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Refractory gastroduodenal ulcers: investigating non-peptic etiologies

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ABSTRACT

This article presents two clinical cases of gastroduodenal peptic ulcers refractory to medical treatment. In both cases, malignancy was excluded following persistent lesions observed in repeated endoscopies, leading to the use of surgery as both a diagnostic and therapeutic approach. These refractory cases require a multidisciplinary approach with a broad differential diagnosis, including etiologies such as toxic substance exposure, persistent Helicobacter pylori infection, or poor adherence to medical treatment, along with less common conditions such as malignancy, acid hypersecretion syndromes, vascular disorders, or immune-mediated diseases.

INTRODUCTION

Although the most common causes of gastroduodenal ulcer are Helicobacter pylori (HP) infection and nonsteroidal anti-inflammatory drugs (NSAIDs), in some cases, these are either not identified or do not respond to medical treatment. In such cases, less frequent etiologies should be investigated, and in the absence of a response to

conventional medical and endoscopic treatment, surgical intervention should be considered as both a diagnostic and therapeutic option.

CLINICAL CASES

The first case concerns a 55-year-old male with a history of stage IV lung adenocarcinoma undergoing chemotherapy and immunotherapy (Pembrolizumab). An upper endoscopy performed to investigate dyspepsia revealed an ulcerated stenosis in the duodenal bulb extending to the gastric antrum (Figure 1A), with no evidence of malignancy on histology and a negative HP test. Despite double-dose proton pump inhibitors (PPIs) for 8 weeks, he was admitted with a secondary obstructive condition. A repeat upper endoscopy revealed persistence of the antral ulcer, with new biopsies again negative for malignancy. Due to refractoriness to medical treatment, surgical intervention was performed, and histological analysis revealed acute and chronic inflammatory components with foci of abscess formation, suggestive of an immune-mediated phenomenon.

The second case involves a 60-year-old male who underwent evaluation for constitutional syndrome. Endoscopy revealed a 30mm excavated ulcer on the greater curvature of the stomach (Figure 1B), with histological findings negative for malignancy and HP infection. Further workup, including endoscopic ultrasound and thoracoabdominal CT, suggested T3N2 gastric neoplasia. Biopsies were repeated three times, all of which were negative for malignancy. Despite eradication therapy and high-dose PPIs for more than 12 weeks, there was no improvement, leading to surgical treatment. The surgery revealed a penetrating ulcer into the pancreas, with no evidence of malignancy.

DISCUSSION

Between 5-10% of gastroduodenal peptic ulcers can be classified as refractory to medical treatment. The most common causes are persistent or undiagnosed HP infection, toxic substance use, or poor adherence to medical therapy. However, other causes, such as acid hypersecretion syndromes, systemic diseases, vascular causes, infections, or radiotherapy side effects, should also be considered. Immunotherapy is a

rare cause, but given the increasing use of these drugs, it should be suspected in cases of refractory gastroduodenal ulcers. Furthermore, malignancy must be excluded, particularly in gastric ulcers. In the presented cases, surgical treatment provided both therapeutic resolution and definitive histological diagnosis.

REFERENCES

1. Chung CS, Chiang TH, Lee YC. A systematic approach for the diagnosis and treatment of idiopathic peptic ulcers. Korean J Intern Med. 2015 Sep;30(5):559-70.
2. Kim HU. Diagnostic and Treatment Approaches for Refractory Peptic Ulcers. Clin Endosc. 2015 Jul;48(4):285-90.
3. Lanas AI, Remacha B, Esteva F, Sáinz R. Risk factors associated with refractory peptic ulcers. Gastroenterology. 1995 Oct;109(4):1124-33.
4. Napolitano L. Refractory peptic ulcer disease. Gastroenterol Clin North Am. 2009 Jun;38(2):267-88.

FIGURES

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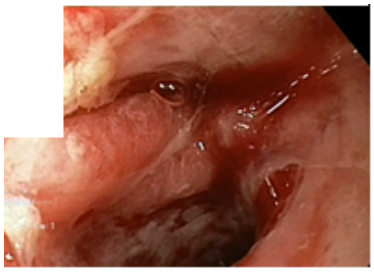

Figure. 1A

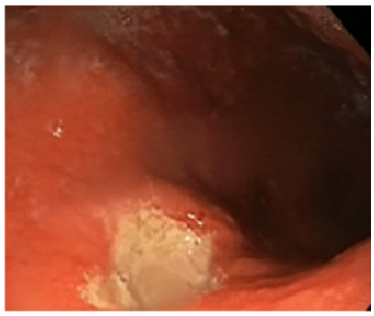

Figure. 1B