Case Report

Monomorphic Epitheliotropic Intestinal T-Cell Lymphoma Mimicking Benign Lymphocytic Infiltrates: A Pathologic Masquerade

Kuljeet Kaur[1], Maitrayee Roy[2], Vishesh Dhawan[2,*], Ayushi Kediya[2]

[1]Department of Pathology, Maharishi Markandeshwar Centre of Medical Sciences and Research, Maharishi Markandeshwar Deemed to be University, Sadopur-Ambala, Haryana, India

[2]Department of Pathology, Maharishi Markandeshwar Institute of Medical Sciences and Research, Maharishi Markandeshwar Deemed to be University, Mullana-Ambala, Haryana, India

***Correspondence:** drvishesh93@gmail.com

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Abstract

Monomorphic Epitheliotropic Intestinal T-cell Lymphoma (MEITL) is a rare aggressive T-cell lymphoma mostly found in Asia. It accounts for less than 5% of primary gastrointestinal malignant lymphomas, is rapidly progressing, and has a poor prognosis with a median survival of 7 months. The relatively small size of atypical cells coupled with brisk cryptitis can result in a misdiagnosis of lymphocytic proctocolitis. A strong index of suspicion is required to employ an appropriate IHC panel for this diagnosis. In this case report, we want to describe a 50-year-old patient who presented with chronic lower gastrointestinal symptoms and was diagnosed with MEITL involving the large intestine and ileum.

Keywords: monomorphic epitheliotropic intestinal t-cell lymphoma; immunohistochemistry; lymphoma

Introduction

Monomorphic Epitheliotropic Intestinal T-cell Lymphoma (MEITL), previously known as type II enteropathy-associated T-cell lymphoma (EATL), is a rare, aggressive T-cell lymphoma predominantly found in Asia, accounting for less than

5% of primary gastrointestinal malignant lymphomas. The revised 2016 World Health Organization classification of lymphoid neoplasms lists MEITL and EATL as separate entities.[1] The patients of MEITL typically exhibit vague clinical symptoms, such as altered bowel habits, persistent stomach discomfort, weight loss, persistent diarrhea, intestinal blockage or perforation, as well as bleeding.[2] MEITL is characterized as a tumor with significant intestinal epithelial infiltration and tiny to medium-sized monomorphic cells with round nuclei and a rim of pale cytoplasm. However, unlike EATL, there is no necrosis or significant inflammation.[3] Immunophenotyping demonstrates that the tumor cells are usually $CD3^+$, $CD8^+$, $CD56^+$, $CD5^-$, $CD4^-$, $CD30^-$, gamma-delta T-cell receptor $(TCR)^+$, alpha-beta TCR^-, T-cell intracellular $antigen^+$, megakaryocyte-associated tyrosine $kinase^+$, Epstein-Barr virus (EBV) encoded small nuclear RNAs $(EBER)^-$, and approximately 80% of cases exhibit gene rearrangements for TCR-γ (T cell receptor gamma) and TCR-δ (T cell receptor delta).[4] Mutations that activate the JAK-STAT (Janus kinase–signal transducer and activator of transcription) pathway are a hallmark of MEITL, with STAT5B (Signal Transducer and Activator of Transcription 5B) mutations being the most prevalent. Additional frequently altered genes implicated in the pathophysiology of MEITL include JAK3 (Janus kinase 3), GNAI2 (Guanine nucleotide-binding protein G(i) subunit alpha-2), CREBBP (cAMP response element-binding protein), and SETD2 (SET domain-containing 2).[1] MEITL is mostly seen in the small intestine, but in our case, the large intestine and the ileum were involved. In this case report, we describe a 50-year-old patient who had long-term lower gastrointestinal (GI) symptoms, a large ulcer in the large intestine and ileum, which on biopsy was diagnosed as MEITL.

Case report

A 50-year-old male presented to our gastroenterology outpatient department (OPD) with chief complaints of recurrent diarrhea and weight loss for the past 4-5 months. He had a history of episodes of haematochezia and underwent a colonoscopy at another hospital, which showed widespread ileo-colonic ulcers. A biopsy was performed in the same hospital, where histological findings were reported as suggestive of ulcerative colitis (UC). He was started on treatment for UC, but with no symptomatic improvement.

He underwent a repeat colonoscopy at our institute, revealing a large circumferential ulcer involving the caecum, sigmoid, ascending colon, and erosions in the ileum. Segmental biopsies were taken from the rectum to the terminal ileum. All biopsies showed dense chronic inflammatory cells in the lamina propria, comprising predominantly small-sized lymphoid cells with uniform round nuclei having clumped chromatin, and exhibiting brisk lymphocytic cryptitis as well as extensive lymphocytic infiltration of surface enterocytes.

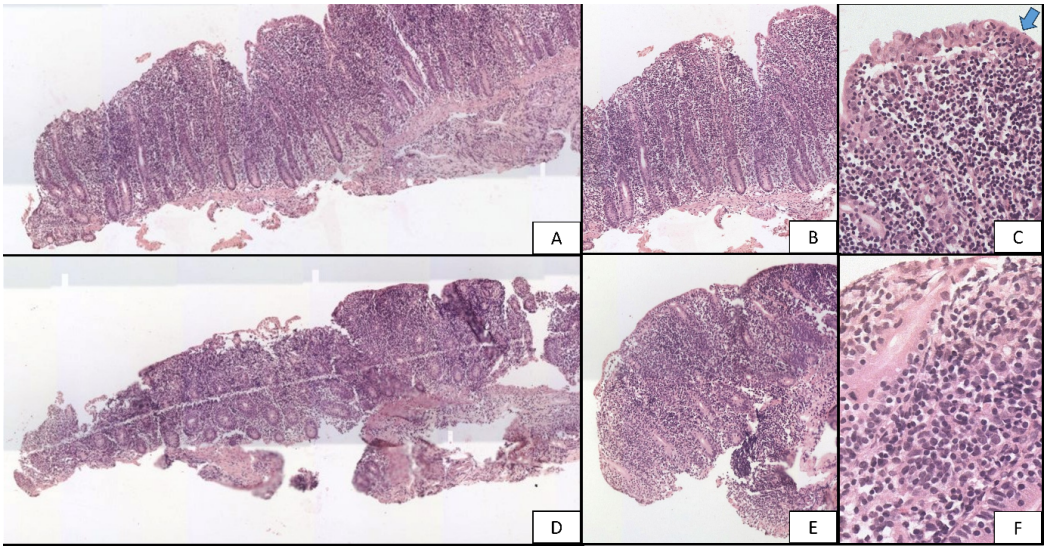

Figure 1: Colonic mucosa with largely intact crypt architecture showing dense lymphoplasmacytic inflammation, brisk lymphocytic cryptitis, and prominent surface epithelial infiltration (arrow). (H&E, 40× A,D; 100× B,E; 400× C,F).

We did not observe any architectural distortion, neutrophilic activity, or granuloma in any of the biopsies. Morphological features prompted us to entertain the possibility of severe microscopic lymphocytic colitis; however, the same was quickly rejected because of colonoscopic findings of erosion and ulceration. A panel of IHC was initially undertaken, keeping in mind the possibility of non-Hodgkin lymphoma (NHL).

The neoplastic cells stained strongly and diffusely with CD3 and CD7, while negative for CD2, CD5, and CD20, indicating a T-phenotype of the lymphoid cells with a Ki67 proliferative index of 30%. A diffuse expression of pan-T markers CD3 and CD7, while loss of CD2 and CD5 supported the monoclonal neoplastic nature of the T lymphocytes, suggesting GIT involvement by T-NHL. Additionally, the tumor cells were diffusely immunopositive for CD8 and CD56, while negative for CD4. A diffuse infiltrate by a monomorphic population of neoplastic CD8 & CD56 positive T lymphoid cells, coupled with prominent epitheliotropism, favored a diagnosis of MEITL.

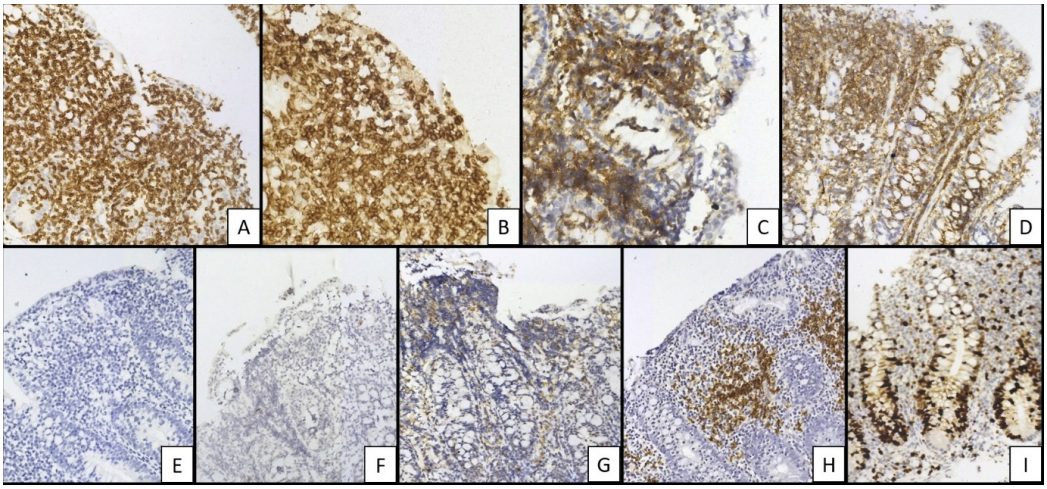

Figure 2: Immunohistochemistry demonstrating strong, diffuse positivity for CD3 (A), CD7 (B), CD8 (C), and CD56 (D), with a Ki-67 proliferative index of approximately 30% (I). The neoplastic lymphoid cells are negative for CD2 (E), CD5 (F), CD4 (G), and CD20 (H). (200×).

A celiac serology was, however, recommended to definitively exclude the possibility of enteropathy-associated T-cell lymphoma, despite the absence of pleomorphism amongst the neoplastic lymphoid cells and CD56 positivity on biopsy. This was promptly performed, and IgA-tTg (3.5 g/L, ELISA, normal range 0.7-4.0 g/L), IgG-Ttg (ELISA, negative $<$20 U/mL), and IgA-endomysial antibodies (Indirect immunofluorescence, Fluorescence at a titer $\geq$ 1:10) were all within normal limits.

Keeping in view the rarity of MEITL, we also recommended a TCR-γ IHC/ T cell receptor gene clonal rearrangement study to confirm the diagnosis. The patient, however, declined further tests and was briefly lost to follow-up. He ultimately succumbed to his condition 6 months later. Written informed consent was obtained from the patient, and ethical approval was obtained from the institutional ethics committee. The entire clinical timeline has been condensed in Table-1.

Table 1: Clinical timeline of the patient.

Time Point	Event
4–5 months before current OPD visit	Onset of recurrent diarrhea and progressive weight loss.
Initial evaluation at outside hospital	Episodes of hematochezia → Colonoscopy shows widespread ileo-colonic ulcers.
	Biopsies reported as ulcerative colitis → UC therapy (oral mesalamine) initiated.
	No symptomatic improvement on treatment.
Presentation to our institute (OPD)	Persistent symptoms → Repeat colonoscopy reveals large circumferential ulcers (caecum, ascending, sigmoid) and ileal erosions.
	Segmental biopsies taken from rectum to terminal ileum.
Histopathology	Dense monomorphic small lymphoid infiltrate with marked epitheliotropism; no architectural distortion, neutrophilic activity, or granulomas.
	Microscopic lymphocytic colitis considered but ruled out due to extensive ulceration.
Initial IHC panel	$CD3^+$, $CD7^+$, $CD2^-$, $CD5^-$, $CD20^-$; Ki-67 ∼30% → T-cell NHL suspected.
	Additional IHC: $CD8^+$, $CD56^+$, $CD4^-$ → favors MEITL.
Further work-up	Celiac serology (IgA-tTG, IgG-tTG, IgA-EMA) normal → EATL unlikely.
	TCR-γ IHC / T-cell clonality study advised → patient declined.
Follow-up & Outcome	Patient lost to follow-up; ultimately died 6 months later.

Discussion

Initially, in 2008, the World Health Organization (WHO) classified two types of EATL: EATL type I (lymphoma developing in patients with celiac disease, a chronic autoimmune GI tract disorder) and EATL type II (a comparable bowel lymphoma that is unrelated to celiac disease). Later in 2016, the WHO categorized these lymphomas as different entities, referring to the lymphoma not linked with celiac disease as MEITL and the lymphoma associated with celiac disease as EATL.[1, 5] MEITL has an aggressive course and a dismal prognosis.[4] MEITL patients are predominantly male and are in the sixth decade of life. The common presenting signs and symptoms of patients are altered bowel habits, weight loss, abdominal pain, and complications like intestinal ulcers/perforation/ obstruction.[6] For our patient, a similar was the situation.

MEITL is hypothesized to originate in intraepithelial lymphocytes, which develop abnormalities over time. These malignant T cells harbor various genetic abnormalities, including a gain of the chromosomal region 9q33-q34 and an amplification of the chromosome locus 8q24, which results in the proliferation of neoplastic cells.[7] and IHC is $CD3^+$, $CD5^-$, $CD4^-$, $CD8^+$, $CD56^+$, $CD103^{+/-}$, $CD30^-$, MATK (Megakaryocyte-Associated tyrosine Kinase)$^+$, and $EBER^-$, and approximately 80% of cases show TCR-γ and TCR-δ rearrangement.[4] Although these ancillary tests are integral to establishing a definitive

diagnosis, they could not be performed in our case because the patient declined further investigations, representing a limitation of this report.

MEITL's endoscopic characteristics are comparable to those of other forms of colitis, and most patients have ulcerations and erosions, which were consistent with our case.[8] According to the literature evaluation, diffuse infiltrating lesions were more likely to occur during endoscopy than ulcerative and polypoid lesions.[9] Microscopically, tumor cells are monotonous, small to medium in size, with round or slightly irregular nuclear membrane, dispersed chromatin, inconspicuous nucleoli, and a thin rim of cytoplasm. Transmural infiltration and prominent epitheliotropism are typical; inflammatory cells and necrosis are rarely seen unless mucosal ulcers exist.[3]

The differential diagnosis includes ulcerative colitis and microscopic colitis; however, several critical discordances between the clinical, endoscopic, and histologic findings necessitated further evaluation. The biopsies lack the hallmark features of ulcerative colitis—namely crypt architectural distortion, basal plasmacytosis, and neutrophil-mediated injury—and the presence of extensive ulcers visualized endoscopically is distinctly atypical for microscopic colitis, which generally exhibits preserved architecture and minimal macroscopic abnormalities. Instead, the mucosa demonstrates a dense and monomorphic lymphoid infiltrate with pronounced epitheliotropism, a pattern not consistent with reactive inflammatory conditions. These atypical features, particularly the uniform cytology of the infiltrating cells, diffuse lamina propria replacement, and marked epithelial involvement, constitute key histologic triggers for immunohistochemical evaluation, ultimately directing the diagnosis toward MEITL.[10]

It is important to differentiate MEITL from other lymphoma and this can be achieved by focusing on important features like monomorphic cell shapes, epitheliotropic patterns, and immunopositivity for CD8 and CD56. Also, it is equally important to differentiate MEITL from cryptitis and microscopic colitis, as they share similar endoscopic pictures of normal colonic mucosa and histologically have a presence of intraepithelial lymphocytes. The minimum number of intraepithelial lymphocytes that is considered alarming is 20 per 100 epithelial cells. However, lymphocytes in lymphoma are way more in number and are associated with cytological atypia.[11]

With a median survival of seven months, MEITL has a poor prognosis and advances quickly.[12] Since there is currently no defined standard of care, autologous stem cell transplantation or chemotherapy after surgical resection has produced better results than surgery alone.[9] Certain clinical trials also advocate the addition of IVE/MTX (ifosfamide, vincristine, etoposide/methotrexate), followed by stem cell transplant to increase the outcomes with a 65% complete remission and 60% 5-year survival rate.[13]

Fluorine-2-fluorodeoxyglucose positron emission tomography (^{18}F-FDG PET) acts as a useful modality in staging and follow-up for the recurrence of aggressive lymphomas, but in our case, sadly, the patient succumbed to the illness.

Conclusion

The relatively small size of atypical lymphoid cells coupled with brisk cryptitis can cause MEITL to be misdiagnosed as proctocolitis/ microscopic colitis. A strong index of suspicion is required to employ an appropriate IHC panel for this diagnosis. Because of the relatively novel entity and its diagnostic challenge, we would like to contribute one such case to the English literature to assist the treating physician in providing appropriate therapy for such individuals.

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