CASE REPORT

Iron-induced gastric ulceration with radiological and endoscopic appearance of carcinoma

Iain M Smith,¹ Gareth Bryson,² Paul Glen¹

¹Department of General Surgery, Queen Elizabeth University Hospital, Glasgow, UK

²Department of Pathology, Queen Elizabeth University Hospital, Glasgow, UK

Correspondence to

Paul Glen,
paul.glen@ggc.scot.nhs.uk

Accepted 16 September 2015

SUMMARY

Erosive injury of the upper gastrointestinal tract resulting from therapeutic oral iron supplements is an uncommon phenomenon. We present a case of a large gastric ulcer with clinical, endoscopic and radiological features suggestive of malignancy, which resolved completely on cessation of iron therapy.

BACKGROUND

While erosive injury to the mucosa of the upper gastrointestinal (GI) tract is a well-recognised consequence of overdose with oral iron supplements,^{1 2} similar injuries can result from doses in the normal therapeutic range. In this case, the associated endoscopic and radiological features were highly suggestive of malignancy—a presentation that has not previously been reported.

CASE PRESENTATION

A 60-year-old man was referred to the general surgical clinic with a 9-month history of vitamin B₁₂ and iron deficiency. He reported 9 kg weight loss over this time and reported constipation and lower abdominal pain. Prior to referral, his weight loss had been attributed to thyrotoxicosis and iron deficiency due to poor diet, but his situation had failed to respond to good control of thyroid function, dietary improvement and iron supplementation.

Abdominal examination was unremarkable, however, a supraclavicular node was palpable.

INVESTIGATIONS

The patient's presentation appeared highly suspicious of advanced GI malignancy. A CT of the chest, abdomen and pelvis was arranged as a non-invasive test to localise the presumed lesion and to guide definitive diagnostic investigation. The scan revealed a large gastric antral mass with a large central ulcer component. Infiltration of perigastric fat and enlarged coeliac and perigastric lymph nodes was consistent with a locally advanced gastric malignancy with nodal metastases (figures 1 and 2).

DIFFERENTIAL DIAGNOSIS

Gastroscopy was performed; the endoscopic appearance was consistent with an established antral carcinoma with central ulceration. However, biopsies consisted predominantly inflamed gastric mucosa and ulcer slough with no malignancy seen. The intense lymphoid infiltrate raised the possibility of lymphoma, however, this was not supported by immunohistochemistry. Repeat biopsies revealed

Figure 1 Transverse CT sections through stomach. Black arrows indicate ulcer with thickened surrounding tissue. White arrows indicate associated lymphadenopathy.

antral-type gastric mucosa with severe active chronic gastritis and extensive ulceration. There was a moderate lymphoid population with lymphoid follicles and germinal centres, but no convincing evidence of lymphoma and none of carcinoma. On this occasion, iron deposition was

Figure 2 Coronal CT section through stomach. Black arrow indicates ulcer with thickened surrounding tissue.

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To cite: Smith IM, Bryson G, Glen P. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2015-211997

Figure 3 Gastric mucosal biopsy showing (A) neutrophil-rich ulcer slough, (B) haemorrhage (C) crystalline iron (black/brown) within ulcer slough and (D) regenerative epithelial atypia (H&E, ×40).

noted on the epithelial surface and within the ulcer slough (figures 3–5). The possibility of oral iron-induced ulceration mimicking carcinoma was raised.

The CT scan was repeated after 6 weeks and showed no interval progression.

TREATMENT

Given the benign histological findings and the static interval CT appearance, a further gastroscopy was performed. The endoscopic appearance remained concerning, however, further biopsies again suggested iron-associated ulceration. On this basis, the patient was advised to stop taking iron sulfate tablets with a further endoscopy scheduled for 1 month later.

OUTCOME AND FOLLOW-UP

One month after cessation of oral iron therapy and addition of omeprazole 40 mg twice daily, endoscopy showed regenerative mucosa at the ulcer. This suggested early healing. After a further 6 months, the ulcer had healed, with endoscopy revealing only scarring at the previous ulcer site.

DISCUSSION

Erosive injury to the mucosa of the upper GI tract is well known in the context of overdoses of oral iron supplements.^{1 2}

Figure 4 Gastric mucosal biopsy demonstrating extensive iron deposition (blue) (Perls stain, ×40).

Figure 5 Gastric mucosa with (A) vascular congestion and (B) mucosal iron deposition (brown) (H&E, ×200).

However, such injury in the context of therapeutic dosing is less well recognised.

Mechanism

Oral iron therapy (taken as tablets) results in deposition of oxidised crystalline ferric iron (Fe^{3+}) on the epithelial surface.^{3–5} This may be seen endoscopically as a yellow-brown streak.⁶ This causes a chemical burn, which, on biopsy, appears as an erosion, with brown-black crystalline material within the ulcer slough. Additional deposition can be found within the lamina propria and submucosal vasculature.^{3 4} Deposits can be highlighted with the use of a Perls stain. However, the distribution of iron within tissue is distinct from that found in iron overload or haemochromatosis, in which finer intracellular iron deposits (as haemosiderin) accumulate deep in the mucosa.^{3 7}

A direct corrosive effect by crystalline iron contact is suggested by case reports of localised necrosis due to impaction of single tablets more distally in the GI tract³ and by the absence of pathology associated with liquid iron supplements (presumably due to faster clearance from the stomach). In addition, intracellular iron is likely to contribute to cellular injury.

Ferrous (Fe^{2+}) iron is normally taken up into duodenal enterocytes by the energy-dependent Divalent Metal Transporter-1 carrier protein,⁸ but, in high concentrations, it is also absorbed in a concentration-dependent fashion.³ This latter mechanism is likely to explain gastric intracellular ferric and ferrous ions. These catalyse production of reactive oxygen metabolites and lipid peroxidation, resulting in necrosis and inflammation. In combination with local ischaemia, due to iron-induced submucosal vascular thrombosis, ulcer healing is compromised.⁴

Mucosal injury resulting from iron tablets may occur at 1/3 of the normal prescription dose, with endoscopic and histological features present from within 5 days of the start of therapy.³ It is likely that pre-existing injury, comorbidity and other medication contribute, as histological features were not detected after 2 weeks of high-dose therapy in young test subjects with no other risk factors for gastritis.⁹

In a study of approximately 1300 unselected endoscopic examinations, 12 (1%) revealed evidence of crystalline iron deposition, with 9 showing mucosal injury.³ However, in a separate study, 15 of 93 recipients (16%) of oral iron therapy showed iron deposition. Six of these had endoscopically noticeable erosions.

Significantly, up to 30% of patients receiving oral iron therapy report heartburn, epigastric discomfort and nausea,¹⁰ though no study has yet investigated any association between

symptoms and endoscopic or histological findings. Nonetheless, in patients with identified iron-associated injury, cessation of therapy was associated with resolution of clinicopathological features.³

In our case, we postulate that the presence of a palpable supraclavicular lymph node was due to gastric inflammation, with the radiologically concerning features resulting from chronicity.

Learning points

- ▶ Oral iron supplements should be considered in the differential diagnosis of erosive mucosal disorders of the upper gastrointestinal tract.
- ▶ Such injury may present with endoscopic and radiological features suggestive of locally advanced malignancy.
- ▶ Histological confirmation of malignancy is essential prior to initiating treatment.

Contributors PG was responsible for the investigation and treatment of the patient described, and initiated this report. GB reported the histology and provided the histological images. IMS drafted the manuscript. PG and GB critically reviewed the manuscript.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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