

Lymphocytic Phlebitis of the Stomach – A Case Report with Literature Review –

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Lymphocytic phlebitis of gastrointestinal (GI) tract is a rare disease. Approximately 50 cases of lymphocytic phlebitis of the GI tract have been reported. Most of these involved the colon or small intestine and presented as acute abdomen. We report the second case of lymphocytic phlebitis of the stomach. A 73-year-old female complaining of dizziness had endoscopic and computed tomography findings strongly suggested gastric cancer, while gastric biopsy was negative for carcinoma. The partial gastrectomy specimen showed lymphocytic phlebitis involving veins in the submucosa, muscularis propria, and serosa while the adjacent arteries were spared. The veins were mainly surrounded by lymphocytes. When a patient has a lesion in the GI tract that is suggesting cancer without biopsies revealing any carcinoma, the pathologist should recommend a deeper biopsy for a proper examination of the submucosa.

Key Words: Lymphocytic phlebitis; Gastric vasculitis; Localized vasculitis

Vasculitis is an inflammatory disease of blood vessels that can affect all types of vessels in any organ of the body, including the vessels of the gastrointestinal (GI) tract. It may be secondary to systemic disorders, such as connective tissue disease (e.g., systemic lupus erythematosus, and rheumatoid arthritis), infection (e.g., bacterial endocarditis), malignancy, or drugs.¹ Primary localized vasculitis of the GI tract is a rare condition.²⁻⁴ Vasculitis involving only the venous system of the GI tract is even more uncommon. Approximately 50 cases of lymphocytic phlebitis of the GI tract have been reported.⁵⁻¹⁵ Most of these involved the colon or small intestine,⁵⁻¹⁵ the stomach was involved in only one case.⁹ Most of these cases presented as acute abdomen. Here, we report a case of lymphocytic phlebitis of the stomach, which presented with an unusual symptom and was clinically and radiologically suspected as a cancer.

CASE REPORT

A 73-year-old female visited the emergency department com-

plaining of dizziness. She had no other symptoms other than dizziness and chronic pain in both knee joints. She had been taking antihypertensive medications for 7 years, and she used non-steroidal anti-inflammatory drug for osteoarthritis of the knees. On laboratory tests, her hemoglobin was 3.3 g/dL, and the peripheral blood morphology showed microcytic hypochromic red blood cells. The iron, total iron binding capacity, and ferritin level were 4 µg/dL, 216 µg/dL, and 12.7 ng/mL, respectively. These findings were consistent with an iron deficiency anemia. As part of the search for the cause of the anemia, the patient underwent an upper GI endoscopy.

Endoscopic findings included superficial ulcers in the posterior wall along the greater curvature, a diffuse, elevated lesion starting from the antrum to the body of the stomach, and severe nodular edema of the pyloric region, which the 0.9 cm-diameter endoscopic fiber barely passed through. Two random biopsies were taken from the prepyloric and pyloric regions. The histopathological report was chronic active gastritis with intestinal metaplasia. As the gross endoscopic findings had been very suggestive of advanced gastric cancer, the patient underwent a

second endoscopy, and two other random biopsies were taken from the anterior wall of the antrum and the lower body. The histopathological examination was again negative for carcinoma. In addition to the endoscopic findings, the computed tomography (CT) scan of the abdomen showed irregular wall thickening of the pylorus and antrum, again consistent with gastric cancer. In spite of the negative biopsies, the endoscopic findings and the CT scan were strongly suggestive of an advanced gastric cancer, and partial gastrectomy was recommended. During the operation, the surgeon sent three small fragments of gastric mucosa for frozen section biopsy. Again, these were negative for carcinoma. The operation finished uneventfully and the patient recovered well. The diagnosis of lymphocytic phlebitis was made from the partial gastrectomy specimen. The patient had no evidence on blood tests, such as antinuclear antibody, rheumatoid factor, or cryoglobulin, of the systemic diseases known to be associated with vasculitis.

The specimen measured 15 cm on the greater curvature and 12 cm on the lesser curvature. In the posterior wall of the body, the prepyloric, and the pyloric regions, the mucosa was diffusely erythematous and irregular in contour, showing some superficial ulcers, from the proximal margin to the distal margin. These irregular erythematous lesions were suspicious for carcinoma. The gastric wall, including the otherwise unremarkable portions, was diffusely edematous (Fig. 1).

Histological examination revealed chronic gastritis with intestinal metaplasia in most of the sections, some with chronic active gastritis with erosion in the mucosa. Submucosal edema was observed throughout. Lymphocytic phlebitis involved veins in the submucosa, the muscularis propria, and the serosa (Fig. 2). Among these, the veins in the submucosa were predominantly affected. The veins and venules were surrounded by dense infiltrates of lymphocytes with occasional plasma cells and eosinophils. Both concentric and eccentric patterns were seen. Adjacent arteries were completely spared. These findings were not confined to the grossly abnormal mucosa; the otherwise unremarkable edematous mucosa was also affected. No fibrinoid necrosis in the vessel wall, granulomatous inflammation, or thrombus was identified.

The immunohistochemistry showed that the lymphocytes were a mixture of CD3+ and CD20+ cells (Fig. 3). The ratio of CD20:CD3 positivity was approximately 1:1. Among the CD3+ T-cells, most were CD8+ T-cells, and some of the CD8+ T-cells showed reactivity for granzyme B, one of the markers for activated cytotoxic T-cells.

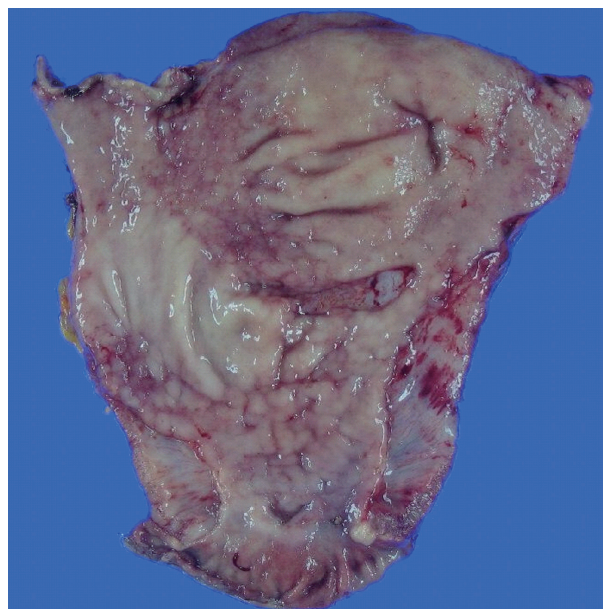


Fig. 1. Gross appearance of the specimen. The gastric wall is diffusely edematous. In the posterior wall of the body, the prepyloric, and the pyloric regions, the mucosa is diffusely erythematous and irregular in contour. Superficial ulcers in the posterior wall of the lower body are observed along the greater curvature. The mucosal defects are due to frozen section biopsies taken during the operation.

DISCUSSION

In 1976, Stevens *et al.*⁶ first reported a case of a 37-year-old female who underwent a hemicolectomy for sudden abdominal pain and diarrhea. They described lymphocytic phlebitis throughout the venous system of the bowel wall; the arteries were completely spared. Thirteen years later, Saraga and Costa³ described three cases, introducing the term “enterocolic lymphocytic phlebitis.” Since then, approximately 50 cases of lymphocytic phlebitis in the GI tract have been reported.⁵⁻¹⁵

Most patients with enterocolic lymphocytic phlebitis (ELP) present with acute abdomen: severe abdominal pain, diarrhea, and/or GI bleeding.⁵⁻¹⁵ The age range is broad, 25-77 years, and there is no gender predilection.^{7,14} The most frequent site affected is the right colon, but other parts of the colon, the ileum, the appendix, and the stomach, can also be involved.⁵⁻¹⁵ None of the patients reported to date have had any known underlying systemic diseases associated with vasculitis. Most recover quickly after the surgery.⁵⁻¹⁵ No reports of recurrence have been noted, except in one case, which was considered to be due to incomplete resection of the initial lesion rather than spontaneous recurrence.¹⁵

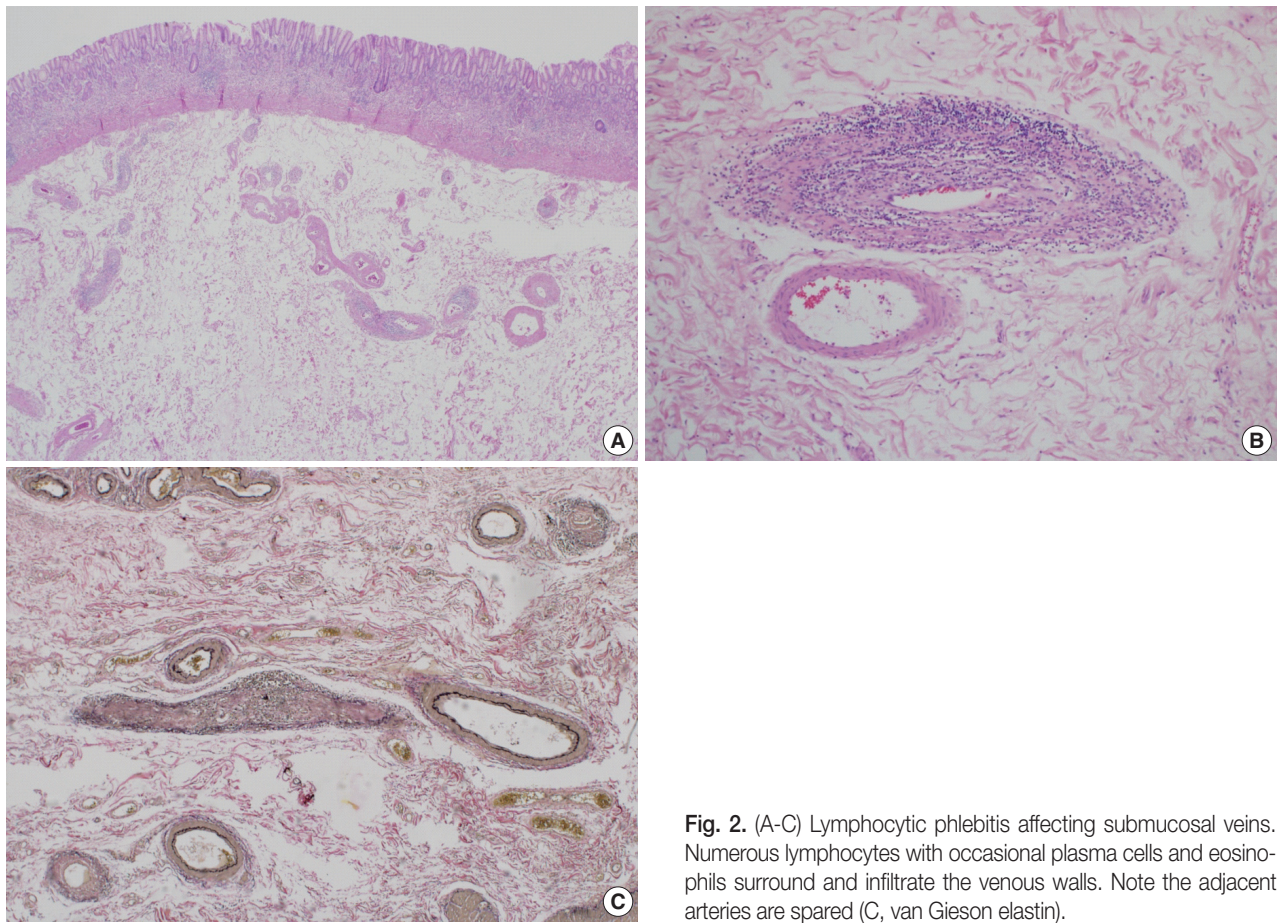


Fig. 2. (A-C) Lymphocytic phlebitis affecting submucosal veins. Numerous lymphocytes with occasional plasma cells and eosinophils surround and infiltrate the venous walls. Note the adjacent arteries are spared (C, van Gieson elastin).

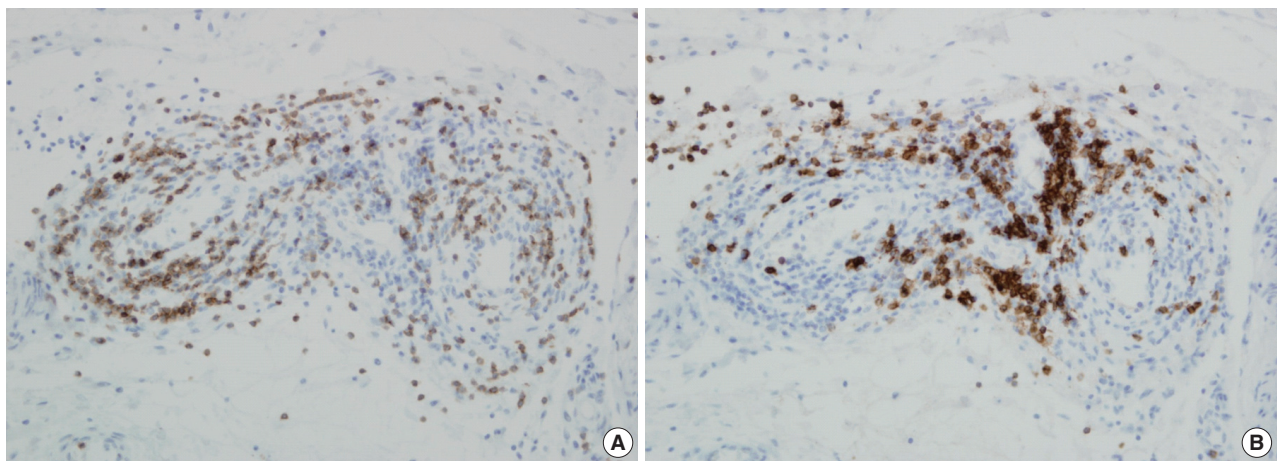


Fig. 3. The immunohistochemical stain shows no zonal distribution of B- and T-cells (A, CD3; B, CD20).

The histological appearance of ELP shows extensive phlebitis of the submucosal, mural, and serosal veins with complete arterial sparing. Some reports have described thromboses and fibrinoid necrosis in the wall of the vein,^{7,11-13,16} but this was not present in the case reported here. Other authors have mentioned

that even in cases in which the macroscopic appearance of the mucosa is normal, microscopic changes have been found at the surgical resection margin.^{5,13,14} In the present case, examination of both grossly abnormal areas and relatively normal areas at surgical resection margins revealed lymphocytic phlebitis. How-

ever, patients with incomplete resection did not complain of any symptoms after the surgical interventions in previous reports.^{5,13,14} This suggests that incomplete resection does not always cause recurrent disease. Abraham *et al.*⁹ and Paik *et al.*¹³ reported that the majority of the lymphocytes were T-cells, whereas Tuppy *et al.*¹² found no zonal distribution of B- and T-cells. And Medlicott *et al.*¹⁶ described T-cell dominance in ischemic areas and no zonal distribution in the margins and intact areas. In the present case, was no zonal distribution of B- and T-cells in either the grossly abnormal regions or the unremarkable edematous regions was seen.

The pathogenesis of lymphocytic phlebitis is unknown. A case of a patient who presented with ELP and lymphocytic colitis was reported in which the specific causative agent was determined to be flutamide, an antiandrogen drug.¹¹ Chetty *et al.*¹⁷ have reported incidental ELP in the rectal stump of patients who have undergone diversion for inflammatory bowel disease. In fact, they discovered that ELP occurred frequently in patients with diversion colitis compared with patients without diversion colitis.¹⁷ They have proposed that altered bowel flora and immune dysregulation may cause lymphocytic phlebitis in diversion colitis. Stevens *et al.*⁶ have suggested that ELP might represent an immunological reaction to materials absorbed from the bowel, and Saraga and Bouzourenne⁷ have suggested a hypersensitivity reaction associated with lymphocyte-mediated vascular damage. Tuppy *et al.*¹² have also reported that among the population of lymphocytes, T-cells expressing T-cell restricted intracellular antigen-1, a protein found in cytotoxic granules, are present, along with a small subgroup of T-cells containing granzyme B, another protein of cytotoxic granules found in activated cytotoxic T-cells. They have proposed that these findings revealing T-cells of the cytotoxic lineage support the possibility that lymphocyte-mediated vascular damage may be of central importance in the pathogenesis of this disease. In view of the finding of granzyme B-positive T-cells reported in the current study, this assumption might be valid.

No specific endoscopic or imaging findings indicate a diagnosis of lymphocytic phlebitis of the GI tract. Some authors described that CT and/or transabdominal ultrasonography showed an edematous and thickened bowel wall which was also observed in our case.^{11,14} Some papers also reported that the lesions in the bowel were suspicious for carcinoma clinically and radiologically because they presented as abdominal masses due to edema and inflammation.^{8,12} On gross examination, lesions appeared to be edematous with wall thickening and some of them showed granular mucosa, hemorrhage, and/or ulcers.^{8,9,11-14,16} It

seems difficult to distinguish lymphocytic phlebitis of the GI tract from carcinoma clinically and radiologically when it forms a mass-like lesion due to edema and inflammation. Therefore, the lack of cases is one of the reasons that a large group study would be helpful for indicating a diagnosis of lymphocytic phlebitis of the GI tract using endoscopy and radiology.

Since most of the reported cases presented with acute abdomen, the patients underwent on surgical interventions. However, cases with chronic courses were also seen. Abraham *et al.*⁹ reported a gastroduodenal lymphocytic phlebitis with epigastric pain and gastric ulceration for 9 months, and in a series of Saraga and Bouzourenne,⁷ 4 out of 6 patients had abdominal pain, weight loss, and/or rectal bleeding for several weeks to months before onset of acute abdomen. This suggests that lymphocytic phlebitis of the GI tract might not always present as acute abdomen, but can present as chronic illness and might not always require surgical intervention.

In the present case, the patient had iron deficiency anemia. To evaluate the cause of the anemia, she underwent a gastroduodenal endoscopy and the endoscopic finding was highly suspicious for carcinoma. The clinicians pointed out that gastric cancer may be responsible for the origin of the anemia, but, unexpectedly, it turned out that the patient was negative for carcinoma. Since her hemoglobin level was very low and the gastric ulcers were superficial, lymphocytic phlebitis did not seem to be the origin of the anemia. Further evaluation was required to find out the cause of the anemia, but the patient refused to go through any more procedures.

This is the second reported case of lymphocytic phlebitis in the stomach and the first case to be mistaken for cancer in stomach. If both the pathologist and the clinicians are aware of this disease entity, are reminded of it when a patient has a lesion in the GI tract that is suggesting cancer, and if multiple biopsies are negative for carcinoma, the pathologist may recommend a deeper biopsy for a proper examination of the submucosa. Furthermore, the clinician might try other modalities to evaluate the lesion, such as positron emission tomography/CT, or the clinician may obtain a deeper biopsy sample even without the recommendation of the pathologist. In this way, any unnecessary operations in an asymptomatic patient with a suspicious lesion may be avoided. Even so, as Will *et al.*¹⁸ have suggested, if the clinical features and imaging findings are suspicious for carcinoma when the results of the histological examination are negative for carcinoma, an exploratory laparotomy is still indicated.

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