

Gastric MALT-Lymphoma: more than Helicobacter Pylori

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Abstract

In this case report, we describe two cases of gastric mucosa-associated lymphoid tissue (MALT) lymphoma. The first patient, who presented with complaints of indigestion, nausea and epigastralgia, had a solid ulcer on endoscopy. Biopsies showed, next to MALT, presence of Helicobacter Pylori. The second patient was admitted with hematemesis. The multiple ulcerations in his stomach were thought to be cocaine-induced. Only after multiple biopsies the diagnosis of MALT was made. No presence of Helicobacter Pylori could be detected. The first patient was successfully treated with Helicobacter Pylori eradication therapy. Localized radiotherapy resulted in complete remission in our second patient. Hence, in absence of Helicobacter Pylori, more aggressive treatment modalities are needed. (*Acta gastroenterol. belg.*, 2021, 84, 657-659).

Keywords: MALT-lymphoma, stomach, Helicobacter Pylori, eradication.

Introduction

Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma) of the stomach is a rare entity with an estimated incidence of 0.41/100,000/year (1). This subtype of non-Hodgkin lymphoma accounts for 50% of the primary gastric lymphomas (PGL). Primary gastric lymphoma's are estimated to represent 2-8% of all malignancies of the stomach (2). A gastric MALT-lymphoma is typically a low-grade B-cell neoplasia. Most of the cases are Helicobacter pylori (*H. pylori*) associated (3). Therefore first line therapy in early stages is the eradication of *H. pylori*. In advanced stages radiotherapy, chemotherapy, immunotherapy, or combination chemoimmunotherapy is recommended (4,5).

Case descriptions

Case 1

A 75-year-old female, presented at the outpatient gastro-enterology clinic with persistent complaints of indigestion, nausea and epigastralgia. She had lost more than 5kg over the last 6 months. In her medical history, only a sterilization procedure was withheld. Treatment with omeprazole 20mg daily, started by her general practitioner had been unsuccessful. Abdominal ultrasound didn't show any abnormalities. A gastroduodenoscopy showed a solid Forrest III ulcer in the gastric corpus with a malignant aspect (Fig 1). Gastric biopsies showed an Helicobacter pylori-associated

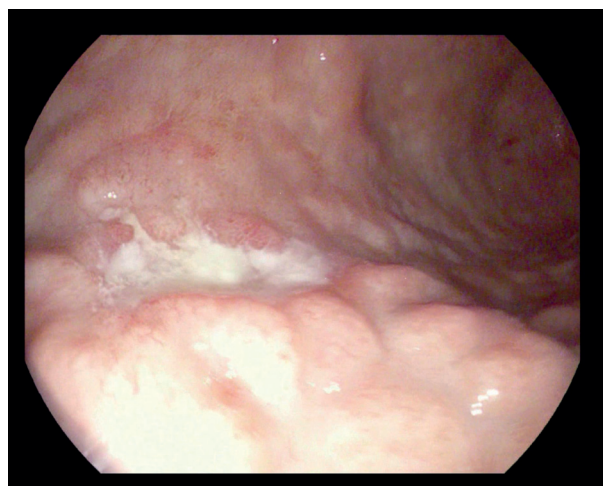


Figure 1.

active and ulcerative gastritis. Biopsies of the ulceration showed the presence of a non-Hodgkin B-cell lymphoma, mainly compatible with a MALT-lymphoma. The immunohistological staining of the tissue was positive for CD20 and negative for CD5, CD10 and Cyclin D1. CT-scan of the thoracic and abdominal region didn't show any abnormalities. Eradication therapy with Tryplera (bismuth/metronidazole/tetracycline) 4x3 tablets/day for 10 days and double dose PPI was started.

Patient was re-evaluated after 2 months with resolution of her complaints. Gastroduodenoscopy showed healing of the ulcer. Repeat biopsies couldn't demonstrate the presence of *H. pylori*. However, there was a lingering B-cell infiltrate in the lamina propria, compatible with the MALT lymphoma, on this biopsy. Treatment with intermediate dose PPI was continued.

Endoscopic re-evaluation after one year showed no visible alteration with normal random biopsies. Low dose PPI was continued as patient suffered from pyrosis after weaning of PPI.

Case 2

A 31-year-old male, was admitted to the emergency department with hematemesis since 3 hours. He had

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Figure 2.

an unremarkable medical history and didn't take any medication. Occasionally he used cocaine. An urgent gastroduodenoscopy was performed and showed multiple ulcers of which two were Forrest Ib ulcers. Hemostasis with adrenalin and aethoxysklerol was successfully performed. Biopsies from gastric corpus and antrum showed mild chronic inflammation. *H. pylori* was negative on biopsies. The patient promised to quit his cocaine use and single dose PPI (pantoprazole 40mg) was initiated.

Two months later, a new gastroscopy still showed multiple small ulcers. Pantoprazole was continued. Four months after the first gastroscopy, a new endoscopy only showed a minimal gastritis at the angular incisure of the stomach. PPI was stopped.

However, 7 months afterwards patient was re-admitted to the emergency department with coffee ground vomitus. A gastroduodenoscopy revealed multiple antral ulcerations and a deep irregularly shaped ulcer with active bleeding (Forrest Ib) in the gastric corpus (Fig 2). Hemostasis was successfully achieved using 5 hemoclips. Urinary toxicology screening was positive for cocaine. Awaiting the result of the gastric biopsies, the tentative diagnosis of an ischemic gastritis due to cocaine use was made and the patient was discharged with in stable clinical condition with pantoprazole 40mg. However, biopsies of the deep ulcer however showed a dense reactive lymphoid infiltrate, possibly compatible with a MALT lymphoma. No signs *H. pylori* infection were withheld on biopsy. One month later a new gastroduodenoscopy was performed and multiple biopsies were taken from the ulcerative zone in the gastric corpus. Immunohistochemical examination confirmed the presence of a MALT lymphoma with CD20 positivity on staining. Staining for CD5, CD10 and Cyclin D1 was negative. On this repeat biopsy *Helicobacter pylori* was also negative. A PET-CT scan was performed and showed a hypermetabolic diffuse thickening of the gastric corpus with multiple locoregional enlarged lymph nodes against the greater and lesser curvature. The lymphoma was staged IIE (Lugano classification) (6). Radiotherapy

(12x2 Gy) of the stomach and adjacent lymph nodes was initiated two month later. A gastroduodenoscopy five months after radiotherapy showed a normal gastric mucosa. Repeat biopsy showed no arguments for a residual MALT-Lymphoma. A mild chronic gastritis was still demonstrated, but IHC for *Helicobacter pylori* once was again negative. An MRI scan didn't show lymphadenopathy.

Discussion

Like we could notice in this two cases, symptoms of a gastric MALT lymphoma are ranging from vague dyspepsia and discomfort in the upper abdominal region to alarm symptoms such as hematemesis or coffee ground vomitus (7). Endoscopic appearance can vary from hyperemic gastric mucosa, mucosal petechial hemorrhages, to multiple erosions or even a nodular pattern (5). Zullo A et al. proposed an endoscopic classification of gastric MALT-lymphoma in 2014 (table 1) (2). According to this proposed classification, our two cases presented as an ulcerative type. The presence of *Helicobacter pylori* is estimated to be around 90% in patients with gastric MALT lymphoma. In our second case, the presence of *H. pylori* could not be demonstrated on repeated biopsies. According to the European Society of Medical Oncology (ESMO) guidelines, a fecal antigen or breath test and serology studies are recommended when the results of histology are negative (4). In this case, the absence of *H. pylori* on multiple biopsies supports the hypothesis that *H. pylori* may be present in early lymphoma stages, but may disappear with tumor progression (8). Our patient with the *H. pylori* negative MALT-lymphoma was treated with radiotherapy (RT). RT is described as the preferred treatment for localized disease in patients who do not achieve lymphoma regression following antibiotic therapy. Also, MALT-lymphomas with deep mucosal invasion, like in our case, are less likely to respond to eradication therapy (9). A systematic review in 2014, including data of 11 studies with 110 patients with low-grade gastric lymphoma, showed that eradication therapy achieved complete lymphoma regression in 15.5% of

Table 1
Endoscopic classification of gastric MALT-lymphoma after
Zullo A. et al (2)

Lymphoma type	Endoscopic presentation
Normal/hyperaemic mucosa	Normal mucosa/hyperaemic modification
Petechial haemorrhages	Presence of mucosal petechial haemorrhages
Hypertrophic	Nodular pattern; large or giant folds
Exophytic	Irregular mucosa – tumor-like appearance or polypoid mass
Ulcerative	Multiple erosions/single or multiple ulcerations
Mixed	A combination of more than one pattern

the patients, although *H. pylori* infection was initially excluded with at least 3 different diagnostic tests (10, 11). Therefore ESMO states that a trial of anti-*Helicobacter* therapy is still worthwhile in *H. pylori* negative patients (4).

Conclusion

MALT lymphoma of the stomach is a rare, mostly low-grade, B-cell neoplasia. Like we showed in our cases, clinical and endoscopic presentation can be very diverse. Most of the cases are *H. pylori* associated and therefore eradication therapy should be considered as first line treatment in every patient with localized disease (4). Our second case is notable because *H. pylori* infection could not be demonstrated. *H. pylori* negative cases often present in a more advanced stage and require more aggressive treatment.

Authors declaration

The authors whose names are listed certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial

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