Agent Orange as a Possible Cause of *Helicobacter pylori* Negative Gastric Mucosa-associated Lymphoid Tissue Lymphoma

Samantha Wu, MD[1], Justin Roy, MD[2], Victoria Jackson, MD[2], Vance Hartke, MD[2], Leela Nayak, MD[3]

[1]Department of Internal Medicine, Tulane University Health Sciences Center, New Orleans, LA

[2]Department of Gastroenterology, Tulane University Health Sciences Center, New Orleans, LA

[3]Chief, Department of Gastroenterology, Southeast Louisiana Veterans Health Care System, New Orleans, LA

Introduction

- Gastric mucosa-associated lymphoid tissue (MALT) lymphoma is the most common extranodal site of non-Hodgkin lymphoma (NHL)
- *Helicobacter pylori* (*H. pylori*) infection is a cause of 90% of all gastric MALT lymphoma cases
- Agent Orange (AO), with traces of oncogenic 2,3,7,8-tetrachlorodibenzo-p-dioxin, has been implicated in NHL, which includes gastric MALT lymphoma

Case Presentation

75-year-old Caucasian male veteran with history of chronic gastroesophageal reflux disease (GERD) who served in the Vietnam War with significant AO exposure was referred for endoscopy to evaluate a reported history of un-staged Barrett's esophagus 5-years prior but with two subsequent normal endoscopies at an outside facility. He noted symptoms of burning chest pain and dyspepsia following large meals, all of which were worsened with spicy foods and improved with omeprazole. Family history was negative for a history of gastric cancer, and he had a 25-pack year smoking history but quit 20 years prior to presentation.

Initial esophagogastroduodenoscopy (EGD) revealed abnormal folds in the gastric fundus and erythema in the gastric antrum but was otherwise normal. Random gastric biopsies and biopsies of the abnormal folds were consistent with gastric MALT lymphoma, negative for *H. pylori* and t(11;18)(q21;q21) (reviewed by the Joint Pathology Center in Bethesda, MD). Repeat EGD 1 month later demonstrated identical findings (Figure 1). Stool testing for *H. pylori* antigen was also negative.

Agent Orange exposure should be considered a risk factor for development of gastric MALT lymphoma.

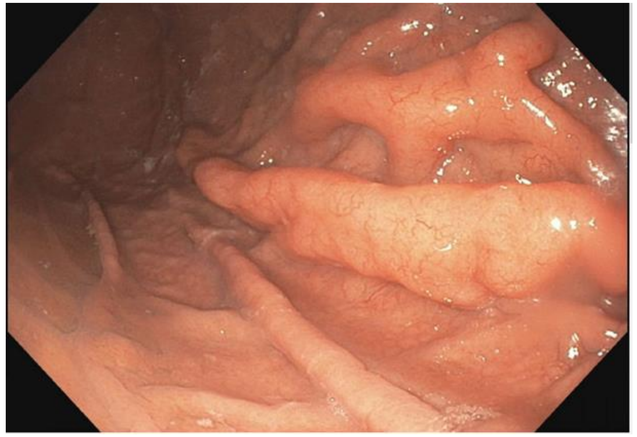

Figure 1. Pre-radiation EGD demonstrating abnormal gastric mucosa with prominent gastric fundus folds seen on retroflexion during EGD prior to ISRT (radiation) therapy

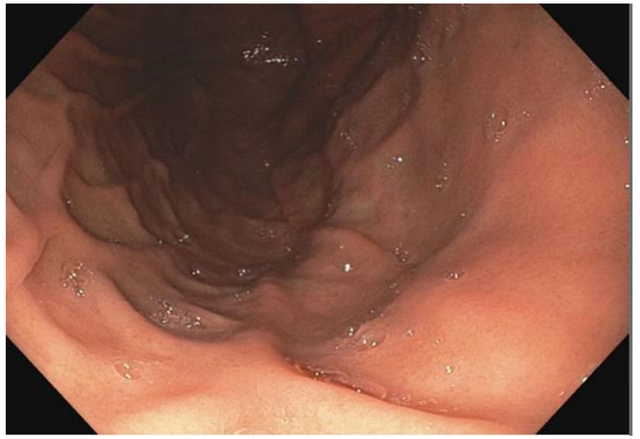

Figure 2. Post-radiation EGD demonstrating resolution of the abnormalities seen with the pre-treatment EGD including disappearance of the prominent gastric fundus folds

Patient Course

The patient was referred to oncology and after staging imaging was found to have stage IE gastric MALT lymphoma. He was treated with involved site radiation therapy and EGD 3 months later showed both endoscopic and pathologic resolution (Figure 2).

Discussion

- The 10% of cases of *H. pylori* negative gastric MALT lymphoma have an unclear etiology
- Dysregulation of nuclear factor-kappa B (NF-κB) principally via translocations t(11;18)(q21;q21) is thought to be a potentially causative genetic alteration
- Neither *H. pylori* nor the common t(11,18) genetic alteration were present in this patient
- Since AO is implicated in NHL and the most common site of extranodal non-Hodgkin lymphoma is the gastric mucosa, patients with a history of significant AO exposure may be at increased risk for developing gastric MALT lymphoma

References

1. Nakamura S, Matsumoto T. Helicobacter pylori and gastric mucosa-associated lymphoid tissue lymphoma: recent progress in pathogenesis and management. *World J Gastroenterol*. 2013;19:8181–8187.
2. Institute of Medicine. 1994. *Veterans and Agent Orange: Health Effects of Herbicides Used in Vietnam*. Washington, DC: The National Academies Press
3. Asano N, Iijima K, Koike T, Imatani A, Shimosegawa T. Helicobacter pylori-negative gastric mucosa-associated lymphoid tissue lymphomas: A review. *World J Gastroenterol*. 2015;21(26):8014-8020.