Case Report

Type II Enteropathy-Associated T-Cell Lymphoma: A Case Report and Literature Review

L Zhao, Y Yang, Y Zhang

Department of Gastroenterology, West China Hospital of Sichuan University, Chengdu, China

ABSTRACT

Type II enteropathy-associated T-cell lymphoma (Type II EATL) is a rare peripheral T-cell lymphoma of the gastrointestinal tract. Here, we report a case of Type II EATL, in which the patient with repeated diarrhea was diagnosed as ulcerative colitis and amebic infection at the beginning, but her symptom had no improvement after therapy. The diagnosis of Type II EATL was confirmed by the repeated biopsies and immunohistochemistry. This case suggests that Type II EATL is difficult to diagnose due to lack of specific symptoms and endoscopic features. It reminds us that for patients with increased intraepithelial lymphocytes and thickened bowel wall, lymphoma should be highly suspected and biopsy should be repeated if necessary.

KEYWORDS: *Enteropathy-associated T-cell lymphoma, intraepithelial lymphocytes, repeated diarrhea, thickened bowel wall*

Date of Acceptance:
25-Oct-2017

INTRODUCTION

Enteropathy-associated T-cell lymphoma (EATL) is a rare peripheral T-cell lymphoma of the gastrointestinal tract, which can be divided into two types.[1] Type I is closely associated with celiac disease, of which tumor cells are large, pleomorphic, and positive for CD3 and CD7 but negative for CD4, CD8, or CD56.[2,3] Type II occurs sporadically, of which tumor cells are small to intermediate in size and displays CD8+, CD56+, and CD3+.[4] The latter is rare in Western countries but has already been reported in Asia.[5,6] However, it is difficult to diagnose due to lack of specific symptoms. The diagnosis of EATL was mainly made by laparotomy, and most of them had an emergency procedure because of perforation.[7] Here, we reported a case of Type II EATL, which was diagnosed by endoscopy and repeat biopsy.

CASE REPORT

A 47-year-old female came to our hospital with repeated diarrhea and weight loss for 3 months. She had watery diarrhea, 500–700 ml/day, without abdominal pain, hematochezia, or fever. She was healthy before, without a history of other diseases such as diabetes, hypertension, and medication exposures. Two months before presentation, she went to a local hospital. Colonoscopy showed scattered congestion, edema, and erosion in the rectum. Biopsies showed inflammatory necrosis, lots of lymphocytes, and plasma cells. Tests for infection were negative. Ulcerative colitis (UC) was diagnosed, and 5-aminosalicylic acid was given, but her symptoms had no change.

On admission, her physical examination was unremarkable. Laboratory tests showed normal erythrocyte sedimentation rate 31.0 mm/h, elevated C-reactive protein 16.6 mg/L, mild anemia (hemoglobin: 75 g/L), and albumin 23.7 g/L. Other laboratory results were shown in Table 1. Microscopic examination of stool showed occult blood +, pus cells +++, and leukocytes+++/HP. Endoscopy was repeated. Gastroscopy was normal. Colonoscopy revealed scattered congestion and erosion in the whole colon, especially in the rectum; and the ileocecal valve was deformed. The biopsies from rectum showed the infiltration of numerous small/medium lymphocytes in the lamina propria. Immunohistochemistry showed

Address for correspondence: Dr. Y Zhang, Department of Gastroenterology, West China Hospital of Sichuan University, No. 37, Guoxue Alley, Chengdu, China.
E-mail: hxzyan@163.com

How to cite this article: Zhao L, Yang Y, Zhang Y. Type II enteropathy-associated T-cell lymphoma: A case report and literature review. Niger J Clin Pract 2017;XX:XX-XX.

Access this article online	
Quick Response Code:	**Website**: www.njcponline.com
	DOI: 10.4103/njcp.njcp_280_17
	PMID: *******

Table 1: The patient's laboratory results of blood chemistry and tumor markers

Items	Results on admission	Reference value
Red blood cell count ($\times10^{12}$/L)	2.92	3.8-5.1
Hemoglobin (/L)	75	115-150
Mean corpuscular volume (fL)	76.7	82-100
Platelet count ($\times10^{9}$/L)	325	100-300
White cell count($\times10^{9}$/L)	10.78	3.5-9.5
Neutrophils (%)	82.7	40-75
Lymphocytes (%)	10.7	20-50
Eosinophils (%)	0.2	0.4-8.0
Monocytes (%)	6.3	3-10
Total bilirubin (umol/L)	5.0	5.0-28.0
Direct bilirubin (umol/L)	0.9	<8.8
Indirect bilirubin (umol/L)	4.1	<20
Alanine aminotransferase (IU/L)	9	<40
Aspartate aminotransferase (IU/L)	9	<35
Total protein (g/L)	47	65.0-85.0
Albumin (g/L)	23.7	40-55
Globulin (g/L)	23.3	20.0-40.0
Glucose (mmol/L)	6.06	3.9-5.9
Urea (mmol/L)	9.99	2.95-7.70
Creatinine (umol/L)	108	37-110
Serum cystatin C (mg/L)	1.37	0.51-1.09
Uric acid (umol/L)	390.0	160.0-380.0
Triglyceride (mmol/L)	1.09	0.29-1.83
Cholesterin (mmol/L)	2.67	2.8-5.7
High-density lipoprotein (mmol/L)	0.73	>0.9
Low-density lipoprotein (mmol/L)	1.28	<4.0
Na (mmol/L)	137.0	137.0-147.0
K (mmol/L)	3.85	3.5-5.3
Cl (mmol/L)	113.6	99-110
Ca (mmol/L)	1.70	2.1-2.7
Mg (mmol/L)	0.59	0.67-1.04
Fe (umol/L)	7.3	6.6-30.4
Total iron binding capacity (umol/L)	33.60	48.3-68.0
Transferrin (g/L)	1.37	2.5-4.3
Ferritin (ng/ml)	310.5	24-336
Erythropoietin (mIU/ml)	9.47	3.7-29.5
Serum iron saturation (%)	21.7	20-55
Anti-intrinsic factor antibody (AU/ml)	1.02	1.02-1.53
Serum Vitamin B12 (pg/ml)	306.0	180-914
Serum folic acid (ng/ml)	11.52	3.2-18.5
IgA (mg/L)	2970.0	836-2900
IgG (g/L)	14.00	8.00-15.50
Immunoglobulin M (mg/L)	1710.00	700-2200
Immunoglobulin E (IU/ml)	11.02	0.1-150.0
KAP (g/L)	8.48	6.98-13.00
LAM (g/L)	6.03	3.80-6.50
EBV-CA-IgA	Negative	
EBV-CA-IgG	Negative	
EBV-DNA	Negative	
T-SPOT.TB	Positive	
Lymphocyte culture + IFN (T) (pg/ml)	21.21	
Lymphocyte culture + IFN (P) (pg/ml)	277.92	
IGRA (P-N)	Normal	
IGRA (N/4)	Normal	
TB-IGRA (T-N) (pg/ml)	17.43	0-14
Lymphocyte culture + IFN (N) (pg/ml)	3.78	
GBM antibody (RU/ml)	<2.00	<20
Procalcitonin (ng/ml)	0.26	<0.046
Carcinoembryonic antigen (ng/ml)	5.81	<3.4
CA 19-9 (U/mL)	8.84	<22
CA-125 (U/mL)	9.52	<35
Alpha fetoprotein (ng/ml)	1.57	<8

IgA=Immunoglobulin A; IgG=Immunoglobulin G; EBC=Epstein-Barr Virus; INF=Interferons; TB=Tuberculosis; GBM=Glomerular basement membrane; KAP=Kinase activator protein; LAM=Lipoarabinomannan; CA= Cancer antigen; T-SPOT=Enzyme-linked immunospot assay; IGRA=Interferon Gamma Release Assay

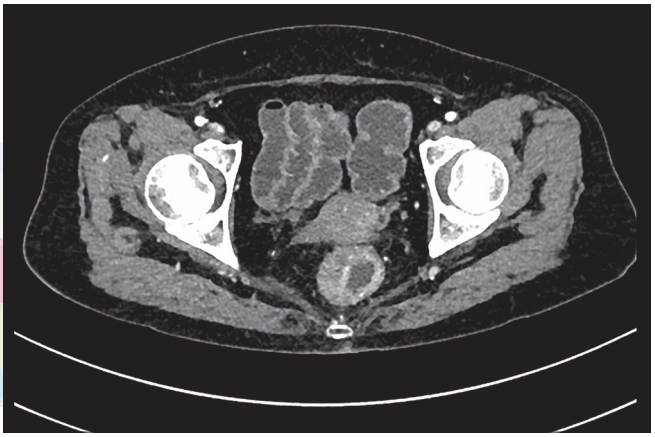

Figure 1: The walls of rectum were unevenly thickened and enhancement

CD20 (+), CD43 (partial positive), CD3ε (−), CD5 (−), CD10 (−), CD23 (−), Cyclin D1 (−), Ki-67 (MIB-J, +, 3%), IgH, and TCRγ gene rearrangement did not show clonal amplification. Samples from the local hospital were checked again. The results also suggested numerous lymphocytes in the mucosal and submucosal. Immunohistochemistry showed CD3ε (partial positive), CD20 (partial positive), CD5 (−), CD10 (−), Cyclin D1 (−), Ki-67 (15%–20%). IgH, and TCRγ gene rearrangement did not show clonal amplification. Then, we went through her history again. She had her symptoms during a trip. We checked her stool again. Amebic cyst was found. Metronidazole was prescribed, but her symptom still remained no change.

Computed tomography enterography (CTE) was ordered and showed the walls of distal ileum, ileocecum, sigmoid colon, and rectum were unevenly thickened with enhancement, and the mesenteric lymph nodes were enlarged [Figure 1]. Small bowel endoscopy

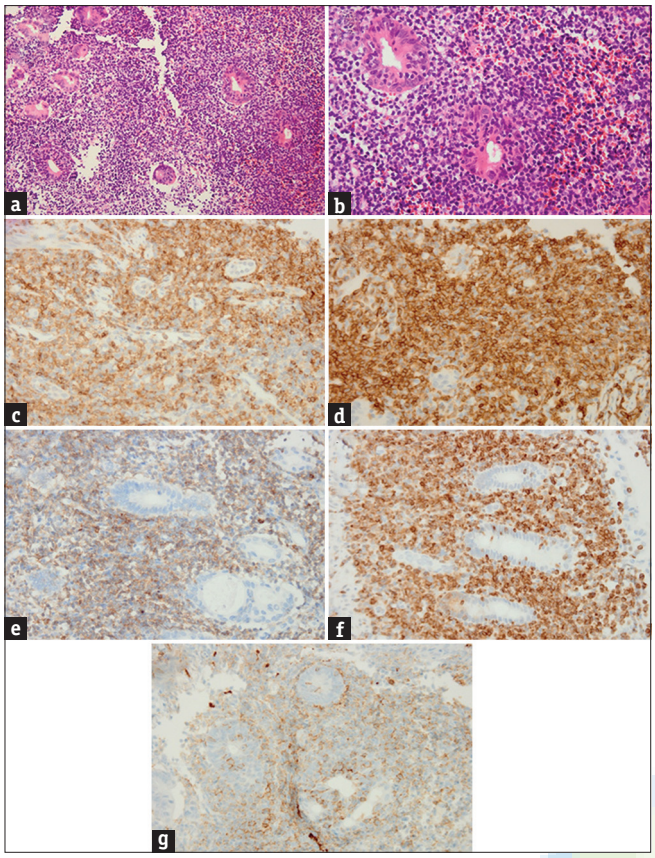

Figure 2: Pathologic and immunohistochemistry pictures of the colon. (a and b) Diffuse infiltration of small lymphoid cells with slightly irregular nuclei extends to the submucosa. (c-g) Immunohistochemical stains for CD2, CD7, CD8, BCL-2, and CD56 were positive. (a: HE (Hematoxylin-eosin staining), ×200; b: HE, ×400)

was performed and revealed normal mucosa of the small bowel. Colonoscopy was performed again, and multiple deep biopsies were taken from the involved bowel (rectum, sigmoid colon, and distal ileum) based on the results of CTE. The results revealed diffuse infiltration of small lymphoid cells which extended to the submucosal. Immunohistochemistry showed that CD8 (+), CD2 (+), CD7 (+), CD20 (some positive), CD56 (±), bc1-2 (+), Granzyme B (−), CD4 (−), CD5 (−), Cyclin D1 (−), CD10 (−), and Ki-67 (the positive rate was 15%) [Figure 2]. TCR-γ gene rearrangement showed clonal amplification peak. *In situ* hybridization for Epstein–Barr virus-encoded RNA was negative. Type II EATL was diagnosed. However, the patient refused chemotherapy and died 4 months later.

Discussion

For lack of specific symptoms and endoscopic features, Type II EATL is difficult to diagnose. In our case, the patient was diagnosed as UC at the beginning, then amebic infection later. However, she had no typical clinical symptoms of UC (diarrhea with blood and mucus) or no typical colonoscopy features (diffuse inflammation in the colon). In addition, 5-ASA did not help her. The diagnosis of amoebic infection was based on the evidence of trophozoites, and metronidazole did not work. It was noticed that her biopsies always showed increased intraepithelial lymphocytes (IEL) and CTE showed bowel wall thickening. Papers were reviewed and it was found that many diseases can cause IEL increase such as celiac disease, EATL, cow's milk intolerance, food allergy, cryptosporidiosis, and giardiasis.[4,8,9] The diseases contributing to the walls of bowel thickening include inflammatory bowel disease, celiac disease, tumors (adenocarcinoma, carcinoid tumor, lymphoma, and gastrointestinal stromal tumor).[10] Celiac disease was ruled out, and lymphoma was highly suspected. Then, multiple deep biopsies were taken from the involved colon based on the results of CTE.

The diagnosis of Type II EATL might pose a challenge because of the features of its pathology. Studies suggested that the neoplasm of Type II EATL could be divided into three zones: central tumor zone, peripheral zone, and intraepithelial lymphocytosis zone (>30 IELs per 100 epithelial cells).[4,8] Monotonous population of lymphomatous cells, which are small sized or medium sized with the slightly larger nuclei and the lighter staining of the chromatin, could be found in the central zone and peripheral zone.[4] While the character of the intraepithelial lymphocytosis zone is the infiltration of small or normal lymphocytes in the epithelium, the lymphocytes have round nuclei and fairly condensed chromatin.[4,8] This zone could be either continuous or discontinuous with the peripheral zone and sometimes far away from the edge of the tumor zone.[8] In addition, the immunophenotype of IEL in this zone can be either identical to or different from the lymphomatous cells.[4,8] Therefore, the increased IEL and the phenotypic variation of IEL might potentially create diagnostic confusion if the physicians happened to biopsy at the intraepithelial lymphocytosis zone. Repeat biopsy at different places may solve this question.

Conclusion

The diagnosis of Type II EATL is difficult due to lack of typical symptoms and specific examination results. This case reminds us that for patients with increased IEL and thickened bowel wall, lymphoma should be highly suspected and biopsy should be repeated if necessary.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will

not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Hong YS, Woo YS, Park G, Lee K, Kang SH, Lee HW, *et al.* Endoscopic findings of enteropathy-associated T-cell lymphoma type II: A Case series. Gut Liver 2016;10:147-51.
2. Delabie J, Holte H, Vose JM, Ullrich F, Jaffe ES, Savage KJ, *et al.* Enteropathy-associated T-cell lymphoma: Clinical and histological findings from the international peripheral T-cell lymphoma project. Blood 2011;118:148-55.
3. Arps DP, Smith LB. Classic versus type II enteropathy-associated T-cell lymphoma: Diagnostic considerations. Arch Pathol Lab Med 2013;137:1227-31.
4. Tan SY, Chuang SS, Tang T, Tan L, Ko YH, Chuah KL, *et al.* Type II EATL (epitheliotropic intestinal T-cell lymphoma): A neoplasm of intra-epithelial T-cells with predominant CD8αα phenotype. Leukemia 2013;27:1688-96.
5. Tomita S, Kikuti YY, Carreras J, Kojima M, Ando K, Takasaki H, *et al.* Genomic and immunohistochemical profiles of enteropathy-associated T-cell lymphoma in japan. Mod Pathol 2015;28:1286-96.
6. Tse E, Gill H, Loong F, Kim SJ, Ng SB, Tang T, *et al.* Type II enteropathy-associated T-cell lymphoma: A multicenter analysis from the Asia lymphoma study group. Am J Hematol 2012;87:663-8.
7. Zhang JC, Wang Y, Wang XF, Zhang FX. Type I enteropathy-associated T-cell lymphoma in the colon of a 29-year-old patient and a brief literature review. Onco Targets Ther 2016;9:863-8.
8. Chan JK, Chan AC, Cheuk W, Wan SK, Lee WK, Lui YH, *et al.* Type II enteropathy-associated T-cell lymphoma: A distinct aggressive lymphoma with frequent γδ T-cell receptor expression. Am J Surg Pathol 2011;35:1557-69.
9. Leon F. Flow cytometry of intestinal intraepithelial lymphocytes in celiac disease. J Immunol Methods 2011;363:177-86.
10. Paulsen SR, Huprich JE, Fletcher JG, Booya F, Young BM, Fidler JL, *et al.* CT enterography as a diagnostic tool in evaluating small bowel disorders: Review of clinical experience with over 700 cases. Radiographics 2006;26:641-57.