

# Gastric Ulcer From Prolonged Oral Iron Therapy: A Case Report and Literature Review

Sandesh R. Parajuli<sup>1</sup>, Fnu Vikash<sup>2, 5</sup>, Shefali Amin<sup>4</sup>, Manish Shrestha<sup>1</sup>, Anish Paudel<sup>1</sup>, Anthony Donato<sup>1</sup>

Review began 06/30/2024

Review ended 08/24/2024

Published 08/27/2024

© Copyright 2024

Parajuli et al. This is an open access article distributed under the terms of the Creative Commons Attribution License CC-BY 4.0., which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

DOI: 10.7759/cureus.67905

1. Internal Medicine, Reading Hospital, Tower Health, Reading, USA 2. Gastroenterology and Hepatology, Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, USA 3. Internal Medicine, Jacobi Medical Center, Albert Einstein College of Medicine, Bronx, USA 4. Internal Medicine, Tower Health Medical Group, Reading, USA

Corresponding author: Sandesh R. Parajuli, sandeshutd@gmail.com

---

---

## Abstract

Iron deficiency is a leading cause of anemia worldwide and is commonly treated with oral iron supplements, which are known for their GI side effects. We present a case of a 66-year-old woman with a history of GI bleeding and multiple comorbidities who developed a gastric ulcer after prolonged oral iron therapy. Although GI side effects are frequent with iron supplements, ulceration is rare, with only a few documented cases. Endoscopic and histopathological evaluations identified iron deposition in the ulcer bed, confirming the diagnosis. Discontinuing the oral iron led to the resolution of symptoms. This case underscores the importance of recognizing and managing iron-induced gastric ulcers to ensure safe and effective treatment of iron deficiency.

---

**Categories:** Gastroenterology, Internal Medicine, Hematology

**Keywords:** oral iron therapy, iron therapy, iron-deficiency anemia, epigastric pain, endoscopy, anemia

## Introduction

Anemia affects nearly one-fourth of the global population, with iron deficiency being the most common cause [1]. Treatment for iron deficiency often starts with oral iron supplements, which are recommended after identifying sources of blood loss [2]. Depending on the clinical situation, different forms of iron delivery may be used, including food fortification, oral supplements, or intravenous therapy [3]. Oral iron, typically administered in pill or tablet form, is widely used but can cause GI side effects such as nausea, abdominal pain, diarrhea, bloating, constipation, and black-colored stools. Gastric mucosal ulceration is a rare but serious side effect that gastroenterologists should be aware of. Patients with such ulcers should be switched to alternative forms of iron supplementation, and iron tablets should be avoided in those with existing gastric ulcers [3,4]. This case report describes a 66-year-old woman who developed a gastric ulcer as a result of oral iron tablets.

## Case Presentation

A 66-year-old morbidly obese female with a history of GI bleeding due to small bowel arteriovenous malformations (AVMs) presented to the hospital with a new melanotic stool. Her medical history included coronary artery disease, heart failure, aortic stenosis, hypertension, hyperlipidemia, and chronic kidney disease stage II. She had recently been prescribed apixaban 5 mg twice daily for paroxysmal atrial fibrillation. Her other home medications included metformin, amiodarone, metoprolol succinate, and pantoprazole 40 mg once daily. She had also been taking ferrous sulfate (325 mg) once daily for over six months. She denied using NSAIDs, bismuth subsalicylate, or additional aspirin or antiplatelet agents. On examination, she was hemodynamically stable, and her blood work, as shown in Table 1, indicated that her hemoglobin and creatinine levels were at baseline.

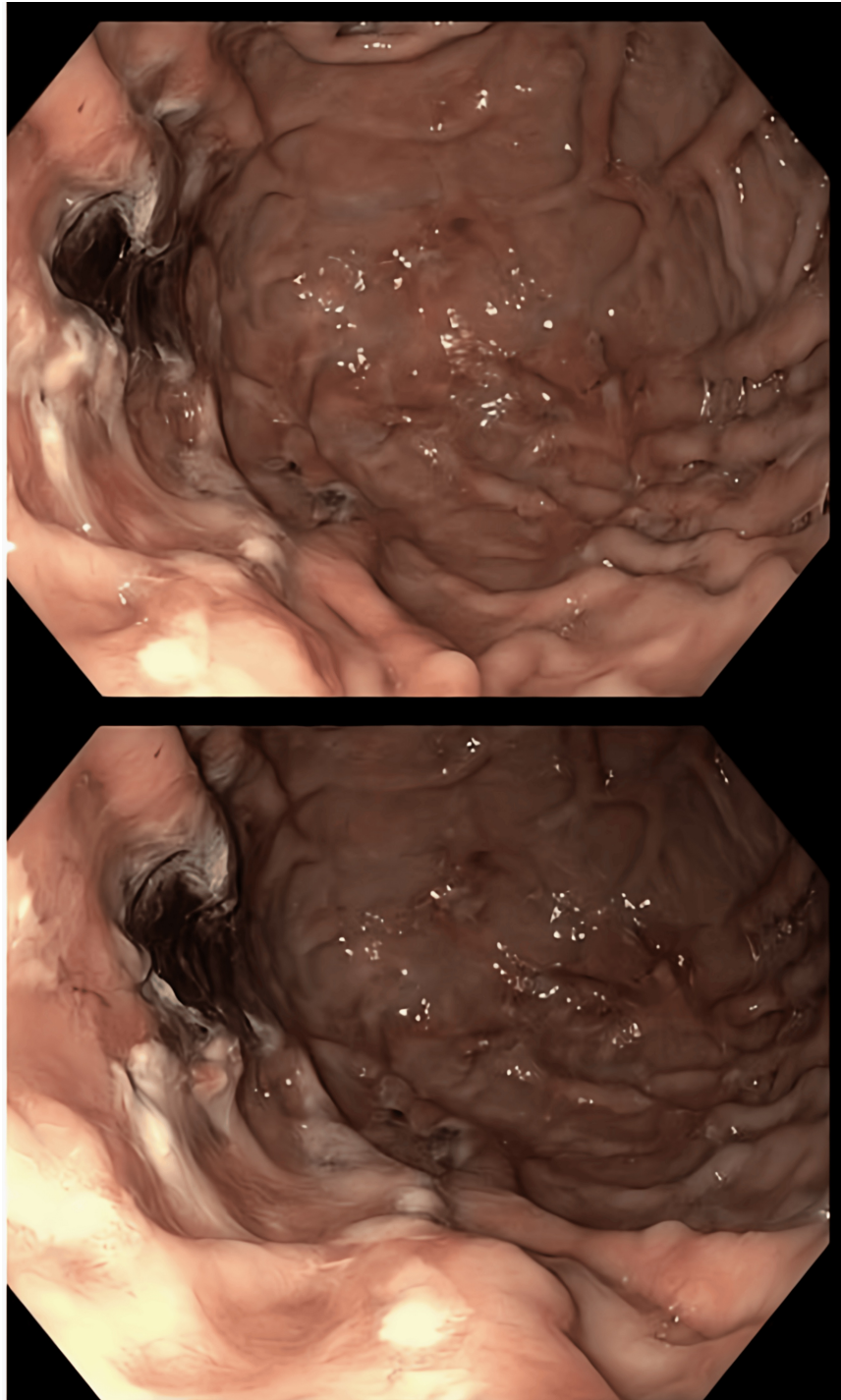
### How to cite this article

Parajuli S R, Vikash F, Amin S, et al. (August 27, 2024) Gastric Ulcer From Prolonged Oral Iron Therapy: A Case Report and Literature Review. Cureus 16(8): e67905. DOI 10.7759/cureus.67905

Lab tests	Result	Reference range
Hemoglobin	9.9	12-16 g/dl
Mean corpuscular volume	97	80-99 fL
Ferritin	150	11-307 ng/mL
Iron saturation	32	11-50%
Total iron-binding capacity	299	284-507 ug/dL
Blood urea nitrogen	19	9-23 mg/dL
Creatinine	0.75	0.55-1.02 mg/dL

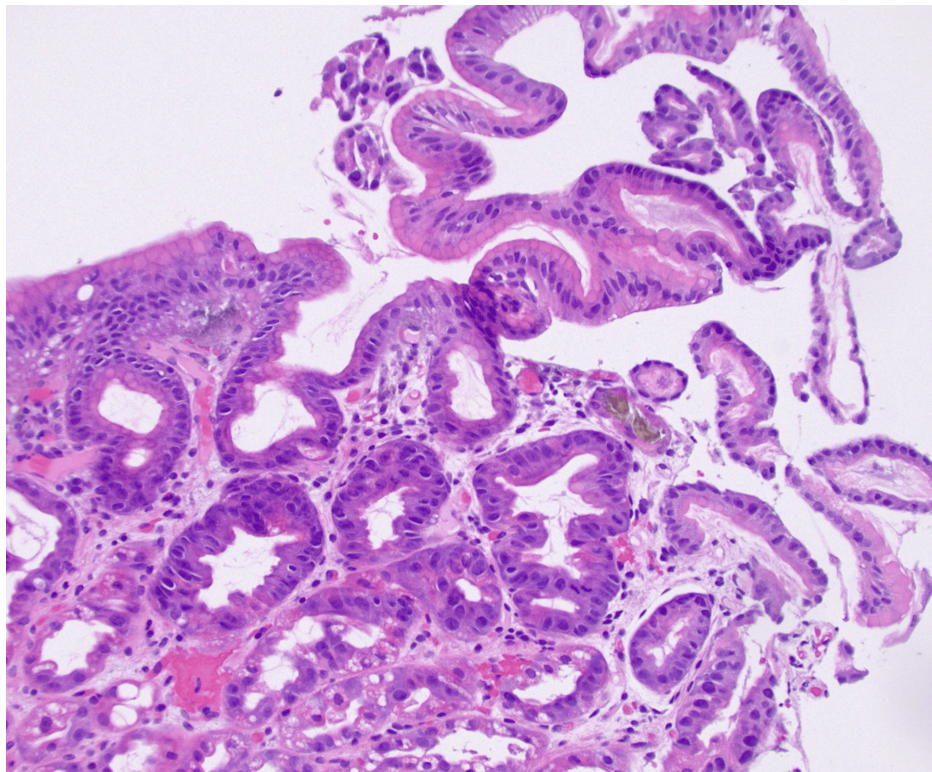
**TABLE 1: Laboratory values**

A CT scan of her abdomen and pelvis with contrast performed in the emergency department did not reveal any obvious source of contrast extravasation. Considering her recent initiation of apixaban, history of AVMs, and low hemoglobin, gastroenterology was consulted for potential endoscopic evaluation. During the upper GI endoscopy, a large (1.5 cm) friable ulcerated mucosa with central eschar was identified along the proximal gastric body (Figure 1).



**FIGURE 1: Esophagogastroduodenoscopy image showing the gastric ulcer situated along the proximal gastric body**

The upper GI endoscopy otherwise appeared normal, with no visible bleeding. A biopsy was performed, showing an eroded epithelial lining with an infiltrated and edematous lamina propria. The presence of brownish to golden crystalline material within the ulcer bed suggested iron deposition, which was further confirmed using Perl's stain (Figure 2).



**FIGURE 2: Microscopic slide displaying brownish to golden crystalline iron deposits on the ulcer bed of the eroded gastric mucosa**

The biopsy results were negative for *Helicobacter pylori* and malignancy. The patient was advised to take pantoprazole 40 mg twice daily until follow-up and to resume oral apixaban. She was instructed to discontinue oral iron supplements, and a follow-up upper GI endoscopy was recommended in two to three months to assess for healing.

## Discussion

Iron-induced gastric ulcers are a notable adverse effect of oral iron supplements used to treat iron deficiency anemia. The GI side effects of these supplements can range from mild discomfort to severe gastric ulceration. The mucosal injury occurs through both direct and indirect mechanisms [4]. Directly, iron supplements can damage the mucosa as they dissolve in gastric acid, releasing free iron ions that catalyze the formation of reactive oxygen species. This disrupts mucosal integrity and contributes to ulcer formation. Indirectly, the increased acidity from oral iron pills can alter the gut microbiota, exacerbating mucosal inflammation. Notably, liquid iron preparations have not been associated with such mucosal ulceration and represent a promising alternative [5-7].

Clinically, iron-induced gastric ulcers present as epigastric pain, often described as gnawing or burning, which may worsen with food intake or improve temporarily with antacids [8]. Nausea, potentially accompanied by vomiting, and, in severe cases, hemoptysis from active bleeding at the ulcer site are also common symptoms [9].

Diagnosis involves a comprehensive approach including patient history, endoscopy, and histopathological analysis. Endoscopy is crucial for visualizing ulcers and differentiating them from other causes, such as *H. pylori* infection or malignancy [6]. Although endoscopic and radiological findings might suggest malignancy, biopsy and histological analysis are necessary for an accurate diagnosis. A key diagnostic clue is the resolution of ulcers following the cessation of oral iron [10].

Management focuses on alleviating symptoms, promoting mucosal healing, and preventing recurrence while meeting the patient's iron needs [9]. Discontinuation of oral iron, which often significantly reduces symptoms and initiates mucosal healing, is the primary step. Proton pump inhibitors (PPIs) are the preferred pharmacologic treatment, as they accelerate healing and alleviate symptoms in cases of iron-induced gastric damage [9]. The development of ulcers despite PPI use suggests that existing ulcers were exacerbated by oral iron, highlighting the importance of avoiding oral iron supplements in patients with gastric ulcers. H2 receptor antagonists, such as ranitidine, may be used but are generally less effective than PPIs [11]. Sucralfate, which forms a protective barrier over gastric ulcers, can also aid in healing and symptom relief.

For patients requiring ongoing iron supplementation, alternative routes like intravenous iron should be considered to prevent further gastric irritation [6]. Additionally, patients should avoid alcohol and smoking, as these can impair mucosal healing [12]. Preventive strategies include using ferrous sulfate with food, prescribing enteric-coated or delayed-release formulations, and appropriate dosing to prevent excessive iron accumulation [13,14].

## Conclusions

Iron-induced gastric ulcers are an underrecognized risk of oral iron therapy, particularly in patients with refractory iron deficiency anemia. Despite the use of PPIs, the risk of mucosal damage persists. Early endoscopic evaluation is crucial for diagnosing these ulcers. Switching to liquid or intravenous iron supplementation can help prevent further mucosal injury and offer a safer management alternative. Early recognition of this complication and timely adjustment of treatment are essential to avoid the severe consequences of iron-induced gastric ulcers.

## Additional Information

### Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

**Concept and design:** Sandesh R. Parajuli, Manish Shrestha, Shefali Amin, Anish Paudel, Anthony Donato, Fnu Vikash

**Acquisition, analysis, or interpretation of data:** Sandesh R. Parajuli, Manish Shrestha, Shefali Amin, Anish Paudel, Anthony Donato, Fnu Vikash

**Drafting of the manuscript:** Sandesh R. Parajuli, Manish Shrestha, Shefali Amin, Anish Paudel, Anthony Donato, Fnu Vikash

**Critical review of the manuscript for important intellectual content:** Sandesh R. Parajuli, Manish Shrestha, Shefali Amin, Anish Paudel, Anthony Donato, Fnu Vikash

### Disclosures

**Human subjects:** Consent was obtained or waived by all participants in this study. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

## References

1. Prevalence, years lived with disability, and trends in anaemia burden by severity and cause, 1990-2021: findings from the Global Burden of Disease Study 2021. *Lancet Haematol.* 2023, 1:e713-34. [10.1016/S2352-3026\(23\)00160-6](https://doi.org/10.1016/S2352-3026(23)00160-6)
2. Ko CW, Siddique SM, Patel A, Harris A, Sultan S, Altayar O, Falck-Ytter Y: AGA clinical practice guidelines on the gastrointestinal evaluation of iron deficiency anemia. *Gastroenterology.* 2020, 159:1085-94. [10.1053/j.gastro.2020.06.046](https://doi.org/10.1053/j.gastro.2020.06.046)
3. Tolkien Z, Stecher L, Mander AP, Pereira DI, Powell JJ: Ferrous sulfate supplementation causes significant gastrointestinal side-effects in adults: a systematic review and meta-analysis. *PLoS ONE.* 2015, 10:e0117383. [10.1371/journal.pone.0117383](https://doi.org/10.1371/journal.pone.0117383)
4. Kaye P, Abdulla K, Wood J, James P, Foley S, Ragunath K, Atherton J: Iron-induced mucosal pathology of the upper gastrointestinal tract: a common finding in patients on oral iron therapy. *Histopathology.* 2008, 53:311-7. [10.1111/j.1365-2559.2008.03081.x](https://doi.org/10.1111/j.1365-2559.2008.03081.x)
5. Koskenkorva-Frank TS, Weiss G, Koppenol WH, Burckhardt S: The complex interplay of iron metabolism, reactive oxygen species, and reactive nitrogen species: insights into the potential of various iron therapies to induce oxidative and nitrosative stress. *Free Radic Biol Med.* 2013, 65:1174-94. [10.1016/j.freeradbiomed.2013.09.001](https://doi.org/10.1016/j.freeradbiomed.2013.09.001)
6. Bordin DS, Voynovan IN, Andreev DN, Maev IV: Current Helicobacter pylori diagnostics. *Diagnostics (Basel).* 2021, 11:1458. [10.3390/diagnostics11081458](https://doi.org/10.3390/diagnostics11081458)
7. Sunkara T, Caughey ME, Nigar S, Olivo R, Gaduputi V: Iron pill gastritis: an under diagnosed condition with potentially serious outcomes. *Gastroenterology Res.* 2017, 10:138-40. [10.14740/gr804w](https://doi.org/10.14740/gr804w)
8. Schümann K, Ettle T, Szegegn B, Elsenhans B, Solomons NW: On risks and benefits of iron supplementation recommendations for iron intake revisited. *J Trace Elem Med Biol.* 2007, 21:147-68. [10.1016/j.jtemb.2007.06.002](https://doi.org/10.1016/j.jtemb.2007.06.002)
9. Laine L: Upper gastrointestinal bleeding due to a peptic ulcer. *N Engl J Med.* 2016, 374:2367-76. [10.1056/NEJMcp1514257](https://doi.org/10.1056/NEJMcp1514257)

10. Smith IM, Bryson G, Glen P: Iron-induced gastric ulceration with radiological and endoscopic appearance of carcinoma. *BMJ Case Rep.* 2015, 2015: [10.1136/bcr-2015-211997](https://doi.org/10.1136/bcr-2015-211997)
11. Scarpignato C, Pelosini I, Di Mario F: Acid suppression therapy: where do we go from here? . *Dig Dis.* 2006, 24:11-46. [10.1159/000091298](https://doi.org/10.1159/000091298)
12. Ko JK, Cho CH: Alcohol drinking and cigarette smoking: a "partner" for gastric ulceration . *Zhonghua Yi Xue Za Zhi (Taipei).* 2000, 65:845-54.
13. Peña-Rosas JP, De-Regil LM, Garcia-Casal MN, Dowswell T: Daily oral iron supplementation during pregnancy. *Cochrane Database Syst Rev.* 2015, 2015:CD004736. [10.1002/14651858.CD004736.pub5](https://doi.org/10.1002/14651858.CD004736.pub5)
14. Zimmermann MB: Global look at nutritional and functional iron deficiency in infancy . *Hematology Am Soc Hematol Educ Program.* 2020, 2020:471-7. [10.1182/hematology.2020000131](https://doi.org/10.1182/hematology.2020000131)