IRB Protocol
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CRC Rotation
11/25/13

Title: ARB's and the risk of lymphocytic gastritis

A. Study Purpose and Rationale

Lymphocytic gastritis is a rare form of chronic gastritis strongly associated with *H. pylori* infection and celiac disease. Lymphocytic gastritis may present clinically with mild dyspepsia, diarrhea and/or weight loss; however patients may be asymptomatic prior to pathological confirmation. As reported by Aggarwal *et al*., the incidence of lymphocytic gastritis has been estimated at 46% and 43% in celiac disease and *H. pylori* infection, respectively. In addition to celiac disease and *H. pylori* infection, lymphocytic gastritis can occur in Crohn's disease, HIV, syphilis, menetrier's disease, inflammatory polyps, lymphoma, and esophageal carcinoma. The use of the ADP receptor inhibitor, ticlopidine, has also been associated with lymphocytic gastritis (see Gastroenterol Clin Biol. 1992;16(3):290). The cause is unexplained in up to 18% of patients. Carmack *et al.* defines lymphocytic gastritis as 25 intraepithelial lymphocytes/100 epithelial cells, regardless of the inflammation in the lamina propria. In a majority of lymphocytic gastritis cases, gross endoscopic inspection shows normal gastric mucosa; yet, thick mucosal folds, nodularity, and aphthous erosions (varioliform gastritis) have historically been cited (see Endoscopy 2013; 45(S 02): E145-E146). Both primary and secondary forms exist depending on etiology of the pathologic finding. The underlying pathophysiology of this form of gastritis is not clear but autoimmune response/antigen sensitivity is thought to play a role based on the known precipitants of the pathologic finding.

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Rubio-Tapia *et al*. found collagenous/lymphocytic gastritis in 31% of patients (7 of 22) with severe sprue-like symptoms who were taking the angiotensin II receptor blocker (ARB), omelsartan. The pathologic finding on biopsy disappeared with the discontinuation of this medication. Although there is some disagreement in the literature regarding the olmesartan-lymphocytic gastritis relationship (see the Mayo Clin Proc. December 2012;87(12):1230-1232), this study will attempt to further elucidate this relationship with a retrospective analysis of ~100 patients diagnosed with lymphocytic gastritis at CUMC.

B. Study Design and Statistical Analysis

This will be a cross-sectional retrospective study of patients with lymphocytic gastritis and matched controls. The cases will be collected using the CUMC Pathology database (WebCIS) from inception to present. using Aa natural language search of the CUMC pathology database using the keywords "lymphocytic gastritis" will be used to locate cases. All patients with biopsy--proven lymphocytic gastritis (defined as per Carmack *et al.*) will be included. Patients who have any disease associated with lymphocytic gastritis will be excluded from the study (see below). Lymphocytic gastritis cases will be matched by age, sex, and year of endoscopic gastric biopsy. The study will have a power of 80% testing at P value of 0.05. Assuming an N = 100 in the control groupcase group and N = 200 in the control group and a 5% ARB use,use; we will have sufficient power to meet statistical significance at 129% ARB use in the case group. This difference is deemed to be meaningful in the context of clinical ARB usage. There is no randomization needed for this study. There is no cross over that will occur in this study.

C. Study Procedure.

This study will require a retrospective chart examination. Cases will be chosen by querying the CUMC pathology database for pathology reports containing the words "lymphocytic gastritis". Appropriate controls will be obtained based on the resultant demographic information of the cases, using the following matching parameters: age, gender, and year of the procedure. The duration of

the entire study will be sixteen to twenty-four weeks. There are no required laboratory measurements or procedures needed for this study. The study will determine whether ARB use is associated with a pathologic diagnosis of lymphocytic gastritis.

D. Study Drugs
N/A

E. Medical Device
N/A

F. Study Questionnaires
N/A

G. Study Subjects
-The inclusion criteria are as follows:

- Age ≥18
- Documented lymphocytic gastritis in CUMC pathology report (defined a 25+ lymphocytes per 100 surface epithelial cells)

-Exclusion criteria include:

- Patients with celiac disease, *H. pylori* infection, crohn's disease, HIV, syphilis, menetrier's disease, inflammatory polyps, lymphoma, esophageal carcinoma and ticlopidine.

H. Recruitment of Subjects
There will be no contact with patients. All data will be collected from patient medical records.
~~Subjects will be identified by examining the CUMC pathology database.~~

I. Confidentiality of Study Data
Patient information will be entered into a computer database which will be encrypted and password-protected; only the principal investigator and co-investigators will have access to the database.

J. Potential Conflict of Interest
There is no conflict of interest with this study.

K. Location of the Study
This study will take place at the Columbia University Medical Center

L. Potential Risks

There is a small risk that patient information could released unintentionally to unauthorized personnel. As noted above, patient information will be stored in a secure computer database; only the principal investigator and co-investigators will have access to this information.

M. Potential Benefits
There will be no immediate potential benefits to the subjects of this study although this study may help elucidate the mechanism by which ARB's cause lymphocytic gastritis.

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N. Alternative Therapies
N/A

O. Compensation to Subjects
There will be no compensation provided to the subjects in this study.

P. Costs to Subjects
There will be no potential risks to the subjects of this study.

Q. Minors as Research Subjects
N/A

R. Radiation or Radioactive Substances
N/A

References

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