

## An uncommon cause of gastro-duodenal ulceration

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### Abstract

Gastrointestinal ulcers occur frequently and are mainly caused by *H pylori* infection. In this report, we present a rare case of gastro-duodenal ulcer following selective internal radiation therapy (SIRT). SIRT is a palliative treatment for unresectable liver tumours. During SIRT, <sup>90</sup>Y-microspheres are infused into the hepatic artery. Pre-treatment evaluation for the presence of arterial shunts to neighbouring organs should be determined in order to avoid complications of SIRT.

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**Key words:** Selective internal radiation therapy; Duodenal ulcer; Colon carcinoma; Hepatic metastases; Gastroscopy

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### INTRODUCTION

Gastric or duodenal ulceration is generally caused by damage to the mucosal barrier of the stomach or duodenum secondary to preponderance of acid valences. In the vast majority of cases, gastric ulceration is an *H pylori*-related disease, especially in the case of duodenal ulceration. Other

causes of gastric or duodenal mucosal damage include excessive use of non-steroidal anti-inflammatory drugs, posttraumatic ischemic mucosal injury, hyperacidity caused by abuse of nicotine or changes in electrolytes, i.e. elevated serum calcium levels<sup>[1,2]</sup>.

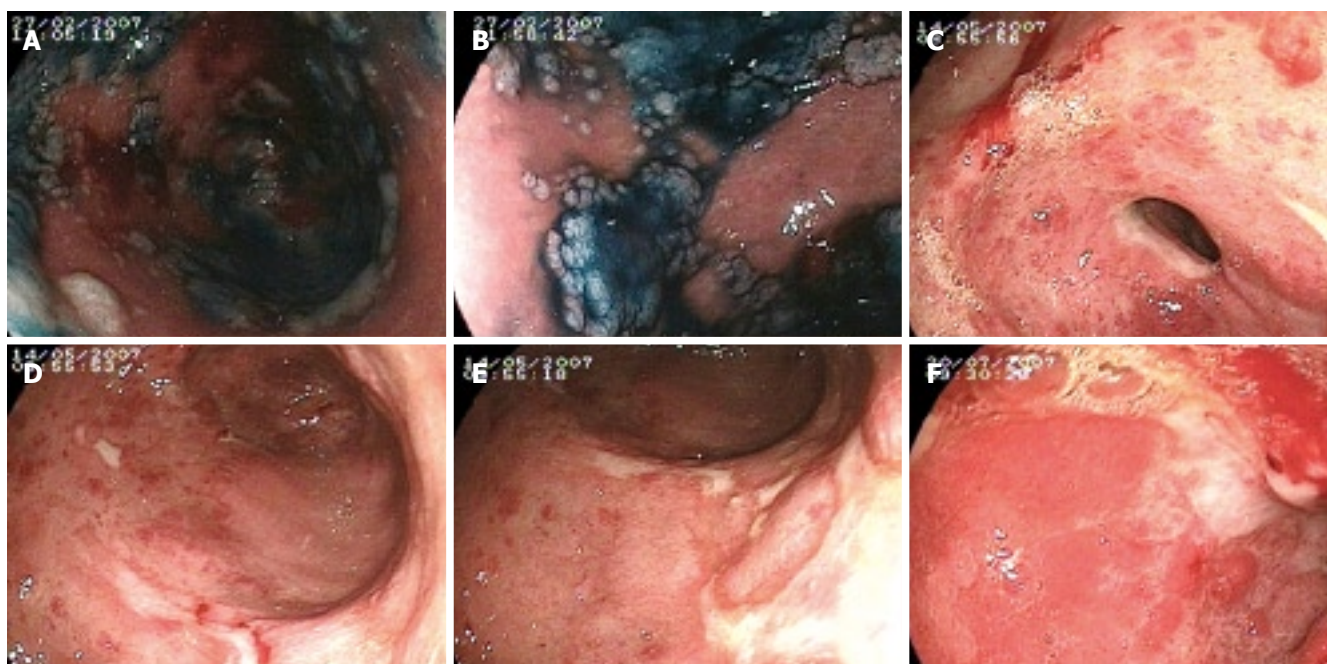
In this report, we present a case of radiation-induced gastro-duodenal ulceration after selective internal radiation therapy (SIRT) for the treatment of hepatic metastases from a sigmoid adenocarcinoma.

Patients with hepatic metastases from a colorectal primary often die from complications associated with the impairment of liver function. Thus, in recent years development of new methods of treatment of non-resectable hepatic tumours has received much attention. External radiation is regarded as ineffective in the treatment of hepatic primary or secondary tumours since the dose of radiation that can be applied to the tumour is limited by the tolerance level of the nontumorous liver tissue<sup>[3-5]</sup>.

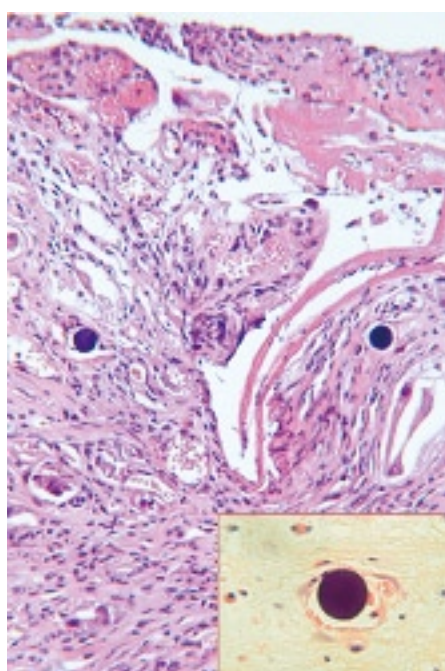
Intra-arterial administration of <sup>90</sup>Yttrium-microspheres, i.e. selective internal radiation therapy, is a palliative treatment for unresectable liver tumours such as hepatocellular carcinoma or liver metastases. This technique allows the application of high radiation dose to hepatic tumours while sparing, for the most part, normal liver parenchyma. During SIRT, <sup>90</sup>Y-microspheres are infused into the hepatic artery either by a surgically placed subcutaneous port or through a percutaneous femoral catheter<sup>[3-6]</sup>. The radiopharmaceutical agent consists of non-biodegradable <sup>90</sup>Y-imprinted microspheres with a glass or a resin matrix with a diameter of 29-35 µm. After injection into the hepatic artery, the microspheres induce microembolization of the hepatic arterioles, mainly in the tumour tissue since its blood supply depends largely on the hepatic artery. <sup>90</sup>Yttrium is a beta-emitter with an average tissue penetration depth of approximately 2.4 mm. Thus, apart from microembolization, a radiation dose from 30 to 60 Gy can be applied to the tumour tissue. Furthermore radiation therapy may be followed by the selective infusion of chemotherapeutic agents into the hepatic artery<sup>[4,7,8]</sup>.

### CASE REPORT

Our patient had sigmoid adenocarcinoma with disseminated hepatic metastases, which responded poorly to systemic chemotherapy with 5-fluorouracil, folinate, irinotecan and bevacizumab. SIRT was applied through a percutaneously placed femoral artery catheter. Several days after the administration of <sup>90</sup>Y-microspheres, the patient developed typical symptoms of upper gastrointestinal ulceration. The patient complained of epigastric pain, nausea and anorexia,



**Figure 1** Chromoendoscopy. **A-B:** Chromoendoscopy with 0.6% Kongored stain showing initial mucosal damage of the gastric antrum; **C-E:** Multiple ulcerations (Forrest III) and severe mucosal inflammation of the gastric antrum, 3 mo after SIRT; **F:** Partially reepithelialized ulcer (Forrest III) in the duodenal bulb, 5 mo after SIRT.



**Figure 2** Gastric biopsy showing ulceration and typical inflammatory eschar at the surface. The mucosa contains granulation tissue with inflammatory cells and several small blood vessels. Two round microspheres can be seen on the right and left side of the figure. Inset:  $^{90}\text{Y}$ -microsphere within a capillary adjacent to an erythrocyte.

followed by increasing weight loss, requiring parenteral nutrition.

Initial gastroscopy showed an extensive pangastritis with mucosal damage and a Forrest type III ulcer in the antrum and proximal duodenum which was confirmed histologically (Figures 1A, B and 2). No *H pylori*-colonization was found in gastric biopsies.

Based on these findings, the patient was treated with high dose proton-pump inhibitor therapy and sucralfate. However, the symptoms persisted and the patient experienced a further weight loss of 7 kg. Two weeks and 3 mo after the initial diagnosis, further gastroscopic examinations were performed and showed progression of the duodenal ulcer with multiple smaller Forrest III ulcers in the gastric antrum (Figure 1C-E). The ulcerations persisted even after 5 mo (Figure 1F).

Because of the close chronological association between the application of SIRT and the development of the patient's symptoms, treatment-related complication was suspected. Pathological examination was expanded to ascertain whether mucosal histological abnormalities may show typical features of radiation damage. Therefore a more detailed histological examination was conducted in order to search for microspheres in the biopsy specimens. Indeed,  $^{90}\text{Y}$ -microspheres embolized into the capillary system were detected and photo-documented as shown in Figure 2.

Clinically, the radiation-induced ulcer persisted despite the continuous use of antacid therapy.

## DISCUSSION

In general, SIRT is a well tolerated technique employed in the treatment of unresectable liver tumours, especially colorectal liver metastases. Nevertheless, complications are seen in about 20% of patients. These include radiation hepatitis and cholecystitis. A Medline literature research using terms as "gastric ulcer", "duodenal ulcer", "internal radiation" and "radiation therapy" revealed that gastroduodenal ulceration occurs in up to 12% patients after treatment with  $^{90}\text{Y}$ -microspheres<sup>[7-12]</sup>. Gastroduodenal ulceration has also been reported after conventional TACE with an incidence of 3% to 5.3%<sup>[13]</sup>. However, the present

report indicates that radiogenic ulceration and radiation-induced side effects persist for a long time and are refractory to pharmaceutical therapy. Radiogenic ulceration led to significant symptoms associated with a sustained decline in the quality of life and an enduring influence on the nutritional status of the patient.

There are several options for pre-treatment planning before the use of SIRT including CT- and PET-scans, visceral angiography and the application of 99m-Technetium macroaggregated albumin to assess tumour vasculature, tumour volume and extrahepatic shunting<sup>[9,14-16]</sup>. With regard to the frequently occurring side-effects of SIRT, the importance of pre-treatment assessment and pre-therapeutic embolization of arterial shunts to neighbouring organs must be established in order to avoid inappropriate loss of quality of life in these patients.

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