Case History

A 58-year-old white male presented with a 2-month history of persistent abdominal pain and 30 pounds weight loss in 3 months. Abdominal and pelvic computed tomography (CT) showed mesenteric lymphadenopathy and a dilated, thick-walled mass in the mesentery communicating with the small bowel. During the surgery, a 17 cm mesenteric mass involving the small bowel with extensive mesenteric lymphadenopathy was identified.

Histologic sections of the lesion are depicted below. Immunohistochemical stains were positive for CD3, CD8, CD56 and negative for CD20, PAX-5, CD4, CD5, CD79a, MUM1, CD30, CD10 and BCL6. Ki-67 was 60-70%.

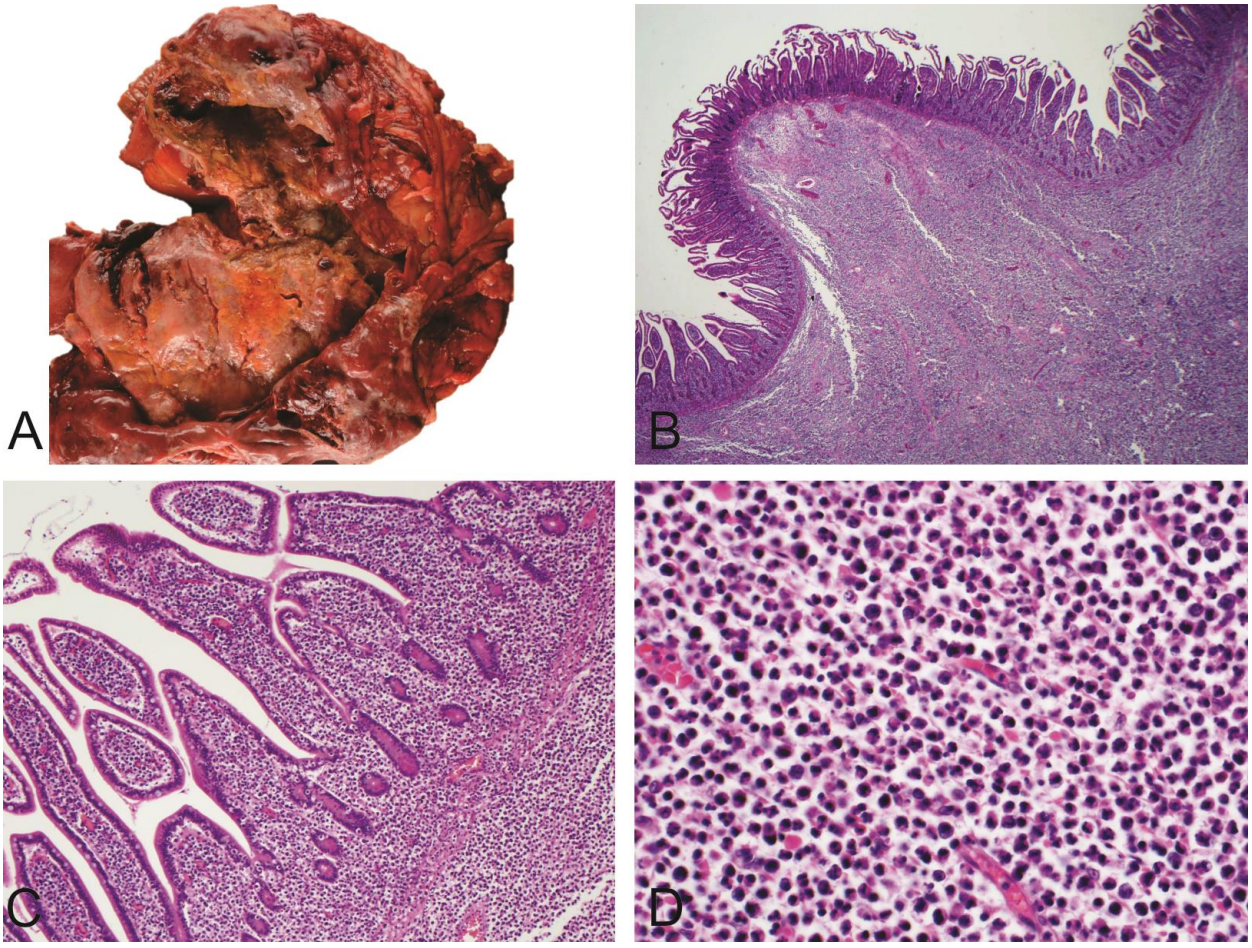

Figure 1. H&E stain. The intestinal epithelium and lamina propria are diffusely infiltrated by relatively monotonous medium-sized to large cells with angulated hyperchromatic nuclei and rim of pale cytoplasm.

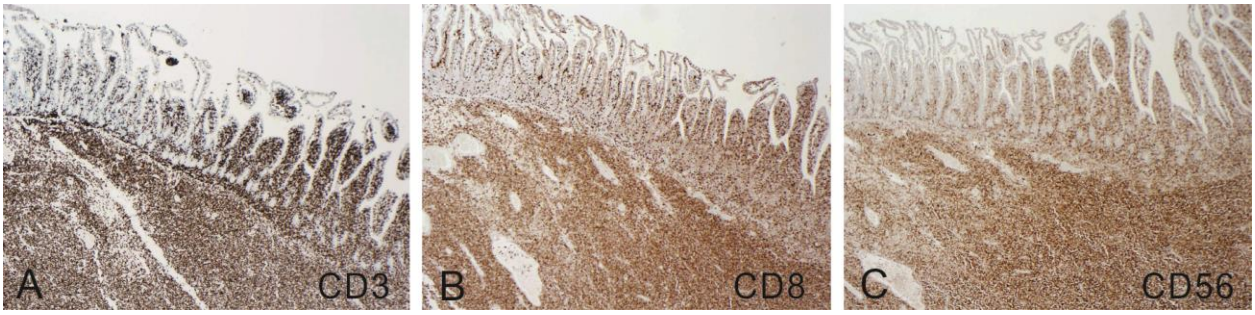

Figure 2. A. CD3 immunohistochemical stain (20x). B. CD8 immunohistochemical stain (20x). C. CD56 immunohistochemical stain (20x).

What is the most likely diagnosis?

A. Diffuse large B cell lymphoma.
B. Enteropathy-associated T-cell lymphoma (EATL).
C. Monomorphic epitheliotropic intestinal T-cell lymphoma (MEITL).
D. Adult T-Cell Leukemia/Lymphoma (ATCL).
E. Peripheral T-cell lymphoma, not otherwise specified (PTCL-NOS).

Correct answer: C. Monomorphic epitheliotropic intestinal T-cell lymphoma (MEITL).

Discussion of monomorphic epitheliotropic intestinal T-cell lymphoma (MEITL)

Grossly, the mass involved the bowel wall extending to the mucosa. Also noted was extensive mesenteric lymphadenopathy as shown in Figure 1A. Histologic sections of the tumor showed transmural infiltration of sheets of relatively monotonous medium-sized to large cells with angulated hyperchromatic nuclei and rim of pale cytoplasm (Figure 1B-D). The tumor cells were positive for CD3, CD8 and CD56 (Figure 2), and negative for CD4 and CD5. Ki-67 showed high proliferation index (60-70%). They were also negative for CD79a, PAX-5, CD20, MUM1, CD30, CD10 and BCL6. The clinical and pathologic findings were diagnostic of MEITL. Small intestinal villi adjacent to the tumor were without significant histopathological abnormalities.

MEITL is a rare primary and highly aggressive gastrointestinal T cell lymphoma which was previously designated as type II enteropathy-associated T cell lymphoma (EATL). Type I EATL, now simply designated as EATL which is highly correlated with celiac disease and is more common in Northern Europe and America. However, MEITL is not associated with celiac disease and is predominant in East Asia. Diagnosis of MEITL is very challenging since the patients do not have celiac disease and the symptoms are non-specific. MEITL most often presents in the small intestine, followed by large intestine. Sstomach can also be involved. Histopathologic examination and specific immunohistochemistry are required for the diagnosis of MEITL.

The main pathologic feature for MEITL includes transmural infiltration of dense monotonous atypical small to medium-sized lymphoma cells. The nuclei are round and regular with finely dispersed chromatin and inconspicuous nucleoli. There is a generous rim of pale cytoplasm and the lymphoma cells show prominent epitheliotropism. Unlike enteropathy-associated T-cell lymphoma (EATL), there is no inflammatory background and the areas of necrosis are uncommon. In general, MEITL has a distinctive immunohistochemical staining pattern with CD3, CD8 and CD56 positive in the majority of cases. Most cases are negative for CD5. TCR-ɣ is often positive, although some cases may be TCR-β positive. More than 90% of cases show T-cell receptor gene rearrangement. Extra signals for *MYC* at 8q24 are commonly identified by fluorescent in situ hybridization (FISH). The most common genetic change is gain at 9q34.3 which is observed in more than 75% cases by FISH or copy number analysis.

In general, patients with MEITL have a very poor prognosis with an overall survival of 7 months and the progression free survival of 1 month. Furthermore, high frequency of extra-intestinal involvement may be one of the reasons for patients with poor prognosis. Currently, there is no standard treatment for MEITL. The CHOP regimen is the most commonly first-line treatment for MEITL.

A. Diffuse large B cell lymphoma

The gastrointestinal tract (stomach and ileocecal region) is the most common extranodal site. Many patients are asymptomatic, but B symptoms such as fever, night sweats and weight loss may be present. Microscopically, the neoplastic cells are medium to large, often with prominent nucleoli. The neoplastic cells typically are positive for CD19, CD20, CD22, CD79a and PAX5- (pan-B-cell markers) and negative for CD3, CD4 and CD8 (pan-T cell markers).

B. Enteropathy-associated T-cell lymphoma (EATL)

EATL, formerly designated as EATL type 1, is a neoplasm of intraepithelial T cells and approximately 80-90% of patients have documented celiac disease. The small intestine is involved in more than 90% of cases with the most common sites being jejunum and ileum. Patients with EATL may present with abdominal pain, diarrhea, weight loss, anorexia or fatigue. Microscopically, the lymphoma cells show pleomorphic medium-sized to large cells with round or angulated vesicular nuclei, prominent nucleoli and moderate to abundant pale-staining cytoplasm. The lymphoma cells are usually CD3+, CD7+, CD103+, TIA1+, granzyme B+, perforin +, CD5-, CD4- and CD8+/-. Most tumors show an inflammatory background, including histiocytes, eosinophils, small lymphocytes and plasma cells. The intestinal mucosa adjacent to EATL, usually shows features of celiac disease (villous atrophy, crypt hyperplasia, intraepithelial lymphocytosis, and increased lymphocytes and plasma cells within the lamina propria.

D. Adult T-Cell Leukemia/Lymphoma (ATCL)

ATCL is a mature T-cell neoplasm caused by the human retrovirus HTLV-1. The disease is usually widely disseminated, involving widespread lymph nodes, peripheral blood, spleen, skin, lung, liver, gastrointestinal tract and CNS. Microscopically, the lymphoma cells show remarkable pleomorphism and are strongly CD25+ in nearly all cases. Most cases are CD2+, CD3+, CD5+, CD4+, CD8-, and CD7-.

E. Peripheral T-cell lymphoma, not otherwise specified (PTCL)

Most patients with PTCL present with peripheral lymph node involvement, but any site can be affected. Extranodal involvement can occur, most commonly in the skin and gastrointestinal tract. The cytological spectrum is extremely broad, from polymorphous to monomorphic. Most cases show numerous medium-sized to large cells with irregular, pleomorphic, hyperchromatic, or vesicular nuclei, prominent nucleoli and many mitotic figures. Most cases are characterized by an aberrant T-cell phenotype with frequent

antigen loss in CD7, CD5, CD4/CD8 and CD52. There is no enteropathy associated changes. T cell receptor gene rearrangement are identified in most cases.

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