

Abstract

The choice of treatment in gastric lymphoma is stage dependent. Endoscopic ultrasound (EUS) is a very accurate technique to assess T- and N-staging of primary gastric lymphoma. Two cases of high-grade gastric non-Hodgkin's lymphoma are documented with videos of upper endoscopy and EUS. The technique for an appropriate staging of the disease with EUS is demonstrated. This article is part of an expert video encyclopedia.

Keywords

Endoscopic ultrasound; Gastric MALT lymphoma; Non-Hodgkin's lymphoma; Video.

Video Related to this Article

Video available to view or download at doi:10.1016/S2212-0971(13)70061-X

Techniques

Esophagogastroduodenoscopy; endoscopic ultrasound (EUS); and contrast harmonic EUS.

Materials

- Gastroscope: GIF-Q165; Olympus, Tokyo, Japan.
- Echoendoscope: GF-UE160; Olympus, Tokyo, Japan.
- Ultrasound unit: Alfa 10; Aloka, Tokyo, Japan.
- Contrast agent: SonoVue; Bracco, Amsterdam, The Netherlands.

Key Learning Points

The gastrointestinal tract is the most commonly involved extra-nodal site of non-Hodgkin's lymphoma (NHL), and the stomach is the most common site. The stomach can harbor a primary NHL or be involved secondarily by a disseminated nodal disease. Considering the special properties of the digestive tract, Isaacson *et al.*¹ introduced the mucosa-associated lymphoid tissue (MALT) concept, classifying primary gastric lymphoma as a distinct entity with peculiar histological and biological features.

In the stomach, tumoral involvement can often be multifocal.² From the mucosa, MALT lymphoma gradually infiltrates the underlying submucosa, muscularis propria, and serosa; simultaneously, malignant cells can reach the regional lymph nodes and other gastrointestinal tracts or the spleen. Moreover, low-grade MALT lymphomas can evolve in high-

grade lymphomas, which have a more aggressive histological and clinical behavior.

Although the stomach is the most common intestinal site of MALT lymphoma, localizations to the duodenum, small and large bowel, esophagus, rectum, larynx, and liver have been reported.³⁻⁶

EUS has been demonstrated to be accurate for the differential diagnosis of large gastric folds. Gastric lymphoma, linitis plastica, Menetrier's disease, inflammatory conditions, and gastric varices account for the most common etiologies that can be accurately identified by EUS.⁷

EUS is very accurate for the diagnosis and staging of gastric MALT lymphoma, which is the most important cause of large gastric folds.⁸

The impact of EUS on clinical outcome of these patients is consistent, as it can predict MALT remission after the simple eradication therapy of *Helicobacter pylori*.⁹⁻¹⁰ In fact, early stage disease infiltrating only the mucosa and/or submucosa, with no involvement of lymph nodes, shows up to 80% response rate. More aggressive therapies, such as chemotherapy and surgery, can now be avoided in the majority of patients affected from low-grade MALT lymphoma.

However, chemotherapy is considered as the treatment of choice in patients with either high-grade lymphoma, advanced disease, or no response to antibiotic regimens.¹¹

It should be kept in mind that EUS is an operator-dependent technique. Suboptimal interobserver agreement has been reported in the staging of gastric lymphoma,¹² as well as with all the other EUS indications described in the guidelines of the American Society of Gastrointestinal Endoscopy.¹³ As a consequence, it is our duty to emphasize that extensive operators' experience and careful examination technique are always warranted to maintain the high levels of accuracy reported in the literature.

Tips and Tricks

- EUS is the most accurate imaging modality for the staging of gastric lymphoma.
- EUS can guide the therapeutic choice according to stage.

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- EUS may also be useful in the follow-up to assess response to therapy and detect early relapse.
- Radial echoendoscopes are more suitable than the linear ones for a complete imaging of the gastric wall.
- To obtain an accurate staging, the stomach should be completely filled with water and debris, and mucus completely aspirated.
- Intravenous injection of antispasmodics improves relaxation of the gastric wall, thereby allowing an adequate assessment of the layers to determine the T-stage.

Scripted Voiceover

<i>Time (min:sec)</i>	<i>Voiceover text</i>
00:01	In this 67-year-old man, EGD reveals a large ulcerated mass originating from the anterior face of the antrum and involving the lesser curvature. Histology is consistent with high grade B cell gastric lymphoma.
00:34	With retroflexion it is appreciated that gastric body and fundus are regular. Endoscopic ultrasound (EUS) is then performed for staging.
00:47	Adequate visualization of the oropharynx should be obtained to ensure a safe intubation of the esophagus with the echoendoscope. Passage through the esophagus is done in a semi-blind fashion due to the oblique endoscopic optic.
01:08	In the stomach, full endoscopic view is achieved allowing proper orientation and positioning of the echoendoscope in relation to the lesion of interest.
01:20	Water filling of the gastric lumen is essential to obtain a good coupling of the ultrasound waves with the gastric layers. Intravenous injection of Buscopan or glucagon is also helpful to obtain relaxation of the gastric wall. Moreover, meticulous aspiration of all residual air pockets and mucus are essential for proper ultrasound imaging. Inadequate distention of the gastric wall and/or incomplete removal of the gastric content may hamper a correct staging of the tumor.
02:14	Once water filling has been completed, EUS imaging begins in front of the pylorus.
02:21	EUS is performed with an electronic radial scanning echoendoscope. The lesion is seen at the 9 o'clock position as a hypoechoic mass infiltrating the gastric wall; the layers are disrupted as typical of lymphoma. The so called transition zone (i.e., the shift from normal to abnormal wall) must be carefully evaluated on both sides of the lesion to obtain an accurate T staging. It is noticed that the lesion has infiltrated the second and third layer (mucosa and submucosa) and has extended into the fourth layer (muscularis propria). The fifth layer (serosa) is still preserved. These features are compatible with a T2 stage gastric lymphoma.
03:27	As gastric lymphoma often presents patchy distribution, the exploration must be completed up to the cardia. For proper visualization of the layers,
	which are normal in this case, the transducer should be kept in the center of the lumen while withdrawing the echoendoscope.
03:55	N staging is subsequently performed. For this purpose, scanning is initiated from the second portion of the duodenum to search for perivisceral and perihepatic lymph nodes. In this case, no lymph nodes are visible. Normal pancreatic parenchyma, common bile duct and portal vein are shown.
04:27	The procedure is completed with transgastric scanning. The image is demagnified to allow deeper investigation of the perivisceral structures and organs. In this case, no lymph nodes are visible. Normal left hepatic lobe, spleen, pancreatic parenchyma, and celiac trunk are shown. These findings are compatible with an N0 stage gastric lymphoma.
05:11	At the end of the procedure all the water is aspirated from the stomach for the sake of the patient's safety and comfort.
05:23	In this 58-year-old woman, EGD reveals two large vegetating lesions in the gastric body. Histology was consistent with high grade B cell gastric lymphoma. EUS is then performed for staging using an electronic radial scanning echoendoscope. The same technique as before is used to accomplish water filling of the lumen and gastric distention.
06:05	The lesions extend over two thirds of the gastric circumference. Upon evaluation of the transition zone it is appreciated that the gastric wall is infiltrated up to the fifth layer (serosa). The latter is disrupted due to tumoral invasion of the perigastric fat, which is seen as pseudopodia. Care is taken to keep the transducer in the center of the lumen to allow appropriate orthogonal visualization of the entire gastric wall, avoiding incorrect staging that can occur with oblique scanning through the neoplastic areas.
07:12	At first sight no clear resection margin is appreciated between the mass and the left lobe of the liver. Close inspection and tissue harmonics allow an optimal discrimination of the layers and tissues with different impedance, revealing that the tumor is contiguous to the liver but is not infiltrating into the parenchyma. As a result T4 disease is ruled out.
07:51	Transduodenal scanning fails to reveal any perivisceral lymph node.
08:01	However, transgastric scanning at the level of the antrum shows a large hypoechoic lymph node outside the greater curvature. This is likely attributable to perigastric extension of the lymphoma. Moreover, multiple small hypoechoic lymph nodes are also visible outside the gastric wall at the 10 o'clock position, nearby the outer margin of the largest lesion. Perigastric tumoral invasion appears in close proximity to the lymph nodes. Slight back and forth movements of the echoendoscope allow careful exploration of the whole area and are essential to assess the TN staging correctly. Overall, these findings are compatible with a T3 N3 stage gastric lymphoma.

- 09:11 Withdrawal of the echoendoscope proximal to the lesions shows additional lymph nodes with pathologic aspect near the liver hilum.
- 09:24 As a note of interest, contrast harmonic EUS after intravenous injection of Sonovue is shown. Gastric lymphoma appears diffusely hyperenhanced with a homogeneous pattern. This behavior might prove useful in evaluating the extension of the disease for staging purposes. This is an off-label use of Sonovue and further research is warranted to establish the role of contrast harmonic EUS in gastric lymphoma staging.

References

1. Isaacson, P.; Spencer, J. Malignant Lymphoma of the Mucosa-Associated Lymphoid Tissue. *Histopathology* **1987**, *11*, 445–462.
2. Wotherspoon, A. C.; Dogliani, C.; Isaacson, P. G. Low-Grade Gastric B-Cell Lymphoma of Mucosa-Associated Lymphoid Tissue (Malt): A Multifocal Disease. *Histopathology* **1992**, *20*, 29–34.
3. Caletti, G.; Togliani, T.; Fusaroli, P.; *et al.* Consecutive Regression of Concurrent Laryngeal and Gastric MALT Lymphoma after Anti-*Helicobacter pylori* Therapy. *Gastroenterology* **2003**, *124*, 537–543.
4. Nagashima, R.; Takeda, H.; Maeda, K.; Ohno, S.; Takahashi, T. Regression of Duodenal Mucosa-Associated Lymphoid Tissue Lymphoma after Eradication of *Helicobacter pylori*. *Gastroenterology* **1996**, *111*, 1674–1678.
5. Fischbach, W.; Tacke, W.; Greiner, A.; Konrad, H.; Müller-Hermelink, H. K. Regression of Immunoproliferative Small Intestine Disease after Eradication of *Helicobacter pylori*. *Lancet* **1997**, *349*, 31–32.
6. Raderer, M.; Pfeffel, F.; Pohl, G.; *et al.* Regression of Colonic Low Grade B Cell Lymphoma of the Mucosa Associated Lymphoid Tissue Type after Eradication of *Helicobacter pylori*. *Gut* **2000**, *46*, 133–135.
7. Caletti, G.; Fusaroli, P.; Bocus, P. Endoscopic Ultrasonography in Large Gastric Folds. *Endoscopy* **1998**, *30*(Suppl. 1), 72–75.
8. Caletti, G.; Ferrari, A.; Brocchi, E.; Barbara, L. Accuracy of Endoscopic Ultrasonography in the Diagnosis and Staging of Gastric Cancer and Lymphoma. *Surgery* **1993**, *113*, 14–27.
9. Ruskoné-Fourmestreaux, A.; Lavergne, A.; Aegerter, P. H.; *et al.* Predictive Factors for Regression of Gastric MALT Lymphoma after Anti-*Helicobacter pylori* Treatment. *Gut* **2001**, *48*, 297–303.
10. Caletti, G.; Zinzani, P. L.; Fusaroli, P.; *et al.* The Importance of Endoscopic Ultrasonography in the Management of Low-Grade Gastric Mucosa-Associated Lymphoid Tissue Lymphoma. *Aliment. Pharmacol. Ther.* **2002**, *16*, 1715–1722.
11. Ruskoné-Fourmestreaux, A.; Fischbach, W.; Aleman, B. M.; *et al.* EGILS group EGILS Consensus Report. Gastric Extranodal Marginal Zone B-cell Lymphoma of MALT. *Gut* **2011**, *60*, 747–758.
12. Fusaroli, P.; Buscarini, E.; Peyre, S.; *et al.* Interobserver Agreement in Staging Gastric Lymphoma by Endoscopic Ultrasonography. *Gastrointest. Endosc.* **2002**, *55*, 662–668.
13. ASGE Standards of Practice Committee; Gan, S. I.; Rajan, E.; Adler, D. G.; *et al.* Role of EUS. *Gastrointest. Endosc.* **2007**, *66*, 425–434.