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Two Cases of Gastric Cancer Treated with Stereotactic Body Radiotherapy Using Cyberknife®

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Abstract

We report two cases of gastric cancer treated with stereotactic body radiotherapy (SBRT) using CyberKnife®. Case 1 was advanced gastric cancer (T3N0M0 stage II_A) in an 80-year-old man. Endoscopy revealed a bulky type 3 tumor on the lesser curvature of the gastric upper body. Case 2 was recurrent gastric cancer in an 82-year-old man who had undergone endoscopic submucosal dissection for a previous tumor. Endoscopy revealed a bulky recurrent tumor on the gastric cardia. Both the patients received SBRT using CyberKnife® for symptom improvement and local control of the tumor. After treatment, both the patients showed early reduction of the tumor and improvement of the symptoms caused by the tumor, without serious complications or tumor progression for 8 and 4 months, respectively. SBRT was useful as a local treatment with low invasiveness and rapid action for locally advanced gastric cancer. Although some issues still require clarification, such as the optimal prescription dose and fractionation of irradiation, we expect SBRT to be a suitable treatment option for locally advanced gastric cancer in cases where other treatments are difficult to perform, such as elderly patients and patients with complications.

Keywords: Stereotactic body radiotherapy; CyberKnife®; Gastric cancer

Abbreviations

SBRT: Stereotactic Body Radiotherapy; CT: Computed Tomography; ESD: Endoscopic Submucosal Dissection; BED: Biological Effective Dose; OAR: Organs at Risk; GTV: Gross Tumor Volume; PTV: Planning Target Volume; DVH: Dose-Volume Histogram; TLS: Target Locating System; CRT: Conventional Radiotherapy

Introduction

Radiotherapy is often used as pre-operative or post-operative adjuvant therapy or as palliative treatment for advanced gastric cancer to improve hemorrhage or passage disorders [1-9]. The use of Stereotactic Body Radiotherapy (SBRT) has made it possible to concentrate the dose on the lesion and reduce the dose to the surrounding organs, thereby resulting in higher local control and fewer adverse events [10]. Moreover, SBRT can be completed in a short period, reducing the patient's physical burden. Accordingly, SBRT is expected to be one of the treatment options used in the multidisciplinary treatment for advanced gastric cancer. Herein, we report our experience of performing SBRT for advanced gastric cancer using CyberKnife®.

Case Presentation

Case 1

An 80-year-old man presented with hematemesis, upper abdominal discomfort, and appetite loss, and was diagnosed with advanced gastric cancer. Endoscopy revealed a bulky type 3 tumor on the lesser curvature of the gastric upper body(Figure 1A). Abdominal Computed Tomography (CT) revealed a bulky tumor on the lesser curvature of the gastric body with a diagnosis of cT3N0M0, stage II_A

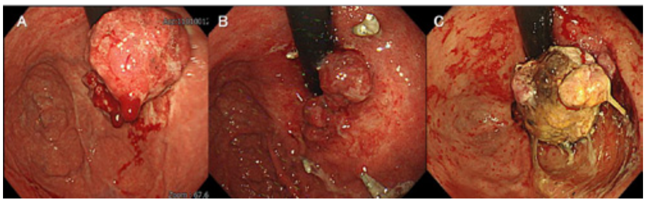

Figure 1: Temporal changes observed on gastroscopy for case 1. (A): Gastroscopy findings before treatment: endoscopy revealed a bulky type 3 tumor on the lesser curvature of the gastric upper body. (B): Gastroscopy findings 1 months after treatment: the tumor was obviously reduced with a remarkable response. (C): Gastroscopy performed 8 months after treatment showed re-growth of the tumor.

Figure 2: Temporal changes on abdominal computed tomography (CT) for case 1. (A): CT scan before treatment: CT revealed a bulky tumor on the lesser curvature of the gastric upper body. (B): CT scan 4 months after treatment: the bulky tumor was flat and obviously reduced. (C): CT scan 8 months after treatment: Re-growth of the tumor was observed, with ascites and liver metastasis.

***** The red arrows point to the tumor.

carcinoma (Figure 2A). Biopsy revealed a well-differentiated tubular or papillary adenocarcinoma. The patient did not undergo surgery because of his advanced age, but instead received a daily dose of 80mg S^{-1}. S^{-1} was administered for 4 weeks, followed by 2 weeks of

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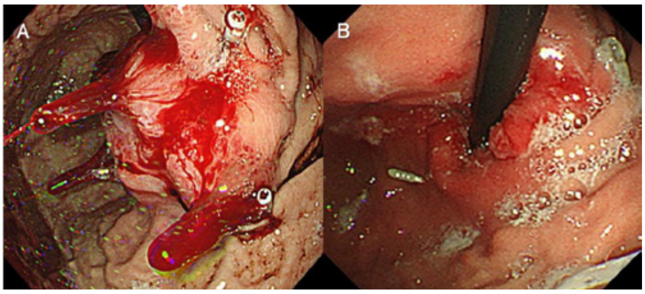

Figure 3: Temporal changes observed on gastroscopy for case 2. (A): Gastroscopy findings before treatment: endoscopy revealed a bulky recurrent tumor on the gastric cardia. (B): Gastroscopy findings 1 month after treatment: the tumor was obviously reduced with a remarkable response.

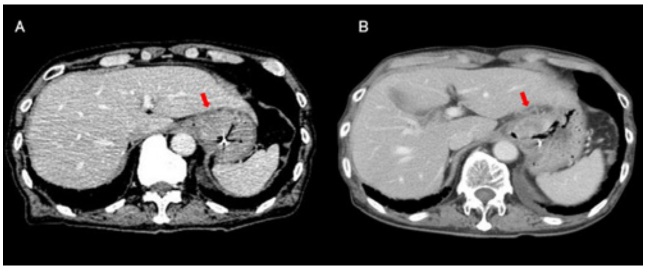

Figure 4: Temporal changes on abdominal computed tomography (CT) for case 1. (A): CT findings before treatment: CT revealed a bulky recurrent tumor on the gastric cardia. (B): CT findings 1 month after treatment: the bulky tumor was flat and reduced.
* The red arrows point to the tumor.

rest. Tumor growth was controlled for 5 months, after which it re-grew. The patient was referred to our hospital for tumor control and symptom improvement.

Case 2

An 82-year-old man who underwent surgery for right renal cancer was diagnosed with gastric cardia cancer (adenocarcinoma, cT1bN0Mx) during follow-up after multidisciplinary treatment for multiple metastases. Although he underwent Endoscopic Submucosal Dissection (ESD), relapse was observed after 6 months. Endoscopy revealed a bulky recurrent tumor on the gastric cardia (Figure 3A). Abdominal CT revealed a bulky gastric cardia tumor with liver metastasis (Figure 4A). The patient presented with hematemesis, upper abdominal discomfort, and passage obstacle. Biopsy showed a well to moderately differentiated tubular adenocarcinoma. The patient wanted to receive CyberKnife® treatment, for which he was referred to our hospital.

Treatment

Stereotactic body radiotherapy: SBRT precisely administers high target doses in a few fractions and minimizes the dose to adjacent normal tissue structures. Case 1 received 42 Gy (10 fractions of 4.2 Gy per fraction) using CyberKnife® G4 (Accuray, Sunnyvale, CA, USA), corresponding to a Biological Effective Dose (BED) of 59.6 Gy (assuming $\alpha/\beta = 10$). Case 2 received 40 Gy (8 fractions of 5 Gy per fraction) using CyberKnife® G4, corresponding to a BED of 60 Gy (assuming $\alpha/\beta = 10$). Although the BEDs prescribed in these cases were lower than those for other cancers were [11-13], we ensured that the dose to the Organs at Risk (OAR) does not exceed the tolerated dose. Table 1 shows the OAR dose constraints (Table 1). Gross Tumor Volume (GTV) was determined by considering endoscopic findings and the visible tumor on CT. The Planning Target Volume (PTV) margin was a 3mm increase in the anterior-posterior right-left direction and a 5mm increase in the superior-inferior direction for GTV. The dose was prescribed using the 95% PTV isodose. The plans were recalculated using the Monte Carlo algorithm. The dose distribution and Dose-Volume Histogram (DVH) of case 1 are shown in Figure 5. Treatment with the CyberKnife® system was performed using fiducial tracking. Metal clips were placed endoscopically around the tumor. Fiducial tracking irradiation was performed using two of five clips in case 1 and two of three clips in case 2. To improve the accuracy further, we frequently acquired images using the Target Locating System (TLS). Patients were irradiated on an empty stomach

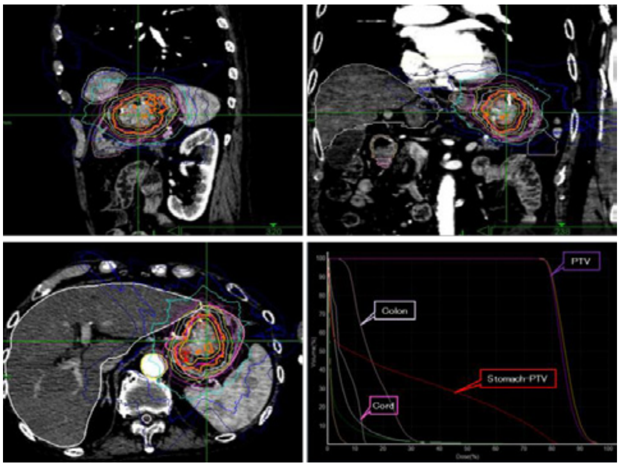

Figure 5: Dosimetric evaluation of computed tomography (CT) images show the dose distribution in the sagittal, coronal, and axial slices, with a D95 isodose involving the tumor. We planned to concentrate the high dose on the target. The lower right figure is a dose-volume histogram (DVH).

Table 1: Dose constraints of organs at risk.

Organs/tissue at risk	Dose-limiting
Liver	V20 <20%
Stomach	36 Gy ≤10 cc
	30 Gy ≤100 cc
Intestine	36 Gy ≤10 cc
	30 Gy ≤100 cc
Spinal cord	Dmax <25 Gy

to ensure the same conditions every time.

CyberKnife®: The CyberKnife® system has a linear accelerator mounted on a robotic arm, providing more flexibility and freedom of motion while delivering the radiation beams. The CyberKnife® system has integrated X-ray imagers that provide continual image guidance and real-time tracking capabilities, ensuring high (i.e., sub-millimeter) accuracy and precision [14].

Treatment response: Although two of the five placed clips fell off in case 1 and one of the three fell off in case 2 during each treatment period, treatment in both the patients was completed without any complications and without reducing treatment accuracy.

The symptoms of hematemesis and upper abdominal discomfort improved from in both cases early after treatment. After 1 month, tumor reduction was confirmed via endoscopic evaluations in both cases. In case 1, the tumors were controlled for 8 months after treatment. However, after 8 months, the tumor rapidly increased in size with ascites retention, and the patient died of disease progression 11 months after treatment (Figures 1B, C, and Figures 2B, C). In case 2, the tumors were controlled for 4 months after treatment. However, the patient died 4 months after treatment owing to deterioration in his general condition (Figures 3B and 4B).

Clinical response

One month after treatment, both cases showed a partial response considering the radiological and endoscopic findings (Figures 1B and 3B).

Adverse event

According to CTCAE scale, v. 4.0., grade 2 gastritis was identified early after treatment in both cases.

Discussion/Conclusion

Although surgery is the standard radical treatment for gastric cancer [15], chemotherapy and palliative treatment are treatment options for inoperable cases owing to advanced stage, advanced age, and complications. Many patients with advanced gastric cancer experience symptoms such as bleeding, obstruction, and perforation of the stomach. These symptoms need to be addressed with topical therapy, as they reduce not only survival but also quality of life. Radiotherapy as palliative treatment is effective for these symptoms [3-5], and higher local tumor control after radiotherapy may benefit patients. The local tumor control rate after radiotherapy is dose dependent. When Conventional Radiotherapy (CRT) was used for palliative treatment of gastric cancer, there was no difference in the palliative effect between high and low BED regimens [16]. In contrast, there was a significant difference in local control when prescription doses were above the BED (assuming $\alpha/\beta = 10$) of 41 Gy [17], and higher BED regimens provided better local control. However, the true irradiated dose was unknown because of inter- and intra-fractional motion of the stomach, and the optimal prescription dose and fractionation for irradiation have not yet been determined. Furthermore, owing to the adverse effects to the surrounding organs due to the tolerable dose and movement of the surrounding organs, prescription doses cannot be easily increased.

Therefore, treatment requires dose concentration and accuracy. We expected that SBRT could be used to resolve these issues, and CyberKnife® was a suitable option. SBRT using CyberKnife® made it possible to concentrate the dose on the lesion and reduce the dose to surrounding organs. The prescription BED (assuming $\alpha/\beta = 10$) was 59.6 Gy in case 1 and 60.0 Gy in case 2. Because of the accuracy obtained via image-guided radiotherapy, it was possible to set a small margin and to quantify more precisely irradiated dose, thereby making it possible to increase the prescription dose. Although these doses exceeded the BED value of irradiation for gastric cancer using CRT considering palliation and local control, the margins are different for CRT and SBRT; hence, it is unclear if the use of increased doses can be generalized for all situations. When SBRT was used to treat cancer at other sites including lung cancer, a BED of ≥100 Gy was effective [18-21], which was less than that. Moreover, the local control period was 8 months in case 1; however, as the tumor size increased rapidly thereafter, the dose seemed insufficient. Furthermore, the optimal prescription dose and fractionation schedule need to be standardized in future studies. However, both the patients that we treated could undergo complete treatment effectively and safely in a short period. In both cases, the tumor reduced rapidly and symptoms of bleeding and obstruction improved. Moreover, tumor progression was controlled for 8 and 4 months, respectively. Adverse events were also mild during the observation period. In addition, as short-term treatment is desirable for elderly patients and patients with poor conditions, SBRT was effective because it involved the use of hypo-fractionated irradiation. Although there are many issues that yet need to be discussed, we expect SBRT to be useful for locally advanced gastric cancer in elderly patients and patients with complications, both of who are difficult to treat.

In conclusion, although treatment planning and dose prescription are difficult because the tolerable dose of normal gastric mucosa and surrounding organs is low, SBRT was highly precise irradiation method and useful as a low-invasive and speedy local treatment for locally advanced gastric cancer. Moreover, SBRT can be useful for elderly patients and patients who have difficulty in undergoing other treatments owing to complications.

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