric fat infiltration was noted on abdominal computed tomography. Increased fluorodeoxyglucose (FDG) uptake (SUV, 6.0) was also noted on 18-FDG positron emission tomography (Fig. 1). To evaluate for obscure gastrointestinal

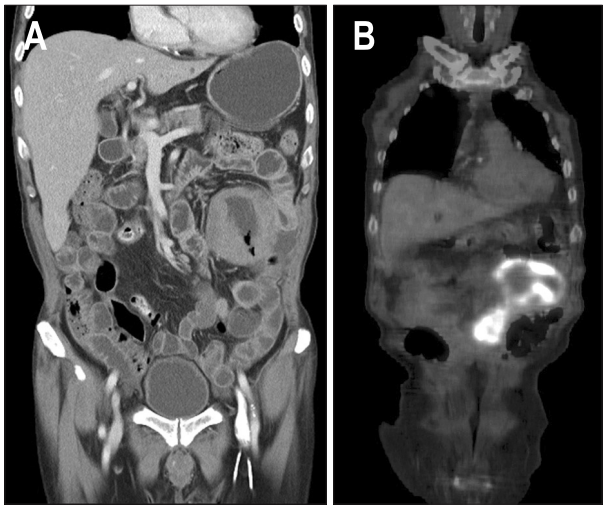

Fig. 1. Abdominal computed tomography (CT) and positron emission tomography (PET) CT. (A) Diffuse enhancing wall thickening and mild dilatation with fluid collection of jejum is noted on abdominal CT. (B) Long segmental hypermetabolism (SUV, 6.0) is noted on 18-fluorodeoxyglucose PET.

Correspondence to: Moon Sung Lee
Department of Internal Medicine, Soonchunhyang University Bucheon Hospital, Soonchunhyang University College of Medicine, 170 Jomaru-ro, Wonmi-gu, Bucheon 420-767, Korea
Tel: +82-32-621-5096, Fax: +82-32-621-5080, E-mail: mslee@schmc.ac.kr
Received on August 19, 2010. Revised on November 22, 2010. Accepted on December 28, 2010.
pISSN 1976-2283 eISSN 2005-1212 http://dx.doi.org/10.5009/gnl.2012.6.4.516

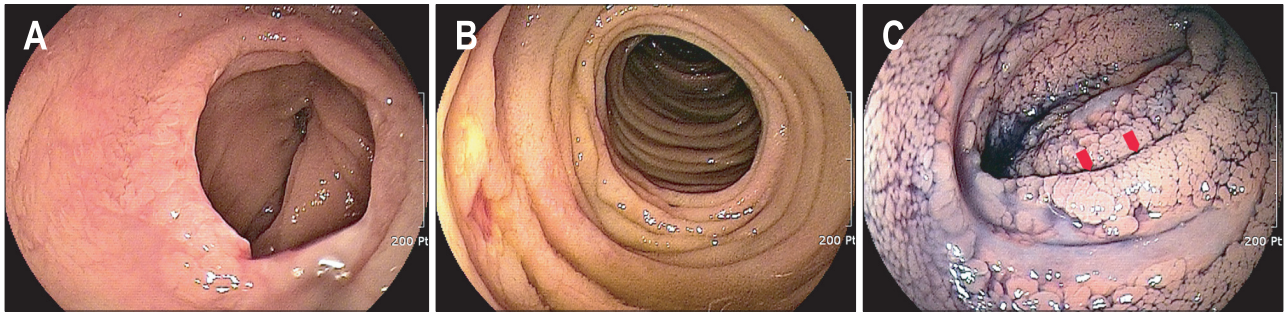

Fig. 2. Double-balloon enteroscopy. (A, B) White light. (C) Chromoendoscopy (indigocarmin). There are multiple small shallow ulcers, mucosal edematous changes, and fusion on villi (red arrows) in the jejunum.

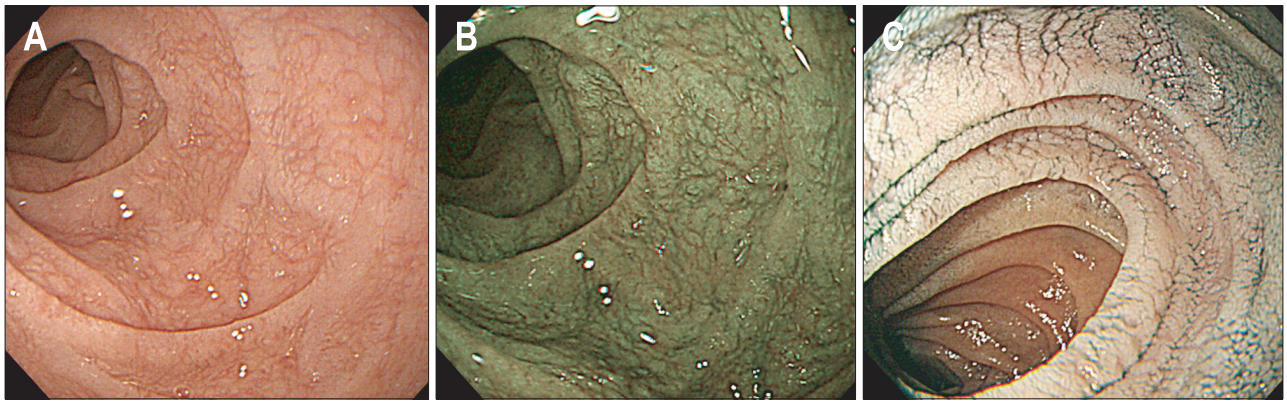

Fig. 3. Push enterocopy. (A) White light. (B) Narrow band imaging (NBI). (C) Chromoendoscopy (indigocarmin). There are mucosal thickening and fine granular mucosa (mosaic or fissured mucosa like pattern) in the jejunum. More prominent nodularity shows with NBI and indigocarmin spray.

bleeding and small intestinal mass, double-balloon enteroscopy (EN-450T5; Fujinon, Saitama, Japan) was performed via oral route and showed multiple small shallow ulcerations, edematous villi and fusion of villi (Fig. 2). Push enteroscopy with conventional colonoscopy via oral route (CF-H260AL; Olympus, Tokyo, Japan) showed mosaic and fissured like villi and more prominent nodularity mucosal pattern with narrow band imaging (NBI) and indigocarmin spray (Fig. 3). The biopsy result was mature T-cell lymphoma. Immunohistochemical staining showed CD3 (+), CD8 (+), CD56 (+), TLA-1 (+), CD4 (-), CD5 (-), CD20 (-), and CD30 (-) (Fig. 4).[13] On bone marrow examination, there was no abnormality.

The patient was treated with rituximab, cyclophosphamide, adriamycin, vincristine, and prednisone (R-CHOP) chemotherapy and radiotherapy. Six months after the initial diagnosis, the patient underwent an operation because of intestinal obstruction with perforation and died from sepsis.

DISCUSSION

Mean age of diagnosed ETL was 60 years old and sex ratio of ETL was about 1:1 (male:female). ETL commonly arises in the proximal jejunum. But, less frequently, ETL can arise anywhere in the small intestine, stomach and colon. About 40% of ETL patients have acute clinical manifestations such as acute peritonitis due to perforation and intestinal obstruction which needs emergent operation. Other clinical manifestations are abdominal pain, weight loss and protein losing enteropathy. In early disease, ETL is localized in gastrointestinal tract or mesenteric lymph node. As progression of disease, it can spread to liver, spleen, skin, or other organs.[5,14] Prognosis of ETL is very poor. Five-year survival rate is 20% to 25%.[2-6]

Few endoscopic findings of ETL were reported by enteroscopy and capsule endoscopy.[7-12] Typical endoscopic findings of ETL are multiple shallow ulcerations and diffuse thickening of mucosa with innumerable coarse or fine granular elevations (mosaic mucosal pattern). No articles have been published about NBI of ETL. In our case of ETL, more prominent mucosal nodularity and scalloing was observed with NBI and indigocarmin spray. The specimen of ETL endoscopic mucosal biopsy shows that mucosal edema and villous distortion by tumor cell infiltration (Fig. 3). This is a reason of nodularity with NBI and indigocarmin spray.

There is no definite treatment guideline of ETL. The surgery for ETL has poor outcomes and its role is limited to debulking and/or treatment of ETL complications such as perforation and obstruction. Radiation therapy has been indicated for bulky disease or incomplete resection. Chemotherapy such as vincristine,

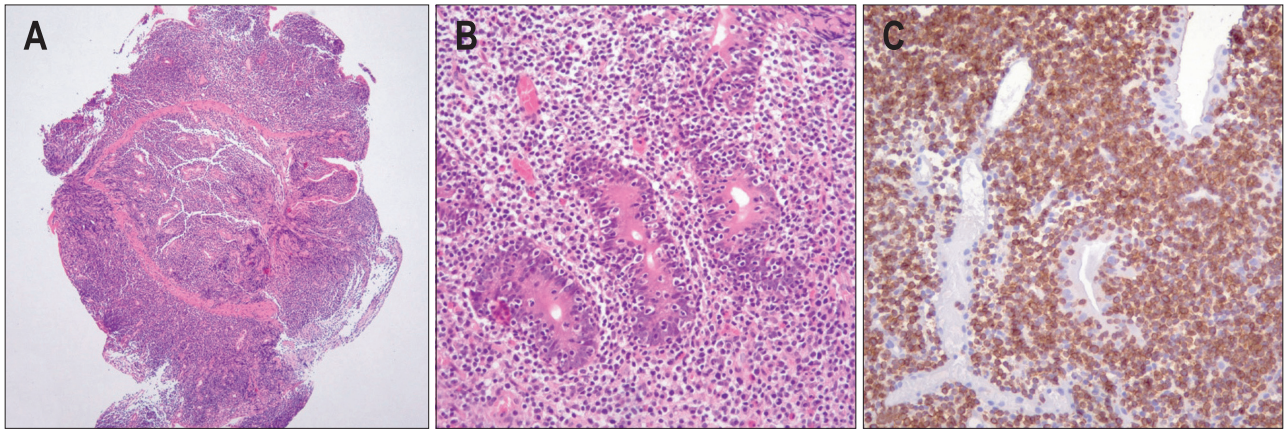

Fig. 4. Histologic pictures of biopsy specimen. (A) Mucosal edema and distortion of villi (H&E stain, ×100). (B) Dense infiltration of small matured lymphocyte in the mucosa and lamina propria is noted (H&E stain, ×200). (C) Immunohistochemical staining of CD3 was positive (×200).

doxorubicin, methotrexate, and prednisolone (VAMP); vincristine, doxorubicin, and prednisolone (VAP); CHOP; procarbazine, etoposide, prednisolone,and doxorubicin (PEPA); cyclophosphamide, etoposide, vincristine, and prednisone (CEOP); prednisolone, cytarabine, lomustine, etoposide, and thioguanine-bleomycin, vincrisitine and methotrexate (PEACE-BOM); and surgery are options for treatment of ETL.[5] But, more than half were unable to complete their planned chemotherapy courses and early treatment failure is frequently occurred because of malnourished state and complications of disease or chemotherapy. Overall response rate of treatment is 58%. But 16% of patients died after first cycle of chemotherapy. Mean recurrence time after chemotherapy or surgery was 6 months.

Recently, some clinical trials for feasibility and activity of high-dose chemotherapy supported by autologous stem cells transplantation (ASCT) as therapeutic option for ETL in small series[15-17] and retrospective studies.[18-20] In these clinical trials, ASCT could increase overall survival rate, even up to 60%. There are two reports of chemotherapy with ASCT about prevention of ETL[21] and reduction in aberrant T-cells in patients with refractory celiac disease.[22]

Alemtuzumab, humanized anti-CD52 monoclonal antibody currently used in treatment of chronic lymphocytic leukemia or T-cell lymphoma, can be another option for ETL.[23,24] Alemtuzumab can treat ETL successfully with chemotherapy. But, all ETL cases who were treated by alemtuzumab were only two. There is the report about increased risk for ETL with using this monoclonal antibody for treatment of refractory celiac disease.[25] So, more clinical studies are needed for alemtuzumab.

In conclusion, ETL is a very rare intestinal tumor. The endoscopic characteristics are edematous vili, fusion of vili, and multiple shallow ulcerations. In chromoendoscopy, indigocarmin and NBI, prominent mucosal noduarity, fissured or mosaic patterns are the characteristics of ETL. There is no treatment guideline for ETL. But, recently, molecular target agent such as alemtuzumab and ASCT can be the treatment options for ETL instead of conventional chemotherapy with poor outcomes.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

REFERENCES

1. O'Farrelly C, Feighery C, O'Briain DS, et al. Humoral response to wheat protein in patients with coeliac disease and enteropathy associated T cell lymphoma. Br Med J (Clin Res Ed) 1986;293:908-910.
2. d'Amore F, Brincker H, Gronbaek K, et al. Non-Hodgkin's lymphoma of the gastrointestinal tract: a population-based analysis of incidence, geographic distribution, clinicopathologic presentation features, and prognosis. Danish Lymphoma Study Group. J Clin Oncol 1994;12:1673-1684.
3. Morton JE, Leyland MJ, Vaughan Hudson G, et al. Primary gastrointestinal non-Hodgkin's lymphoma: a review of 175 British National Lymphoma Investigation cases. Br J Cancer 1993;67:776-782.
4. Daum S, Hummel M, Weiss D, et al. Refractory sprue syndrome with clonal intraepithelial lymphocytes evolving into overt enteropathy-type intestinal T-cell lymphoma. Digestion 2000;62:60-65.
5. Gale J, Simmonds PD, Mead GM, Sweetenham JW, Wright DH. Enteropathy-type intestinal T-cell lymphoma: clinical features and treatment of 31 patients in a single center. J Clin Oncol 2000;18:795-803.
6. Honemann D, Prince HM, Hicks RJ, Seymour JF. Enteropathy-associated T-cell lymphoma without a prior diagnosis of coeliac disease: diagnostic dilemmas and management options. Ann Hematol 2005;84:118-121.
7. Joyce AM, Burns DL, Marcello PW, Tronic B, Scholz FJ. Capsule endoscopy findings in celiac disease associated enteropathy-type intestinal T-cell lymphoma. Endoscopy 2005;37:594-596.

8. Hadithi M, Akol H, Al-Toma A, Jacobs M, Mulder CJ. Indigo carmine chromoendoscopic appearances of enteropathy-associated T-cell lymphoma during double-balloon endoscopy in a patient with celiac disease. Endoscopy 2007;39 Suppl 1:E212-E213.
9. Hadithi M, Al-toma A, Oudejans J, van Bodegraven AA, Mulder CJ, Jacobs M. The value of double-balloon enteroscopy in patients with refractory celiac disease. Am J Gastroenterol 2007;102:987-996.
10. Yanai S, Matsumoto T, Nakamura S, et al. Endoscopic findings of enteropathy-type T-cell lymphoma. Endoscopy 2007;39 Suppl 1:E339-E340.
11. Daum S, Wahnschaffe U, Glasenapp R, et al. Capsule endoscopy in refractory celiac disease. Endoscopy 2007;39:455-458.
12. Sato Y, Ono M, Sagawa T, et al. Endoscopic findings of enteropathy-type T-cell lymphoma by double-balloon enteroscopy and capsule endoscopy. Dig Endosc 2010;22:243-245.
13. Zettl A, deLeeuw R, Haralambieva E, Mueller-Hermelink HK. Enteropathy-type T-cell lymphoma. Am J Clin Pathol 2007;127:701-706.
14. Isaacson P, Wright D, Ralfkiaer E, et al. Enteropathy-type T-cell lymphoma. In: Jaffe ES, Harris NL, Stein H, et al., eds. Pathology and genetics of tumours of haematopoietic and lymphoid tissues. Lyon: IARC Press, 2001:208-209.
15. Okuda M, Nomura J, Tateno H, Kameoka J, Sasaki T. CD56 positive intestinal T-cell lymphoma: treatment with high dose chemotherapy and autologous peripheral blood stem cell transplantation. Intern Med 2002;41:734-737.
16. Al-Toma A, Verbeek WH, Visser OJ, et al. Disappointing outcome of autologous stem cell transplantation for enteropathy-associated T-cell lymphoma. Dig Liver Dis 2007;39:634-641.
17. Rongey C, Micallef I, Smyrk T, Murray J. Successful treatment of enteropathy-associated T cell lymphoma with autologous stem cell transplant. Dig Dis Sci 2006;51:1082-1086.
18. Bishton MJ, Haynes AP. Combination chemotherapy followed by autologous stem cell transplant for enteropathy-associated T cell lymphoma. Br J Haematol 2007;136:111-113.
19. d'Amore F, Relander T, Lauritzen GF, et al. Dose-dense induction followed by autologous stem cell transplant (ASCT) leads to sustained remissions in a large fraction of patients with previously untreated peripheral t-cell lymphomas (PTCLS): overall and subtype-specific results of a phase ii study from the nordic lymphoma group. Haematologica 2009;94(Suppl 2):437.
20. Sieniawski M, Angamuthu N, Boyd K, et al. Evaluation of enteropathy-associated T-cell lymphoma comparing standard therapies with a novel regimen including autologous stem cell transplantation. Blood 2010;115:3664-3670.
21. Meijer JW, Mulder CJ, Goerres MG, Boot H, Schweizer JJ. Coeliac disease and (extra)intestinal T-cell lymphomas: definition, diagnosis, and treatment. Scand J Gastroenterol Suppl 2004:78-84.
22. Al-toma A, Visser OJ, van Roessel HM, et al. Autologous hematopoietic stem cell transplantation in refractory celiac disease with aberrant T cells. Blood 2007;109:2243-2249.
23. Gallamini A, Zaja F, Patti C, et al. Alemtuzumab (Campath-1H) and CHOP chemotherapy as first-line treatment of peripheral T-cell lymphoma: results of a GITIL (Gruppo Italiano Terapie Innovative nei Linfomi) prospective multicenter trial. Blood 2007;110:2316-2323.
24. Soldini D, Mora O, Cavalli F, Zucca E, Mazzucchelli L. Efficacy of alemtuzumab and gemcitabine in a patient with enteropathy-type T-cell lymphoma. Br J Haematol 2008;142:484-486.
25. Vivas S, Ruiz de Morales JM, Ramos F, Suárez-Vilela D. Alemtuzumab for refractory celiac disease in a patient at risk for enteropathy-associated T-cell lymphoma. N Engl J Med 2006;354:2514-2515.