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Subtotal gastrectomy for diffused hemorrhagic gastritis induced by radiation, following liver resection for hilar cholangiocarcinoma. A case report



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ABSTRACT

INTRODUCTION: A rare case of hemorrhagic gastritis induced by radiation is presented, which was resistant to conservative treatment and required subtotal gastrectomy.

PRESENTATION OF CASE: A 56-year-old male was initially undergone right hepatectomy, resection of the extrahepatic biliary tree, hilar lymph node dissection and hepatico-jejunostomy due to advanced hilar cholangiocarcinoma. Because of the extent of the disease, chemo-radiotherapy was administered. The patient received a total radiotherapy dose of 57.6 Gy in 32 sessions. Unfortunately, diffused hemorrhagic gastritis induced by radiation was developed, which was resistant to conservative treatment (endoscopic hemostasis, transfusion). A subtotal gastrectomy was performed. The patient is in good condition 45 months after the liver resection, but with local recurrence.

CONCLUSION: In resistant situations to conservative treatment and recurred bleeding of diffused hemorrhagic gastritis induced by radiation, surgical management may have a role.

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1. Introduction

Radiotherapy is used often for the management of malignant tumors. However its use is not without consequences. Hemorrhagic gastritis induced by radiation is a potential life-threatening complication and the management is challenging. There is no treatment of choice so far. We present a patient who developed severe persistent upper gastrointestinal bleeding three months after radiotherapy for resected advanced hilar cholangiocarcinoma. This complication was effectively managed with subtotal gastrectomy and Roux-en-Y gastro-jejunostomy.

2. Methods

This work has been reported in line with the CARE Guidelines [1].

3. Case report

A 56-year-old male with hilar cholangiocarcinoma (stage IIIA) was submitted to right hepatectomy, excision of the extrahep-

atic biliary tree, hilar lymph node dissection and Roux-en-Y hepatico-jejunostomy in our department, in 09/2011. Histological examination showed hilar cholangiocarcinoma with max diameter 3.5 cm and perineural infiltration (RO resection, without lymph node invasion).

The patient was submitted to chemo-radiotherapy postoperatively due to tumor extension. He received chemotherapy of oxaliplatin and capecitabine (3 cycles). He also underwent 32 sessions of radiotherapy (started on 12/2011, duration: 1.5 months) using external beam radiation of the right hypochondrium and epigastrium. The radiotherapy was held in four fields radiation (anterior-posterior, right-left) using linear accelerator (18 MV). The patient received a total dosage of 57.6 Gy. The daily dosage was 1.8 Gy using shrinkage technique. The whole stomach received a mean dosage of 18.2 Gy (range from 0.3 Gy to 61.5 Gy). The distal part of the stomach received from 0.6 Gy minimum to 61.5 Gy maximum, with a mean dosage of 53 Gy.

Unfortunately, the patient developed upper gastrointestinal bleeding (hematemesis and melena) three months after the completion of radiotherapy. Initially, he was treated at his district hospital using proton pump inhibitors. Esophagogastroduodenoscopy (EGD) showed diffused hemorrhagic lesions in multiple sites in the gastric mucosa (Fig. 1). He was managed there with transfusion of red blood cells (RBCs) and fresh frozen plasma (FFPs), but the bleeding recurred. He was referred to our

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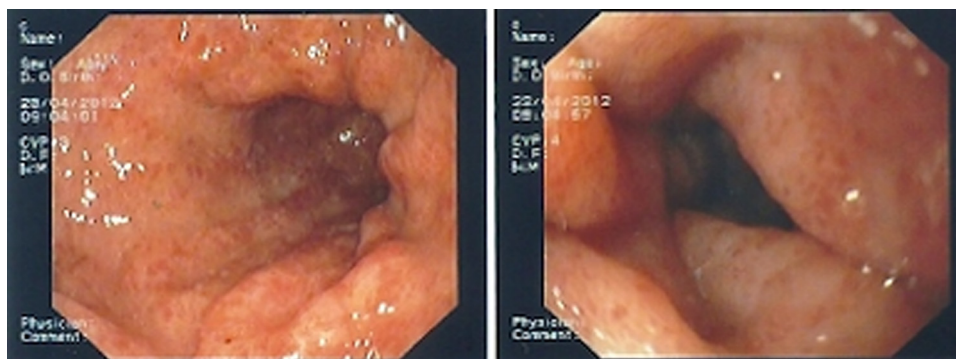


Fig. 1. Esophagogastroduodenoscopy: diffuse vascular lesions in multiple sites of the gastric mucosa, consistent with diffused hemorrhagic gastritis.

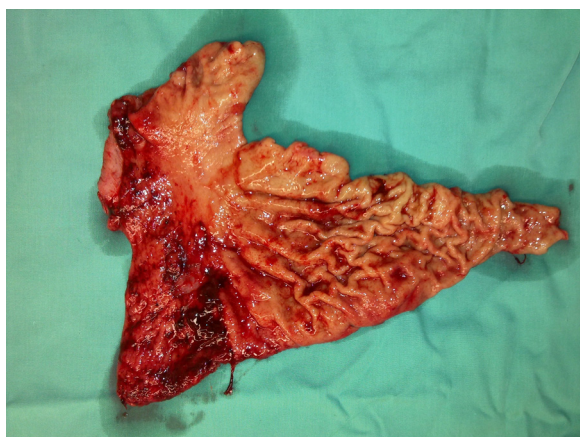


Fig. 2. Surgical specimen of subtotal gastrectomy where findings of diffused hemorrhagic gastritis can be seen.

hospital, where another effort of conservative treatment of upper gastrointestinal bleeding was attempted with several sessions of endoscopic hemostasis (cautery, injection of adrenalin) and transfusion of RBCs and FFPs, but with no success. He totally received 24 units of RBCs and 20 units of FFPs at both hospitals, in 36 days. Unfortunately the bleeding persisted. For this reason surgical management was decided. A subtotal gastrectomy with Roux-en-Y gastro-jejunosomy was performed. Histology showed diffused hemorrhagic gastritis induced by radiation (Fig. 2). The postoperative period was uneventful and the patient was discharged on the 17th postoperative day. He developed a mild myelodysplastic syndrome after radiation; however he had a very good quality of life. Unfortunately, 45 months after the hepatectomy, he developed local recurrence in the liver which is going to be managed with radio-frequency ablation.

4. Discussion

Upper gastrointestinal bleeding, due to diffused hemorrhagic gastritis induced by radiation is very rare. Only two cases required surgical management are reported in the literature. In the first case a total gastrectomy was performed due to post-radiotherapy hemorrhagic gastritis in a patient with primary gastric non-Hodgkin's lymphoma [2]. In the second case a 66-year-old male with carcinoma of the hypopharynx, underwent pharyngo-laryngo-esophagectomy, using the stomach as a replacement conduit. He developed hematemesis and tarry stools 5 months after the completion of radiotherapy. Conservative management was not successful. For this reason he underwent a subtotal gastrectomy

and a portion of jejunum was placed between pharynx and the remaining stomach, as a conduit [3].

Acute vasculopathy at the irradiated stomach may progress to obliterative endarteritis, vasculitis and endothelial proliferation, which leads to mucosal ischemia, telangiectasias and ulceration. The mucosa of irradiated stomach seems friable with multiple telangiectasias leading to a chronic radiation injury causing bleeding [4,5]. The stomach has a thick muscular and mucosal layer and is relatively resistant to radiation. It is likely that the ulceration of the irradiated stomach is caused due to the destruction of the mucosal cells of the gastric mucosa. The prime change is edema, which appears immediately after irradiation. Disruption of the epithelial cells of the mucosa and the stromal cells appears about in 1 week. This is primarily hyperemia, hemorrhage and infiltration with leukocytes. These changes can lead to ulceration from 1 to 3 months [6]. The injury of the stomach varies from mucosal inflammation, causing dyspepsia-nausea-vomiting, to bleeding and ulceration. The majority of symptoms occur within 3 years after the completion of radiotherapy. Patients who were cured from a complication of irradiated stomach are also at risk for future complications [7].

Most of the knowledge about the tolerance radiation dose on the stomach is from clinical studies of radiotherapy in the treatment of Hodgkin's disease [3,6]. In this case the lymph nodes of the upper abdomen are irradiated, however the stomach is also irradiated unintentionally. These studies proved that the big fraction and the great total dose of radiotherapy are related to a higher rate of late radiation complications [3]. Emami et al. suggest that the TD5/5 of the stomach was 60 Gy, 55 Gy, and 50 Gy when one-third, two-thirds and the entire stomach was irradiated, respectively (for ulceration-perforation) [8]. Very few reports demonstrate ulceration under 45 Gy. Other factors that may contribute to the stomach toxicity induced by radiation are previous abdominal surgery and cirrhosis [6,7]. Yet, the reason for such a serious bleeding complication in our patient is uncertain, as both the total dose of radiation and fraction size are within the recommended ranges. The total dose is within Emami's recommended TD5/5 (53 Gy for one third of the stomach irradiated) and the low fraction of 1.8 Gy.

Although, there are several reports with increased incidence of hemorrhagic gastritis after radiation therapy combined with chemotherapy, the influence of chemotherapy on the toxicity of the irradiated stomach is uncertain. The chemotherapy agents that have been reported in such cases are 5-fluorouracil, gemcitabine, mitomycin-C, lomustine (CCNU), paclitaxel and carboplatin, which have been used alone or in combination. In these studies the chemotherapy was given after the completion of radiotherapy or concurrently [4–7,9–11]

There is one case report which shows patient's susceptibility to radiotherapy. That patient who was operated for esophageal adenocarcinoma was postoperatively administered chemotherapy and radiotherapy. Three months after the end of radiotherapy, he

was presented to the emergency department with melena and low hematocrit. Gastroscopy showed diffuse hemorrhagic gastritis presumably secondary to radiation effect. Five months after this episode he was diagnosed with non-metastatic stage V prostate cancer. For this reason, pelvic radiotherapy was applied and a few weeks later he complained about melena and he had low hematocrit. Taking this case into consideration, we can assume that some people are more susceptible to radiation than others. However more evidence is required in order to reach solid conclusions [5].

In most cases the treatment of the upper gastrointestinal bleeding is conservative by endoscopic therapy and blood transfusion. Other treatment methods that have been reported for diffused, hemorrhagic gastritis due to radiation are endoscopic band ligation [4], epsilon-aminocaproic acid (EACA) [5], hyperbaric oxygen treatment [9], radiofrequency ablation and argon plasma coagulation. [10,11] Recent papers have reported the successful use of oral administered prednisolone for intractable bleeding from hemorrhagic gastritis induced by radiation [12,13].

In our case, endoscopic treatment with cautery and adrenaline injection had been attempted several times but failed to control the bleeding. Surgical treatment was necessary because of the failure of conservative treatment and massive requirements in transfusion of RBCs and FFPs in 36 days of hospitalization. Despite the fact that most cases of upper gastrointestinal bleeding can be managed nowadays conservatively, taking into consideration the favorable outcome in our case, we can conclude that surgical management of intractable bleeding for hemorrhagic gastritis induced by radiation may has a role in the armamentarium for the management of this rare and difficult to manage life threatening condition.

Conflicts of interest

None declared.

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Ethical approval

None applicable.

Consent

Written informed consent was obtained from the patient prior to publication.

Author contribution

Michalis Fatouros and Georgios Glantzounis performed the operation and Georgios Papadopoulos was the Anesthetist.

Evaggelia Peponi and Periklis Tsekeris are Radiotherapists who gave the informations about the radiotherapy of our patient. Vasileios Tatsis wrote the manuscript, while the rest of the authors critically revised it.

Research registry

Not applicable.

Guarantor

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