

GIPS Case of the Month

A 69-year-old Hispanic female with a past medical history of non-insulin dependent diabetes, chronic constipation, and dyslipidemia presented to the hospital with diffuse abdominal pain and recent melena. The patient reported having subjective fevers for a month prior to her presentation but no recent weight loss. Abdominal ultrasound demonstrated a 13 x 11 x 10 cm complex mass in the mid-abdomen, and a CT scan noted small bowel wall thickening and dilation proximal to the mass. At surgery the mass was found to involve the jejunum and adjacent mesentery. A gross image, an intra-operative scrape preparation (H&E), H&E photomicrographs, and immunohistochemical stains are provided below.



Figure 1 Representative cross section of mass (post fixation)

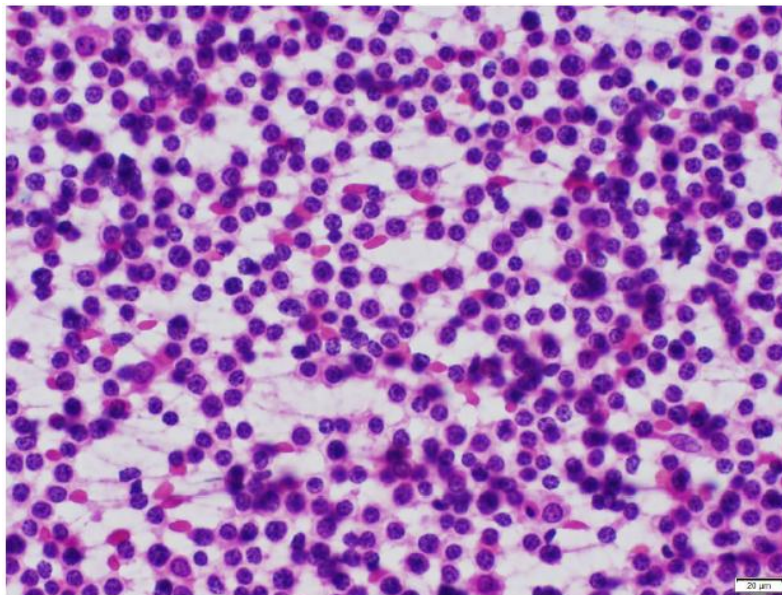


Figure 2 Scrape preparation (H&E)

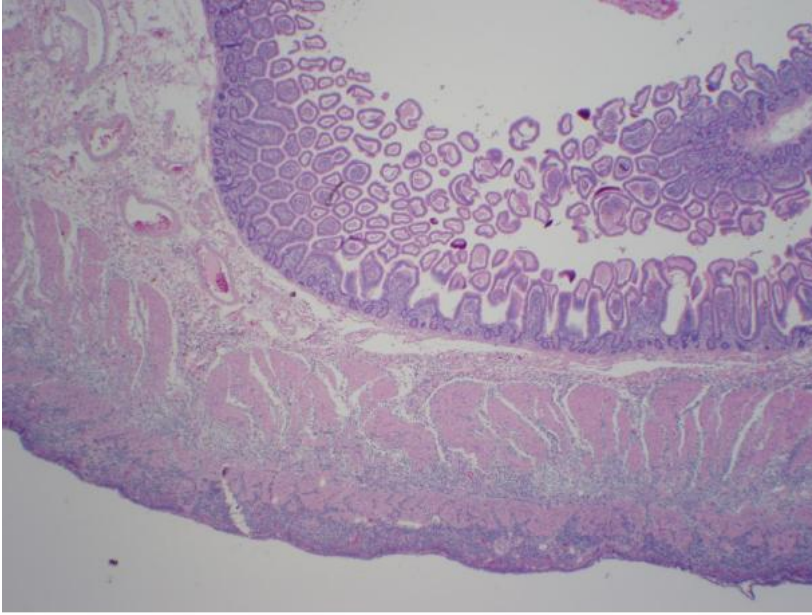


Figure 3 Section from thickened area of bowel (2x)

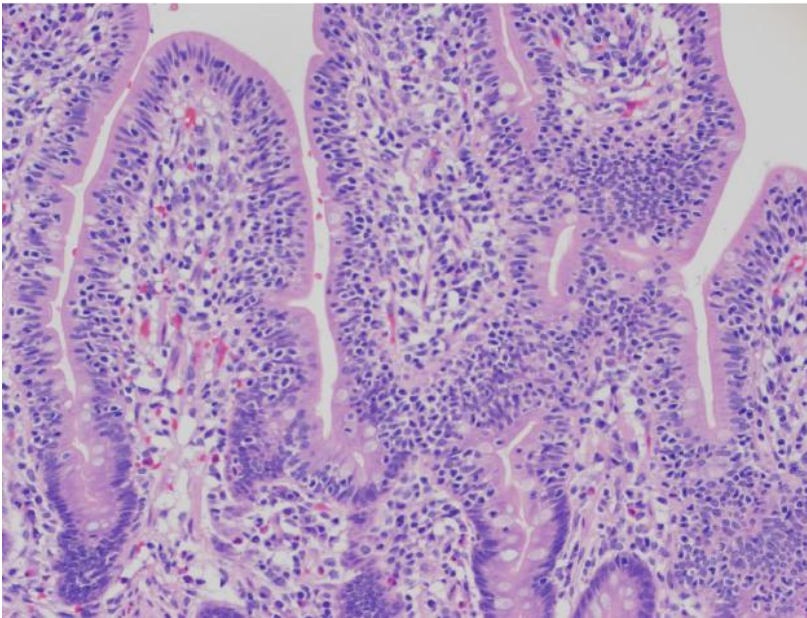


Figure 4 Villi from thickened area of bowel (20x)

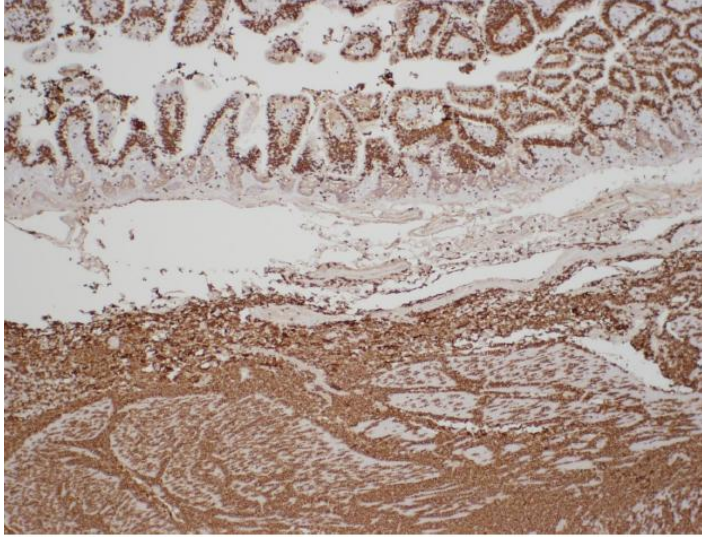


Figure 5 CD8 (2x); Immunohistochemical staining for TIA and CD56 were also positive (immunoreactive)

What is your diagnosis?

- A. Marginal zone lymphoma
- B. Extranodal NK/T-cell lymphoma, nasal type
- C. Enteropathy-associated T-cell lymphoma (Type 1)
- D. Enteropathy-associated T-cell lymphoma (Type 2)
- E. Anaplastic large cell lymphoma

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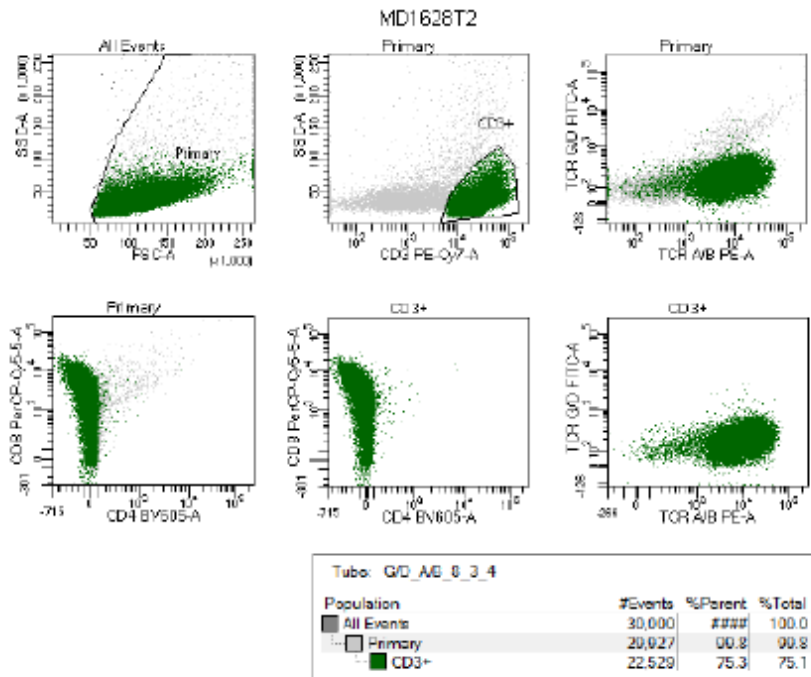
Answer and Discussion:

D. Enteropathy-associated T-cell lymphoma (Type 2)

Enteropathy-associated T-cell lymphoma (EATL), type 2, now designated as monomorphic epitheliotropic intestinal T-cell lymphoma (MEITL) in the revised 2016 WHO classification of lymphoid neoplasms is a rare primary gastrointestinal T-cell lymphoma which shows little to no association with celiac disease. MEITL occurs most frequently in Asian and Hispanic populations with a median patient age of about 60 years. There is a strong male predominance. Patients can present with chronic symptoms including abdominal pain, fever, and weight loss or more acutely with obstruction and/or perforation. The small bowel is the most frequently involved site. Multifocal disease is not uncommon often involving other intra- and extra-abdominal sites including: colon, stomach, pancreas, ovary (our case), omentum, bladder, and rarely bone marrow.

Transmural involvement is a common feature, but villus blunting, if present at all, is usually confined to areas of lymphoma. Necrosis is rare, and usually limited to areas of perforation or ulceration. As the name implies, a prominent feature is the large number of neoplastic intra-epithelial lymphocytes (Figure 4). The lymphocytes are monomorphic, small to medium sized with scant pale cytoplasm and have mildly irregular nuclei, coarse chromatin, and frequent mitosis. Unlike type 1/classical EATL the background does not commonly contain a mixed inflammatory infiltrate.

Tumor cells are CD3+, CD4-, CD8+, CD56+, TIA+, and may express TCR $\alpha\beta$ as in our case (See patient's flow cytometry plot; primarily T-cell markers below) or more commonly TCR $\gamma\delta$. EBER is generally negative though rare EBER positive cases have been reported. Most commonly the lymphocytes within the mass and within the epithelium have the same immunophenotype.



Clinical data is sparse for MEITL, but all of the studies have found the prognosis to be poor with the overall survival time often being less than a year. The few patients eligible for hematopoietic stem cell transplantation have experienced much better outcomes.

EATL, type I, **(Choice C)** now designated as enteropathy-associated TCL, is strongly associated with celiac disease, and primarily affects individuals of northern European origin. It is the most common malignancy seen in patients with celiac disease, and occurs in approximately 2-3% of patients. The disease tends to occur in patients with a brief history of adult onset celiac or dermatitis herpetiformis, and less commonly in patients with a long history of celiac disease. The cells are usually medium to large in size with marked polymorphism, and exist within a prominent mixed inflammatory infiltrate. Necrosis is often present, and the background small intestine demonstrates the histologic findings of celiac disease. The cells are CD3+, CD4-, CD5-, CD7+, CD8+/-, CD56-, EBER- and most commonly express TCR $\alpha\beta$.

Marginal zone lymphoma **(Choice A)** is composed of a monotonous population of small to medium sized cells with clear cytoplasm similar to MEITL. However, a basic panel of immunostains using B- and T-cell markers or flow cytometry easily distinguishes the two entities.

Extranodal NK/T-cell lymphoma, nasal type **(Choice B)** most commonly presents in the aerodigestive tract but can secondarily involve the gastrointestinal tract. NK/T-cell lymphoma tends to be angiodestructive, a feature not seen in MEITL or enteropathy-associated TCL. NK/T-cell lymphoma is immunophenotypically similar to MEITL (CD56+, TIA+) but generally lacks T-cell receptor rearrangements and is virtually always EBER+.

Anaplastic large cell lymphoma (ALCL) **(Choice E)** is a T-cell lymphoma that can be further divided into anaplastic lymphoma kinase (ALK) positive or negative, a distinction important for prognosis. ALCL can be nodal or extranodal. While extranodal involvement of the gastrointestinal tract is possible, other more common sites include: skin, bone, soft tissue, and lung. ALK positive ALCL tends to occur most frequently in the first three decades of life, whereas ALK negative ALCL tends to occur in middle aged to older adults; both have a male predominance. ALCL cells are too large and pleomorphic to be confused with MEITL but the distinction between ALCL and enteropathy-associated TCL maybe challenging if a clinical history of celiac is not provided. ALCL is characteristically CD30+, with only a subset of enteropathy-associated TCLs expressing bright CD30. CD3 tends to be negative in ALCL and positive in enteropathy-associated TCL.

References

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