Duodenal Lymphocytosis with Normal Villous Architecture: How Often Is It Celiac Disease?

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Background: Increased intraepithelial lymphocytes (IELs) with normal duodenal architecture is a common finding (Marsh 1). Many diseases have been implicated in such lesions, including celiac sprue (CS), infection, NSAIDs, and autoimmune conditions. CS incidence in patients with Marsh 1 lesions has varied widely from 9 to 40%. We correlated histologic features with clinical outcome to determine the incidence of CS in Marsh 1 lesions and identify unique, predictive histology.

Design: We identified 134 patients diagnosed with intraepithelial lymphocytosis over 4 years. Inclusion criteria required at least 2 well-oriented biopsies, increased IELs, and available CS serologic data. The remaining 79 cases were evaluated for marsh class, number of IELs, lamina propria inflammation, neutrophils, hemosiderin, lymphoid aggregates, and location (duodenal bulb versus not). Serology results and final clinical diagnoses were obtained from the clinical team and correlated to the histologic findings. Pathologists and clinicians were blinded to each other's collected data.

Results: Six percent (5) of biopsies showed <35 IELs/100 epithelial cells, 13% (10) showed 35-40 IELs, 23% (18) showed 40-50 IELs, 28% (22) had 50-60 IELs, 23% (18) 60-70, and 9% (7) had > than 70 IELs. The diagnoses most commonly associated with IELs were CS (23%, 18), Unknown (29%, 23), NSAID use (24%, 19), and Irritable Bowel Syndrome (13%, 10). Other diagnoses associated with IELs included bacterial overgrowth, common-variable immunodeficiency syndrome, type 1 and 2 diabetes, graft versus host disease, helicobacter pylori infection, inflammatory bowel disease, juvenile rheumatoid arthritis, collagenous colitis, systemic lupus erythematosis, and tropical sprue (each 5% or less of cases). All disease categories were equally distributed amongst the various gradations of intraepithelial lymphocytosis. No other pathologic features were diagnostic of a specific etiology.

Conclusions: The diagnostic categories most commonly associated with IELs were CS, unknown disease, NSAID use, and irritable bowel syndrome. Other conditions including autoimmune disease and immune dysregulatory disorders were also associated in a minority of cases. There was no difference in the amount of lymphocytosis for any given category of disease. A variety of conditions present with Marsh 1 lesions, and no definite histologic differences can be identified among this group. We found that 23% of Marsh 1 lesions were due to CS, a finding that is significantly higher when compared to similar studies.