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Fungal Peptic Ulcer Disease in an Immunocompetent Patient

Ridwaan Albeiruti[1], Fahad Chaudhary[1], Hiren Vallabh[2], Troy Krupica[1], Justin Kupec[2]
[1]Department of Medicine, West Virginia University, Morgantown, WV, USA
[2]Section of Digestive Diseases, West Virginia University, Morgantown, WV, USA

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ABSTRACT

The lifetime prevalence of peptic ulcer disease (PUD) is 5–10%. While PUD in immunocompetent patients is most commonly associated with *Helicobacter pylori* infection or the use of non-steroidal anti-inflammatory drugs (NSAIDs), other common causes of PUD must also be considered in the differential diagnosis. We describe a case of endoscopic and histological resolution of PUD related to *Candida* infection in a healthy, immunocompetent woman.

LEARNING POINTS

- Peptic ulcer disease (PUD) can be secondary to fungal infections, even in immunocompetent patients.
- A higher index of suspicion needs to be maintained for fungal causes of PUD, particularly if symptoms do not improve.
- Recognizing fungal causes of PUD may lead to faster diagnosis and treatment.

KEYWORDS

Peptic ulcer disease, Candida infection

CASE DESCRIPTION

A 50-year-old woman presented with a 3-month history of post-prandial abdominal cramping, vomiting and a 7 lb weight loss. Her medical history was significant for hypertension, hyperlipidaemia, depression, chronic obstructive pulmonary disease (COPD) and gastroesophageal reflux disease. There was no history of HIV (human immunodeficiency virus) or diabetes. She denied non-steroidal anti-inflammatory drug (NSAID) use and alcohol consumption and was not taking corticosteroids. Endoscopic evaluation was performed.

Esophagogastroduodenoscopy (EGD) revealed a 1 cm, non-bleeding, irregular-shaped, deep and clean-based ulcer at the pylorus (*Fig. 1*). The remainder of the examination was unremarkable. Biopsies were taken and revealed an ulcer with necro-inflammatory debris and fungal organisms, consistent with *Candida* species (*Fig. 2*). Periodic acid-Schiff (PAS) fungal stain revealed scattered yeast colonizing the fibrinous debris (*Fig. 3*).

The patient was given a 3-week course of fluconazole and her symptoms had resolved on follow-up. Repeat EGD (2 months later) revealed resolution of her ulcer (*Fig. 4*). Repeat biopsies of the pylorus were negative for any evidence of fungal organisms (*Fig. 5*).

DISCUSSION

Peptic ulcers are breaks in the gastric or duodenal mucosa which penetrate through the muscularis mucosa and create a cavity with surrounding inflammation. Peptic ulcer disease (PUD) is the most common cause of stomach and duodenal perforation. Worldwide, there were 87.4 million new cases of peptic ulcers in 2015 resulting in 267,500 deaths [1]. PUD affects more than 6 million people in the USA each year [2].

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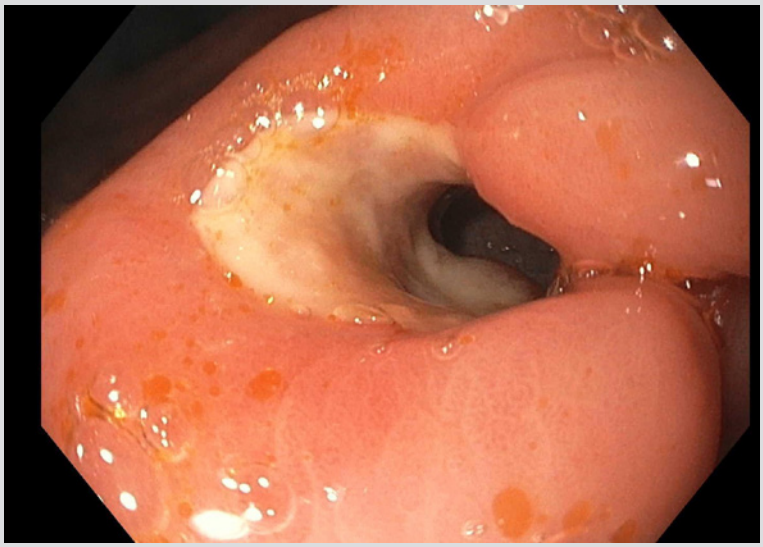

Figure 1. Initial endoscopy findings

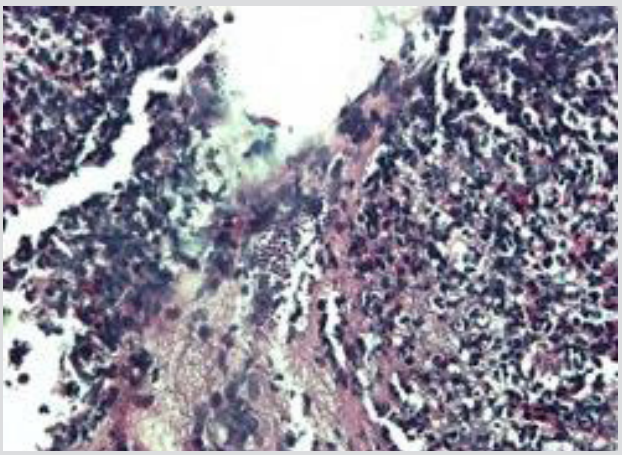

Figure 2 .H&E staining of biopsy specimen

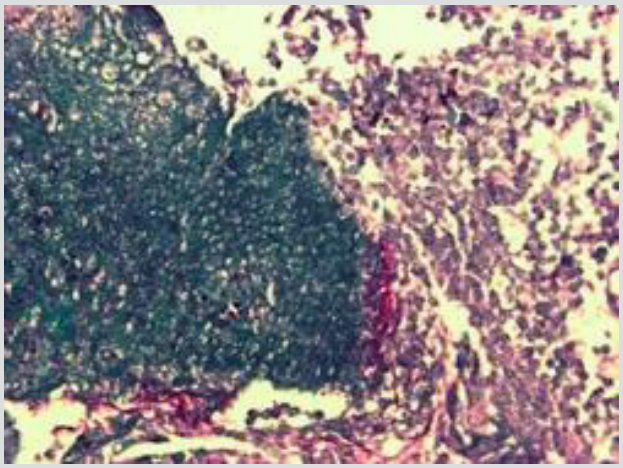

Figure 3. Periodic acid–Schiff (PAS) staining of biopsy specimen

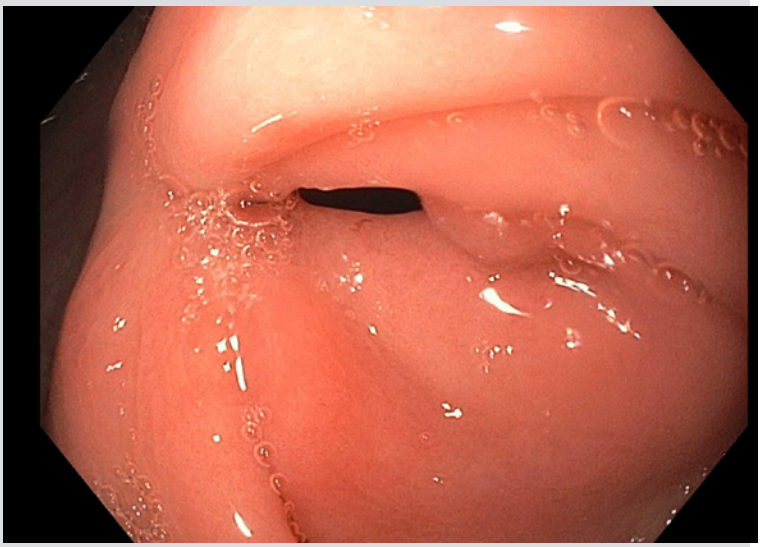

Figure 4. Endoscopy after treatment

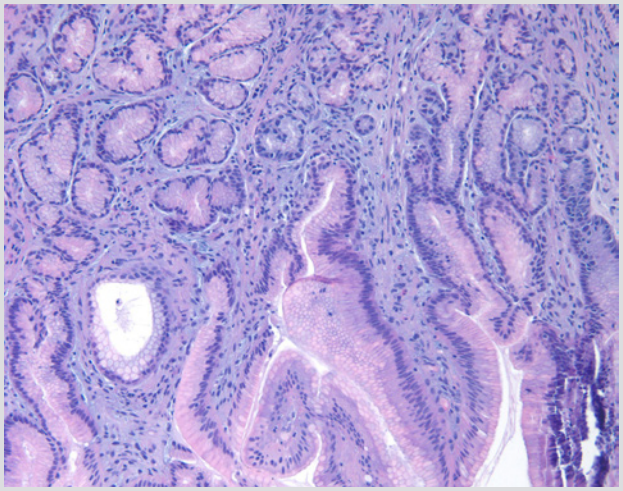

Figure 5. Repeat biopsy after treatment

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A large, retrospective study using the National Inpatient Sample consisting of US inpatient data between 1998 and 2005 showed an average annual PUD hospitalization rate of 63.6/100,000 population.

Helicobacter pylori infection and NSAID use are responsible for the overwhelming majority of PUD cases. However, improved detection with endoscopy has reduced *H. pylori* prevalence. Other causes of non-H. pylori non-NSAID ulcers include antiplatelet drugs, stress, *Helicobacter heilmannii*, cytomegalovirus, Behçet's disease, Zollinger-Ellison syndrome, Crohn's disease and cirrhosis with portal hypertension [3]. Risk factors for the development of PUD are the use of NSAIDs, H. pylori, COPD, chronic renal insufficiency and tobacco use. Even though fungal PUD has a prevalence of 4–36%, the diagnosis is frequently overlooked [4].

Candida is a normal commensal organism in the gut and colonizes the oesophagus in 20% of healthy adults [5]. Few cases of fungal PUD in immunocompetent patients have been reported over the past 10 years (*Table 1*). A review of 16 patients between 1998 and 2007 at a university hospital in Korea revealed that nine cases of gastric candidiasis were benign ulcers and the other seven were malignant. Similar to previous literature, associated conditions included diabetes, cirrhosis, lung cancer and pulmonary tuberculosis [6].

A literature review yielded 10 cases of fungal PUD in immunocompetent patients with risk factors such as smoking, steroid use and heavy antacid use. Antifungal treatment resulted in clinical improvement and ulcer resolution in eight of the 10 patients. One patient, with a perforated fungal ulcer, died post-operatively after cardiac arrest and did not receive any medication. Another patient refused treatment and interestingly was found to have a recurrent Candida-associated gastric ulcer in a different location. One patient was found to have H. pylori on an initial biopsy of a peptic ulcer, followed by Candida albicans on the second endoscopy. Two patients had co-existing infection with both *H. pylori* and *C. albicans* and were both successfully treated with an antifungal agent and a proton-pump inhibitor. Patients with large ulcers may have fungal PUD. Overall, the treatments were varied as regards lengths of treatment and antifungal agents which included fluconazole, caspofungin and amphotericin B (*Table 1*). Our patient eventually achieved clinical and biopsy-proven resolution after completing a course of fluconazole, providing more evidence for the use of antifungals in the treatment of *Candida PUD*.

CONCLUSION

We present a case of EGD and biopsy-proven resolution of PUD secondary to *Candida* infection in an immunocompetent patient. It is important for clinicians to maintain a higher index of suspicion for other causes of PUD for correct and prompt management.

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	Patient age, gender	Presentation	Risk factors	Endoscopy	Histopathology/ culture	Treatment	Outcome
Cascio et al, 2011[7]	62, M	Severe epigastric pain	Heavy smoker	None. Ex-lap with 2.5 cm wide perforation of duodenal bulb	Candida krusei on biopsy and peritoneal fluid culture	Caspofungin	Resolution
Nishimura et al, 2011[8]	73, F	Unknown (article in Japanese)	None	Two gastric ulcers with thick exudates in the fornix	Numerous Candida forms	Antifungal	Resolution
Nagata et al, 2012[9]	82, M	Epigastric pain	None	Ulcerous lesions with thick exudates in the fornix and corpus and severe atrophic gastritis	Candida forms and Helicobacter pylori (confirmed with 13C breath test)	Antifungal and PPI	Resolution
Rai et al, 2012[10]	25, F	Upper abdominal pain, cough, fever	None	Oval to circular 10×6 cm ulcer	1st EGD - H. pylori; 2nd EDG - granulation tissue, numerous yeast and pseudohyphae on PAS consistent with Candida albicans	Amphotericin B+PPI	Survived; following EGD normal
Sasaki, 2012[11]	87, F	Anorexia	Steroid inhaler use, risedronate	Medium-sized submucosal tumour-like elevation covered with erythematous mucosa with an oval, deep central ulcer	Large number of hyphae; Candida tropicalis by culture	None	Recurrent Candida-associated gastric ulcer
Gupta, 2012[12]	50, M	Sudden onset abdominal pain and shock	Strong antacid intake	None. Ex-lap with 1×1 cm prepyloric perforation	Pseudohyphae, suggestive of Candida; peritoneal fluid with C. albicans	Not given antifungal treatment	Died from cardiac arrest
Ince et al, 2014[13]	55, M	Haematemesis and melena	None	Giant gastric ulcer (4 cm diameter) with oozing visible vessel on yellow base in corpus region	H. pylori and positive PAS; C. albicans and Candida kefyr growth	Fluconazole 400 mg on 1st day followed by 200 mg daily for 2 weeks and esomeprazole magnesium 40 mg for 1 month	Almost complete healing of ulcer on 3-week followup EGD. Eradication of H. pylori afterwards
Ukekwe et al, 2015[14]	70, M	Epigastric pain followed by abdominal wall rigidity	None	None. Ex-lap revealed 3.1×1 cm gastric perforation covered with fibrinous exudate	Candida growth (numerous spores and budding hyphae)	Fluconazole, clindamycin, ciprofloxacin, levofloxacin, imipenem	Resolution
Goyal et al, 2016[15]	45, F	Persistent epigastric pain and vomiting , weight loss	NSAID use	Circumferential ulcer at pylorus extending into 1st part of duodenum	Fungal spores and budding yeast forms of Candida species	Fluconazole 200 mg for 2 weeks	Small healing clean-based ulcer on 1-month follow-up EGD
Albeiruti, 2020 (our case)	50, F	Post-prandial abdominal pain, vomiting, weight loss	COPD	1 cm irregular shaped ulcer at pylorus	Necroinflammatory debris and fungal consistent with Candida	Fluconazole	Resolution

Table 1. Published cases of fungal peptic ulcer disease

COPD, chronic obstructive pulmonary disease; EGD, esophagogastroduodenoscopy; ex-lap, exploratory laparotomy; F, female; M, male; NSAID, non-steroidal anti-inflammatory drug; PAS, periodic acid–Schiff; PPI, proton-pump inhibitor.

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