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A Case of Gastric Mucosa- Associated Lymphoid Tissue Lymphoma (Maltoma) with Multiple Gastric Fistulas and Gastrointestinal Bleeding.

Fallahian F*, Rahimi F**, Khedmat H***, Mohammad Alizadeh AH±.

* Baqiyatallah Research Center for Gastroenterology and Liver Disease, Tehran, Iran, ** Professor, Department of Pathology, Shahid Beheshti University of Medical Sciences, Tehran, Iran, *** Associate Professor. Baqiyatallah Research Center for Gastroenterology and Liver Disease, Baqiyatallah University of Medical Sciences, Tehran, Iran, ± Associate Professor. Research Center for Gastroenterology and Liver disease; Shahid Beheshti University of Medical Sciences, Tehran, Iran.

Correspondence: Dr. H. Khedmat, Baqiyatallah Research Center for Gastroenterology and Liver Disease, Baqiyatallah University of Medical Sciences, Tehran, Iran, Telephone: +98(21) 8803-7560, Fax: +98(21) 8803-7560, E-mail: dr.khedmat@gmail.com

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Abstract:

The case study reported here involves a 47 old man who presented with hematochesia, intermittent fever, anorexia, weight loss, and postprandial vomiting at our clinic. A upper gastrointestinal series with water-soluble contrast media was performed in addition to a gastroscopy, an abdominal computed tomography (CT) scan, and surgical examination. These diagnostic tests revealed that the patient had gastric MALTOMA, gastrointestinal bleeding, and gastrocolic, gastropancreatic, and gastrosplenic fistulas, however, multiple fistulization of gastric MALT lymphoma to adjacent organs was not observed.

Keywords: MALT; gastro colic/ gastro pancreatic/ gastro splenic fistulas; gastrointestinal bleeding

Introduction:

Gastric lymphoma is a rare malignancy that accounts for less than 2% of primary gastric cancers.⁽¹⁾ In spite of this, it is the most common extranodal lymphoma, and accounts for anywhere between 4 to 20% of lymphomas of this type.^(2, 3) Gastric lymphomas have the highest prevalence in patients over the age of 50, and men are affected two to three times more frequently than women.^(4, 5) Mucosa-associated lymphoid tissue (MALT) lymphomas are extranodal cancers originating from the B cells of the mucosa and sub mucosa of lymphoid tissue, usually in the stomach and regional lymph nodes.⁽⁶⁾ This type of cancer accounts for approximately 8% of non-Hodgkin's lymphomas. MALT lymphomas are equally prevalent in stage I (localized to the stomach) and stage II (involving regional lymph nodes), with less than 10% occurring in advanced stages.⁽⁷⁾ Because of this, MALT lymphomas rarely lead to systemic metastasis.

Case Report:

A forty-seven year old man was referred to our hospital with hematochesia, intermittent fever, perspiration, anorexia, weight loss of about 30 kg in 4 months, and postprandial vomiting. The patient did not report a history of epigastric pain, smoking, or alcohol consumption. He exhibited wasting due to bitemporal atrophy, but showed no evidence of lymphadenopathy or hepatomegaly. Diagnostic tests revealed that the patient exhibited anemia, leukocytosis, hypokalemia, and

uncompensated metabolic alkalosis. A gastroscopy identified four gastric ulcers in the fundus that were draining a odorous fluid (figure 1). In addition, a colonoscopy detected melena, and abdominal computed tomography (CT) showed a large nonhomogenous mass in the left abdomen, with mass effects on the stomach and left kidney. Other tests revealed ascites and left pleural effusion (figure 2), and an upper gastrointestinal series with water-soluble contrast media revealed a gastrocolic fistula (figure 3).

During surgery, fistulas in the spleen, pancreatic involvement, and a tumor in the left colon were detected and splenectomy, pancreatectomy, partial gastrectomy, and colostomy were performed. Samples from partial gastrectomy, left hemicolectomy, splenectomy, and the distal pancreas showed diffuse immunoblastic B cell lymphoma involving the gastric and colonic walls and splenic tissue. Multiple biopsies showed low-grade gastric MALT lymphoma (figure 4).

Histological examination of the spleen, partial stomach, and large intestine revealed diffuse neoplastic proliferation, as evidenced by with the appearance of vesicular nuclei, prominent nucleoli, and marginal chromatin condensation in the lymphoid cells. The cytoplasm was eosinophilic and scant to moderate nuclei were eccentrically located. Permeating of the neoplastic proliferation in the colonic wall and splenic tissue was also noted. Extensive foci of necrosis was evident in the latter.

Figure 1, Gasteroscopy of the patient.

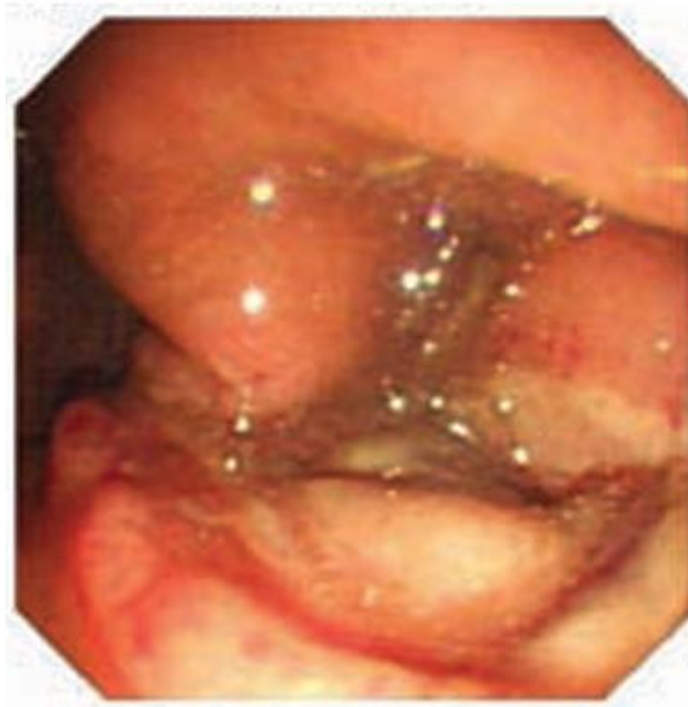


Figure 2, Abdominal CT scan of the patient.

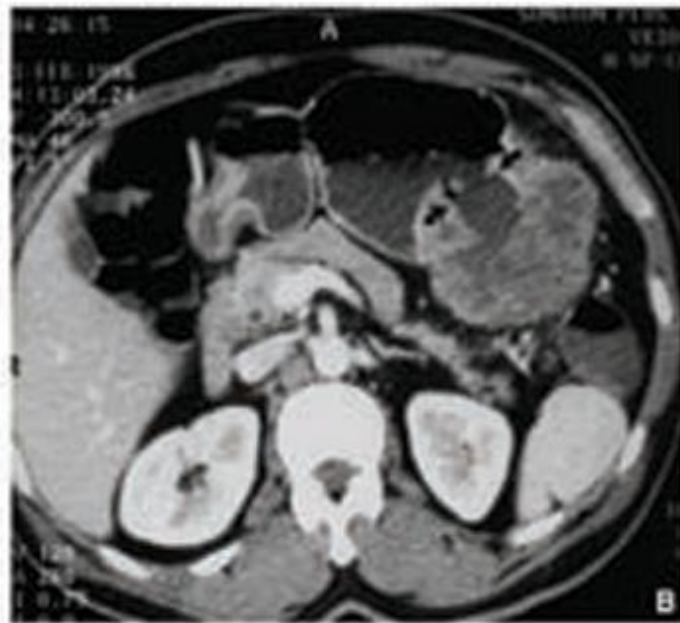


Figure 3, Barium meal of the patient. arrows indicate gastrocolic fistula.

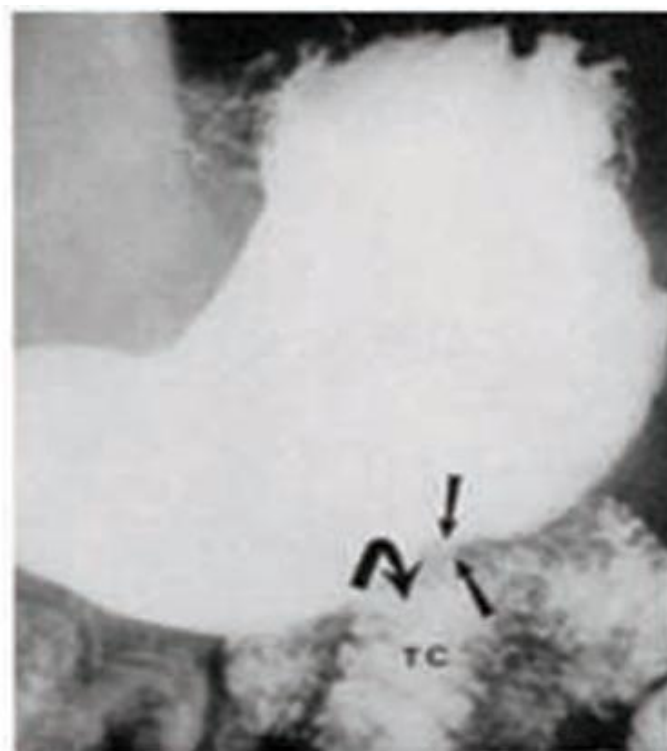
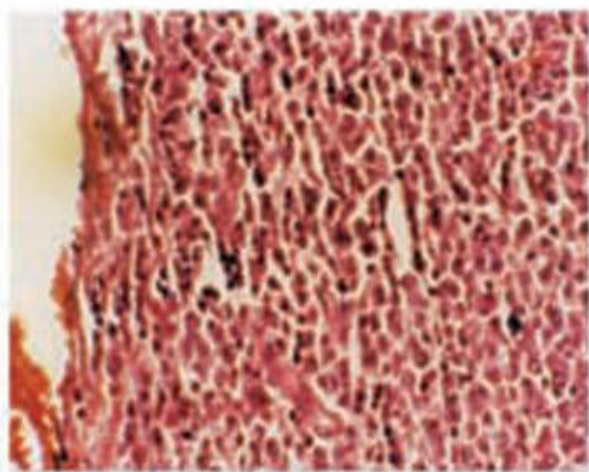


Figure 4, Gastric Histology slide of the patient.



Discussion:

Most cases of gastric lymphoma are of the non-Hodgkin's type. Early symptoms are vague, and many patients go long periods of time before a diagnosis is established and the proper treatment is initiated.⁽⁸⁾ Some common symptoms include abdominal pain, early satiety, nausea, vomiting, anorexia, weight loss, abdominal fullness, weakness, night sweat, jaundice, fever, and dysphagia.⁽⁷⁾ Difficulties in diagnosis occur because these symptoms are often presented in patients with other abdominal pathologies, such as peptic ulcer disease, gall bladder, pancreatic and functional disorders, as well as gastric neoplasms.⁽⁹⁾ In addition, approximately 20 – 30% of patients report bleeding in the form of hematemesis or melena, and on rare occasions, gastric obstructions and perforations.⁽¹¹⁾ To complicate matters further, results from radiographic and endoscopic analysis of gastric lymphomas are often indistinguishable from those produced from peptic ulcer disease, gastritis, and other gastric neoplasms.

A diagnosis can often be supported by contrast enhanced radiographic analysis, however, the sensitivity of such studies is low and the findings are often non-specific for gastric lymphoma. The primary method for diagnosis of gastric lymphoma is esophagogastroduodenoscopy, which not only provides a means for pathologic diagnosis through biopsy, but also is important in the identification of other disorders with overlapping symptoms. It should be noted, however, that obtaining a diagnostic biopsy is difficult because gastric lymphomas spread submucosally and have vague surface qualities. Because of this, several speci-

mens are often required in order to obtain an accurate diagnosis.⁽¹⁾ Prior to initiating treatment of a newly diagnosed gastric lymphoma, it is important to rule out the presence of systemic lymphoma. Bone marrow biopsy, chest radiography, and abdominal CT are necessary for this evaluation, and should also be performed regularly throughout the course of treatment.⁽¹⁾ In addition, all patients suspected of having primary gastric lymphomas should undergo indirect laryngoscopy to rule out involvement of Waldeyer's ring.

The bacteria *Helicobacter pylori* has been identified as an important etiological factor that may increase one's susceptibility to MALT lymphomas, however, some studies have found a low rate of *H. pylori* infection among those with MALT lymphomas. This suggests that not all gastric lymphomas are related to this bacteria. In one study, 31 cases of resected gastric lymphoma were analysed. Tests revealed that 10 cases were low-grade MALT lymphomas and 21 cases were high-grade MALT lymphomas. *Helicobacter pylori* were found in 58% of cases, suggesting that *H. pylori* infection may play a promoter role in the development of MALT lymphoma, even though its presence is not mandatory for the progression of the lymphoma in view of its low frequency in advanced high-grade MALT lymphoma.⁽¹²⁾

Yamasaki R, et al (2004) reported that *Helicobacter pylori* heat-shock protein 60 kilodalton (kDa) is an important antigen in the pathogenesis of MALT lymphoma. In cases of low-grade MALT lymphoma, adaptive immune responses against

heat-shock protein 60 kDa (hsp60) by *Helicobacter pylori* may be enhanced by host factors such as antigen presentation and T-cell activation. This may result in B-cell proliferation and can be demonstrated during chronic *H. pylori* infection.⁽¹³⁾

The strongest evidence for the significance of *H. pylori* in the pathogenesis of low etiological-grade gastric MALT lymphoma is provided by clinical studies where treatment of *H. pylori* infection is followed by a complete regression of these tumors in most patients.⁽¹⁴⁾ Gastrosplenic fistula formation resulting from primary gastric malignancy is rare and should be managed as a matter of emergency. A patient with primary non-Hodgkin's lymphoma of the stomach⁽¹⁵⁾, and another patient with spontaneous gastrosplenic fistula secondary to pathologically proven diffuse splenic large cell lymphoma⁽¹⁶⁾ were identified. The formation of a gastropleural fistula is an uncommon complication that can occur in a number of conditions. In one case, a patient with gastropleural fistula as a complication of gastric lymphoma developed tension pneumothorax and empyema.⁽¹⁷⁾ An additional case of primary lymphoma of the spleen associated with gastrosplenic fistulae was reported.⁽¹⁸⁾

In yet another study⁽¹⁹⁾, it was reported that only four cases of gastrocolic fistula were identified in the literature among patients with primary non-Hodgkin's lymphoma (NHL) of the stomach, and all were associated with disseminated (stage IV) disease. In one of these cases, gastrocolic fistula was suspected due to

feculent vomiting and an examination of the fistula through a CT scan.

The treatment of gastric lymphoma is an area of ongoing controversy. Surgical resection has been the standard therapy. Recent advances, however, have been developed in other treatment modalities.⁽¹⁾ A case of low-grade MALT lymphoma treated with radiotherapy alone is reported. This case highlights treatment issues related to the substantial reduction in the size of the irradiated volume achieved by treating the patient in a fasting state.⁽²⁰⁾ In a previous study⁽²¹⁾, the authors performed pathological examinations in patients diagnosed with primary large cell lymphoma of the stomach, and who had received systemic chemotherapy. The results of the study suggested that the presence of the trademark histological features of MALTOMA in patients with primary large cell gastric lymphoma might be associated with a better response to systemic chemotherapy and a better prognosis. In another study⁽²²⁾, the effects of conservative treatment in 29 patients with non-Hodgkin lymphomas located mainly in the stomach and duodenum was evaluated. The author concluded that complete remission in all cases of stage I, II, and III gastric lymphomas, including MALT lymphomas, could be induced through combination therapy utilizing *Helicobacter pylori* (*H. pylori*) eradication, chemotherapy, and radiation, and that complete remission could be induced in stage IV lymphomas located in the stomach and duodenum in 50% of cases. These cases have many clinical, histopathological, and immunohistochemical features in common, and it is proposed that this is because they

share a common pattern of histogenesis from MALT. The author stated that the clinical and histopathological features of these lymphomas can be understood in the context of the behavioral characteristics and morphology of MALT. The case presented in this paper exhibited positive serology for *H. Pylori*; however, a histological examination of gastric mucosa was negative. Complete worked-up was performed for tuberculosis because of his constitutional symptoms. After surgery, the patient's general condition and weight improved and he was referred to chemotherapy.

In conclusion, endoscopic aspects of MALT lymphoma are nonspecific. Acute upper gastrointestinal hemorrhage may be the first clinical manifestation of the disease. Attention should be paid to infiltrative gastric lymphomas, as it is difficult to diagnose and differentiate them from other gastric conditions such as ulcers and erosions. Efforts should be made to improve the early diagnosis of gastric lymphomas, as early detection is key to a better prognosis

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