Recurrent Gastric Perforation as a Late Complication of Radiotherapy for Mucosa-Associated Lymphoid Tissue Lymphoma of the Stomach

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Abstract

Radiation therapy can be used to treat Helicobacter pylori-negative or eradication-refractory extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue (MALT) of the stomach. We report a case of gastric perforation which occurred more than 1 year after the completion of radiotherapy for H. pylori eradication-refractory gastric MALT lymphoma, and then recurred shortly afterwards. This was considered to be a late complication of radiation toxicity. Although gastric perforation due to radiotherapy has been reported very rarely in the past, even in advanced disease, this case shows that perforation can develop in patients with superficial disease and can relapse.

Key words: MALT lymphoma, radiation-induced gastric perforation, late toxicity, Helicobacter pylori

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Introduction

Treatment of primary gastric lymphoma varies in condition of disease. With respect to extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma) of the stomach, the association with Helicobacter pylori infection has been well established (1). Although H. pylori eradication is efficacious therapy for H. pylori-positive gastric MALT lymphomas with early tumor stages, 20-40% patients were nonresponders (1-4). On the other hand, H. pylori-negative MALT lymphomas have been reported in approximately 30-40% of patients from Asian studies (5, 6), even though the prevalence varies in geographic areas. Radiation therapy can be a therapeutic option for these H. pylori eradication-refractory or H. pylori-negative MALT lymphomas of the stomach (1, 7-11). Radiotherapy for the stomach may lead to several complications. Among these complications, the major concern has been the risk of perforation or bleeding of the stomach. However, these risks appear minimal according to a review of the literature (8, 12, 13, 15-18). We encountered a case of recurrent gastric perforation after completion of radiotherapy for a gastric MALT lymphoma.

Case Report

In August 2001, a 70-year-old woman was diagnosed with MALT lymphoma in the fornix region of the stomach limited to the submucosal layer (Fig. 1). She received triple therapy for eradication of H. pylori because of a coexisting bacterium infection. Despite successful eradication, her lymphoma did not achieve remission. In September 2002, she underwent radiotherapy with a total dose of 40.5 Gy in daily fraction of 1.5 Gy, and achieved remission without any adverse event.

In April 2004, she visited our hospital with abdominal pain. On physical examination, abdominal distension and mild tenderness were present. Blood tests showed an elevated C-reactive protein of 4.5 mg/dL, and a normal white cell count. Plain radiography and abdominal computed tomography showed marked intraperitoneal free gas. She was hospitalized urgently for cryptogenic gastrointestinal perforation. We chose non-surgical treatment using a nasogastric tube, antibiotics, and a proton pump inhibitor because we hypothesized that the perforated site was located in the...
Figure 1. Pretreatment endoscopic image showed the lesion of MALT lymphoma with irregular and bleached gastric mucosa.

Figure 2. Endoscopic finding on the sixteenth hospital day after the first gastric perforation revealed a small ulcer at the lymphoma scar.

Figure 3. On one month before the second perforation, the ulcer reached the scarred stage.

Figure 4. Four days after the second perforation, the endoscopic image demonstrated an open ulcer resembling a hole at the lymphoma scar.

stomach based on her history. We also considered her good general condition and lack of clinical signs of peritonitis to determine the treatment strategy. Esophagogastroduodenoscopy on the sixteenth hospital day revealed a small ulcer at the lymphoma scar, which we diagnosed as the lesion responsible for the perforation (Fig. 2). Following healing of the ulcer, she was discharged with continuation of the proton pump inhibitor. However, in November 2004, she was readmitted for gastric perforation, although we had confirmed that the ulcer reached the scarred stage on endoscopy one month before this second perforation (Fig. 3). She was treated as previously, and again recovered. Four days after reperforation, endoscopy demonstrated a hole-like ulcer at the same location (Fig. 4). Thereafter, no relapse has occurred and remission of the MALT lymphoma has been maintained.

Discussion

For patients with *H. pylori* eradication-refractory or *H. pylori*-negative gastric MALT lymphomas, radiotherapy has shown excellent results. One study demonstrated 100% complete remission for these gastric MALT lymphoma patients at a median follow-up time of 27 months with radiation alone to a median dose of 30 Gy (range 28.5-43.5 Gy) (7). Other studies showed similar results (9, 11). A concern when choosing radiation therapy for primary gastric lymphomas is late toxicity to the preserved stomach. The secretory dysfunction of the stomach, inflammatory reactions in the gastric mucosa, and ulceration or perforation of the gastric wall are all involved in late gastric toxicities, in addition to secondary carcinogenesis. The destruction of gastric mucosa cells as an acute injury from irradiation heals with conservative management in most cases, while it is sometimes followed by submucosal fibrosis with microcirculation damage. These alterations can lead to ulceration or perforation (14). Although we compared the gastric wall circulation before and after perforation with contrast material-enhanced abdominal CT scans, detailed evaluation was difficult.

The risk of radiation-induced gastric perforation is actually small. In 1954 Berger et al (15) reported gastric perforation after irradiation occurring in three gastric malignant lymphoma patients; however, this old report is distinct from the current medical situations. Moreover, two of the three
patients developed perforation in late stage of the clinical course and probably did not have relevance to radiotherapy. Talamonti et al (16) reported one instance of radiation-induced gastric perforation. The patient was an advanced case. As for lymphoma at an early stage, Burgers et al (17) and Taal et al (18) reported one perforated case in Musshoff’s stage I non-Hodgkin’s lymphoma of the stomach a few months after radiotherapy. Therefore, several review articles which referred to the above-mentioned reports described that morbidity of gastric perforation due to irradiation to lymphomas corresponds to <4% at most (8, 12, 13). Moreover, there are only a few reports on perforation as a definite late complication of radiation therapy. Limiting the literature search to gastric MALT lymphoma, to date no case of perforation following irradiation has been reported (7-11, 19, 20).

Total radiation dose is a critical factor for developing ulceration and perforation. Likewise, fractionation is also an important factor as low doses of radiation per fraction (≤ 2 Gy) suppress gastrointestinal complications (14).

The present case shows that radiation-induced gastric perforation might occur in patients with superficial gastric lymphoma who received an adequate dose of radiation therapy. As well, perforations can develop irrespective of the time after completion of radiotherapy and can relapse. Although infrequently occurring, we should be aware of gastric perforation as late irradiation toxicity. Further studies will be required to evaluate the late effect as well as the long-term efficacy of irradiation for gastric MALT lymphoma.

References