Case Report

Primary Hepatic Presentation of Enteropathy Associated T-Cell Lymphoma in a Patient with Established Celiac Disease

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Abstract

Enteropathy associated T–cell lymphoma (EATL) is a high grade non-Hodgkin’s lymphoma arising from intraepithelial T lymphocytes of the intestine. EATL is specifically associated with celiac disease and commonly presents in sixth and seventh decades of life. These lymphomas occur most commonly in the small intestine (90%) and presentation outside gastrointestinal tract is rare. We report a case of a 60-year-old female with a primary hepatic presentation of EATL. To our knowledge, this is the first report of a predominant, possibly primary, hepatic EATL in a patient with celiac disease without documented involvement of gastrointestinal tract, emphasizing awareness of unusual clinical presentations and requiring prompt diagnosis of this aggressive neoplasm.

Keywords: enteropathy associated T–cell lymphoma, EATL, hepatic, lymphoma

Introduction

Enteropathy associated T-cell lymphoma is a rare, aggressive entity that normally presents in the small intestine. Patients usually present with abdominal pain and bowel perforation and have a poor prognosis. In advanced stages it can spread to the surrounding organs via direct extension. The most commonly involved sites at presentation are the small intestine (90%), mesenteric lymph nodes (35%), and the large intestine (16%) with only 0.03% of cases involving the liver [1].

Clinical Presentation

This patient is a 60-year-old female with a complicated past medical history, notable for celiac disease, protein malnutrition, weight loss and abnormal liver function tests. She presented with cough, fever and diarrhea. Her physical stats and vital signs were as follows, height was 63 inches (160.02 cm), Weight was 100 lbs (45.45 kg), BMI was 17.78, pulse rate was 67 beats per minute and blood pressure was 100 / 55 mmHg. Physical exam revealed an elderly female in a wheelchair in no acute distress. Crackles were heard in the lower lungs on pulmonary examination. Abdominal examination revealed a non-distended abdomen with normal bowel sounds. No organomegaly was found on palpation.

Past medical history

In 2009 she presented with weakness, nausea, vomiting, high fever, abdominal pain and lack of appetite leading to dehydration and significant weight loss (100lbs to 85lbs). At the time, esophagogastroduodenoscopy (EGD)
showed gastric inflammation and erythema and flattened duodenal folds. Microscopic sections for the gastric biopsy showed benign gastric mucosa with moderate chronic inflammation within the lamina propria. The inflammation was composed of lymphocytes, plasma cells and few eosinophils. No acute inflammation was seen. Sections of the small bowel biopsy showed flattening of the villi and expansion of the lamina propria by a marked chronic lymphocytic infiltrate. Numerous lymphocytes infiltrated the superficial epithelium as well as the crypt epithelium. No granulomas were seen. No dysplasia was present, thus features were consistent with celiac disease. The differential diagnosis considered included lymphocytic enterocolitis, other protein allergies, long-standing nonspecific chronic duodenitis, autoimmune enteropathy and dermatitis herpetiformis.

In 2015, the patient had EGD/colonoscopy. EGD showed normal esophageal and gastric mucosa, but the duodenal mucosa was congested with scalloped folds. Colonoscopy showed congested mucosa but without any signs of inflammation (Figures 1 and 2). Microscopic evaluation showed sections of gastric biopsy with normal foveolar and glandular architecture with no evidence of Helicobacter pylori. Sections of the terminal ileum demonstrated acute ileitis with ulceration, without atypical features. Sections of the duodenal biopsy demonstrated villous atrophy with decreased villous to crypt ratio, approximately 1/1 with increased intraepithelial lymphocytosis, confirming the diagnosis of celiac disease. No gastrointestinal neoplasm was ever identified.

![Figure 1: Colonoscopy evaluation in 2015 showing congested mucosa and scattered superficial ulcerations in the ileum](image-url)
Work-up and diagnosis

Laboratory studies showed abnormal liver tests which prompted imaging studies. CT showed innumerable new small hypointense lesions especially in the right hepatic lobe that were increased in size and number since the prior CT. A prior 0.6 × 0.5 cm hypointense area in segment 8 had enlarged to 0.9 × 0.5 cm within a period of 20 days (Figure 3). No intrahepatic or extrahepatic biliary ductal dilatation was seen and there were no abnormal findings in the spleen. The sigmoid and distal descending colon showed diffuse wall thickening.

A core liver biopsy was performed to evaluate the liver lesions seen on CT (Figure 4). Microscopic evaluation showed hepatic involvement by 1 T-cell lymphoma. Immunohistochemical studies were performed. The large atypical cells were positive for CD45 (LCA), CD45 RO, CD30, CD3, CD8, CD7, and CD25 and negative for CD4, S100, CD5, CD10, CD20, ALK-1, CD34, CD56, Granzyme B, Tdt, CD21, CD23, CD117 and CD138. The differential diagnosis included Enteropathy-associated T-cell lymphoma, type 1 (EATL, Type 1), hepatosplenic T-cell lymphoma and adult T-cell leukemia/lymphoma. However, in the context of the patient’s celiac disease, the morphologic features of the tumor cells, the absence of sinusoidal involvement of the liver and the above immunophenotypic profile, the tumor was diagnosed as EATL, Type 1. The patient was started on immunotherapy (Brintuximab) and is currently continuing treatment.
Discussion

The 2008 World Health Organization (WHO) classification of haematopoietic and lymphoid neoplasms defines Enteropathy-associated T-cell lymphoma (EATL) as “an intestinal tumor of intraepithelial T lymphocytes,
showing varying degrees of transformation but usually presenting as a tumor composed of large lymphoid cells, often with an inflammatory background” and EATL type II as “10-20% cases in which the lymphoma is composed of monomorphic medium sized cells that may occur sporadically without risk factors for celiac disease”. However, a review of the 2006 revision of the world health organization classification of haematopoietic and lymphoid neoplasms that was published in December 2016 has redefined the EATL type I as enteropathy associated TCL and defined it as being closely linked to celiac disease and primarily it disease of individuals often not being European origin. As for EATL, type II, it has been redesignated as monomorphic epithelioid tropic intestinal TCL (MEITL) and characteristically having no association with celiac disease with increased incidence in Asians and Hispanic populations [2].

This revision is based on a study performed by Deleeuw et al. in which they used whole-genome sequencing to identify the genetic alterations that identify the different subtypes of EATL in 30 cases. They categorized enteropathy associated TCL by non-monomorphic cytomorphology, CD 56 negativity, common gains of 1q and 5q regions, but not of the MYC oncogene. They categorized monomorphic epithelioid tropic intestinal TCL as monomorphic small to medium sized tumor cells morphology with frequent CD 56 expression, MYC oncology locus gain, and rare gains 1q and 5q regions [3]. Their findings support a prior study done in 1998 by Chott et al. in which he concluded that the majority of CD 56 positive intestinal lymphomas are morphologically and phenotypically distinct T-cell lymphomas most likely derived from the activated cytotoxic CD 56 positive, CD8 positive intraepithelial lymphocytes. In addition, Deleeuw et al. found that 73% of type 1 EATLs (73%) expressed HLA-DQB1*02, while only 33% of type 2 EATLs expressed HLA-DQB1*02 and concluded that “Compared with type 2 EATL, type 1 EATL patients more frequently carried HLA-DQB1*02 and were homozygous significantly more often for HLA-DQB1*02” [4].

The non-monomorphic cytomorphology and CD 56 negativity observed in our case, along with a clinical history of celiac disease, are consistent with a diagnosis of the newly categorized enteropathy associated TCL. Since the full description of enteropathy associated TCL has not yet been published by WHO, the remaining discussion will be based on the 2008 “WHO classification of haematopoietic and lymphoid neoplasms” description of enteropathy associated T-cell lymphoma, type I. This lymphoma occurs most commonly in the small intestine, jejunum or ileum with rare presentation outside the gastrointestinal tract. Most patients have adult onset celiac disease and often present with intestinal perforation and abdominal pain. Endoscopically, it is seen as ulcerated raised mucosal masses but the presentation varies and can include ulcers or large exophytic masses. Microscopically they present as medium to large monotonous cells with occasional pleomorphism, infiltrated by inflammatory cells including histiocytes and eosinophils have the potential of obscuring the tumor cells present [4].

Enteropathy associated T-cell lymphoma has poor prognosis with a median survival of 10 months. A large retrospective study by Malamut et al. concluded that aggressive treatment with chemotherapy and or surgery is associated with increased survival. In summary, we report an unusual case of a patient with celiac disease and no intestinal neoplasm presenting with enteropathy associated T-cell lymphoma involving the liver. Given the aggressive biology of this neoplasm and potential for response to appropriate therapy, recognition of unusual presentations may help in better management of these patients.

Conclusion

EATL is an aggressive lymphoma that typically involves the gastrointestinal tract with subsequent dissemination to other organs with only 0.03% of cases involving the liver. To our knowledge, this is the first report of a predominant, possibly primary, hepatic EATL in a patient with celiac disease without documented involvement of
gastrointestinal tract, emphasizing awareness of unusual clinical presentations and requiring prompt diagnosis of this aggressive neoplasm.

References


