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Editorial

Thickened Gastric Wall: Simplifying the Diagnosis

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See "Differential Diagnosis of Thickened Gastric Wall between Hypertrophic Gastritis and Borrmann Type 4 Advanced Gastric Cancer" by Jun-Young Se, et al. on page 961, Vol. 18, No. 6, 2024

Hypertrophic gastropathy is a rare condition characterized by enlarged gastric mucosal folds due to foveolar cell hyperplasia, edema, and variable degrees of inflammation.[1] Two clinical syndromes have been identified to cause hypertrophic gastropathy; Zollinger-Ellison syndrome and Menetrier disease. Differential diagnosis is problematic on a clinical basis, and it is frequently required to distinguish other conditions that can cause mucosal hypertrophy, such as gastric malignancy (adenocarcinoma and lymphoma), granulomatous gastritis, gastric varices, and eosinophilic gastritis. Other rare diseases, such as primary hypertrophic osteoarthropathy and primary Sjogren syndrome, have also been reported to cause hypertrophic gastropathy.

Menetrier disease is frequently associated with protein-losing gastropathy and hypochlorhydria. The etiology is unknown, but cytomegalovirus or *Helicobacter pylori* infections have been associated. A previous case-control study reported increased mortality and risk of gastric cancer in Menetrier disease.[2] The mucosa of patients with Menetrier disease demonstrates irregular hypertrophic folds that involve the entire gastric corpus and can mimic linitis plastica gastric cancer.[3] The differential diagnosis of these two diseases can be difficult as a gastric biopsy can be inconclusive in many cases unless full-thickness gastric mucosa is acquired.

In the current issue of *Gut and Liver,* Seo *et al.*[4] provide valuable insights into the differential diagnosis of hypertrophic gastritis (HG) with Borrmann type 4 advanced gastric cancer (AGC B-4). Specifically, the authors performed a retrospective study and compared the two diseases' unique endoscopy and endoscopic ultrasonographic (EUS) features.

The authors reported that AGC B-4 showed male dominance and more frequently reported symptoms such as weight loss, nausea or vomiting, and dyspepsia compared with HG. Hemoglobin, total protein, and albumin levels were significantly lower in AGC B-4. *H. pylori* infection was more frequent in HG but must be interpreted with a caveat as half the cases of AGC B-4 were not investigated for *H. pylori*. Endoscopic findings reported antral wall thickenings and the presence of ulcers to be more frequent in AGC B-4. EUS findings reported the destruction of wall layers or thickened proper muscle (PM) layers in AGC B-4. Multivariable analysis revealed thickened PM layers (≥2.39 mm) and the presence of ulcer as significant risk factors of AGC B-4 with a preserved wall layer.

A previous study reported that HG's endoscopic findings were enlarged folds only in the gastric corpus, reddened mucosa, erosions, adherent mucus layer, and varioliform erosions in the antrum.[5] The present study reported a significant difference in antral wall thickening (39.1% in AGC B-4 vs 4.0% in HG) and ulcer (59.1% in AGC B-4 vs 4.0% in HG). The authors report that simple biopsy at the ulcer showed a 92.6% success rate but fell to 42.6% in patients without ulcers. This suggests the need for other diagnostic methods in patients with thickened gastric walls without ulcers.

The EUS findings of HG have only been described in isolated cases, probably due to the rarity of the disease.[3,5,6] Few studies have directly compared EUS findings between HG and AGC B-4, making this study a valuable contribution. Previous studies reported marked thickening and

increased echogenicity of the second layers with no abnormal echogenicity or thickening of other layers, as EUS findings suggestive of HG. Echogenic thickening (>13 mm) of the mucosal layer has also been reported as a possible characteristic feature of HG.[6] In the current study, HG showed a thickening of the mucosal layer, but the PM layer was not thickened. Meanwhile, AGC B-4 shows thickening of the PM layer more often than HG, and the authors suggest a cutoff of 2.39 mm.

This study has some limitations that must be acknowledged, and the results should be interpreted accordingly. It is well known that the diagnostic accuracy of EUS depends on the endoscopists' skill, and the EUS findings' generalizability in this study must be validated. As the authors acknowledge, EUS images were retrospectively reviewed by one endosonographer, which may have led to bias. It is unclear if EUS is more helpful or required than imaging modalities such as abdominal computed tomography, as the latter can be more helpful in evaluating metastasis to lymph nodes or distant organs.

This study demonstrates valuable endoscopic and EUS findings that discriminate HG with AGC B-4. Endoscopic findings of antral involvement and the presence of ulcers, and EUS findings of destroyed wall layers and thickened PM suggest AGC B-4. Forceps biopsy should be performed at the ulcer in patients with thickened gastric folds, and other diagnostic modalities should be considered in patients without ulcers. While future studies are needed to reinforce these findings, the rarity of the condition may limit large-scale research opportunities.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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