advances
in radiation oncology

Teaching Case

Carbon Ion Radiation Therapy for Postoperative Pelvic Recurrence of Rectal Cancer With a Large Tumor Infiltrating and Compressing the Rectum: A Case Report

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Introduction

Surgery offers the highest potential cure for a postoperative pelvic recurrence of colorectal cancer. However, a pelvic exenteration is often performed, which is highly invasive and its postoperative management is challenging.[1,2] Although radiation therapy (RT) is a less invasive treatment option, the clinical outcomes of RT for pelvic recurrence of rectal cancer remain unsatisfactory with local control rates of 68% to 74%, even with stereotactic body RT (SBRT) for relatively small recurrent tumors.[3,4]

In the last decade, favorable clinical outcomes have been reported with carbon ion (C-ion) RT for pelvic recurrences of rectal cancer, with 3-year local control rates of 85% to 93%.[5-7] In previous reports, patients with a recurrence of colorectal cancer and tumor involvement or compression of the gastrointestinal (GI) tract were usually not included due to the risk of serious toxicities, such as GI perforation. Additionally, patients with tumors infiltrating the rectum or tumors located with little-to-no space for inserting a spacer (eg, pelvic floor) were not suitable for insertion of a spacer that physically separates the tumor and the rectum to avoid severe rectal toxicities.[8,9] Therefore, to treat pelvic recurrences of rectal cancer without causing severe toxicities in cases where the tumor infiltrates or compresses the rectum, lowering the administration dose, rectal dose adjustment, and colostomy before C-ion RT might be necessary.

However, there have been no previous reports of C-ion RT for recurrent rectal tumors infiltrating and compressing the GI tract. Herein, we report on a case of a postoperative pelvic recurrence of rectal cancer with a large tumor infiltrating and compressing the rectum treated by C-ion RT, wherein a drastic clinical response was achieved without severe toxicities.

Case Report

The patient

A 57-year-old male Japanese patient with rectal cancer underwent an internal anal sphincter resection (ISR) and colostomy, and the pathologic diagnosis included type 1, por1 > tub1, pMP, int, INFb, ly1, v1, pN0(0/7), pPM0, pDM0, TmpN0M0 pstage I, surgical margin negative, estimated glomerular filtration rate negative, K-ras mutation codon 12 (+), and GTT: codon 13 (-). After surgery, the patient did not receive adjuvant therapy. Eleven months after the ISR, the patient underwent a colostomy closure, and there was no evidence of recurrence upon examination by computed tomography (CT), colonoscopy, and tumor marker until this time.

Fifteen months after the ISR, the patient experienced a defecation disorder, anal pain, and rectal bleeding, after which the patient underwent magnetic resonance imaging (MRI) and a colonoscopy. The MRI revealed a tumor (90 × 80 × 75 mm) located in the pelvic floor, compressing a wide area of the rectum, and the tumor showed good contrast in gadolinium-enhanced T1-weighted images (Fig. 1a and 1b). The colonoscopy revealed pelvic tumor infiltration with extension to the rectum, as well as rectal bleeding. Simultaneously, a biopsy was performed on the exposed tumor in the rectal wall, and the pathologic diagnosis was adenocarcinoma.

Subsequently, the patient underwent contrast-enhanced CT and fluorodeoxyglucose (FDG)−positron emission tomography (PET). Contrast-enhanced CT showed a tumor with slight contrast enhancement, and FDG-PET showed abnormal FDG uptake, which is consistent with a pelvic floor tumor (Fig. 1c and d). Contrast-enhanced CT and FDG-PET showed no evidence of metastasis to the lymph nodes or distant organs. The patient showed high levels of serum carcinoembryonic antigen (38.1 ng/mL; normal: 0-5.0 ng/mL). Finally, the patient was diagnosed with a postoperative pelvic recurrence of rectal cancer, with a tumor infiltrating and compressing the rectum and no distant metastases.

The patient underwent a colostomy to treat the defecation disorder. Then, the patient was referred to Gunma University Heavy Ion Medical Center for C-ion RT, because curative surgery was unsuitable, chemotherapy was refused by the patient, and x-ray RT was not an option due to poor local control. Spacer placement surgery before C-ion RT was not suitable because the tumor was infiltrating and compressing a wide area of the rectum, and there was no space to insert the spacer on the pelvic floor. C-ion RT was chosen as a treatment approach with a clear understanding of the high risk of severe rectal toxicities, such as rectal perforation, bleeding, and abscess. Informed consent for this treatment was obtained from the patient before the initiation of therapy,

and the ethics committee of Gunma University Graduate School of Medicine approved this case report.

C-ion radiation therapy and dose−volume histogram

Before C-ion RT, the patient was immobilized using tailor-made fixation cushions and thermoplastic shells to acquire treatment planning CT images, and respiratory-gated and 4-dimensional CT images were acquired. The treatment planning CT images were merged with the MRI and FDG-PET to precisely delineate the gross tumor volume (GTV). The clinical target volume (CTV) had a margin of at least 5 mm around the GTV to include microscopic disease. The internal margin was assessed using 4-dimensional CT images for tumor movement. The planning target volume (PTV) was defined as the sum of the CTV, internal margin, and setup margin. The rectum included the CTV and PTV because anastomotic recurrence could not be ruled out. Therefore, to avoid severe rectal toxicities, we reduced the prescription dose from 73.6 Gy (relative biologic effectiveness [RBE]) of the standard recommended dose to 64.0 Gy (RBE) in 16 fractions for 4 weeks.

C-ion RT was performed using conventional broad beam with passive irradiation and C-ion beams from one direction per fraction for a total of three directions in 16 fractions. The standard dose constraints were defined as the mean dose (D_{mean}) of <50 Gy (RBE) and the maximum dose (D_{max}) of <60 Gy (RBE) to the rectum and the dose delivered to a 1 cm^3 volume of the bladder (D_{1cc}) of <60 Gy (RBE).[7] Figure 2 shows the dose distribution and dose-volume histogram (DVH) of the C-ion RT. The DVH parameters of the GTV, CTV, PTV, bladder, and rectum are shown in Table 1. Although this treatment plan exceeded the standard dose constraint of the rectum and bladder, C-ion RT was performed with priority for GTV coverage. Toxicities were assessed using the Common Terminology Criteria for Adverse Effects (version 4.0).[10] The tumor response was assessed by the Response Evaluation Criteria in Solid Tumors (version 1.1).[11]

Results

After completion of treatment, the patient did not receive adjuvant therapy. During the C-ion RT, the patient experienced no acute toxicities. Three months after C-ion RT, the tumor showed a complete response (Fig. 3c) and serum carcinoembryonic antigen levels improved to normal limits (1.9 ng/mL). Anal pain and rectal bleeding improved, and no late rectal toxicities developed. The colostomy was not closed, and the patient was defecating with a colostomy during the last follow
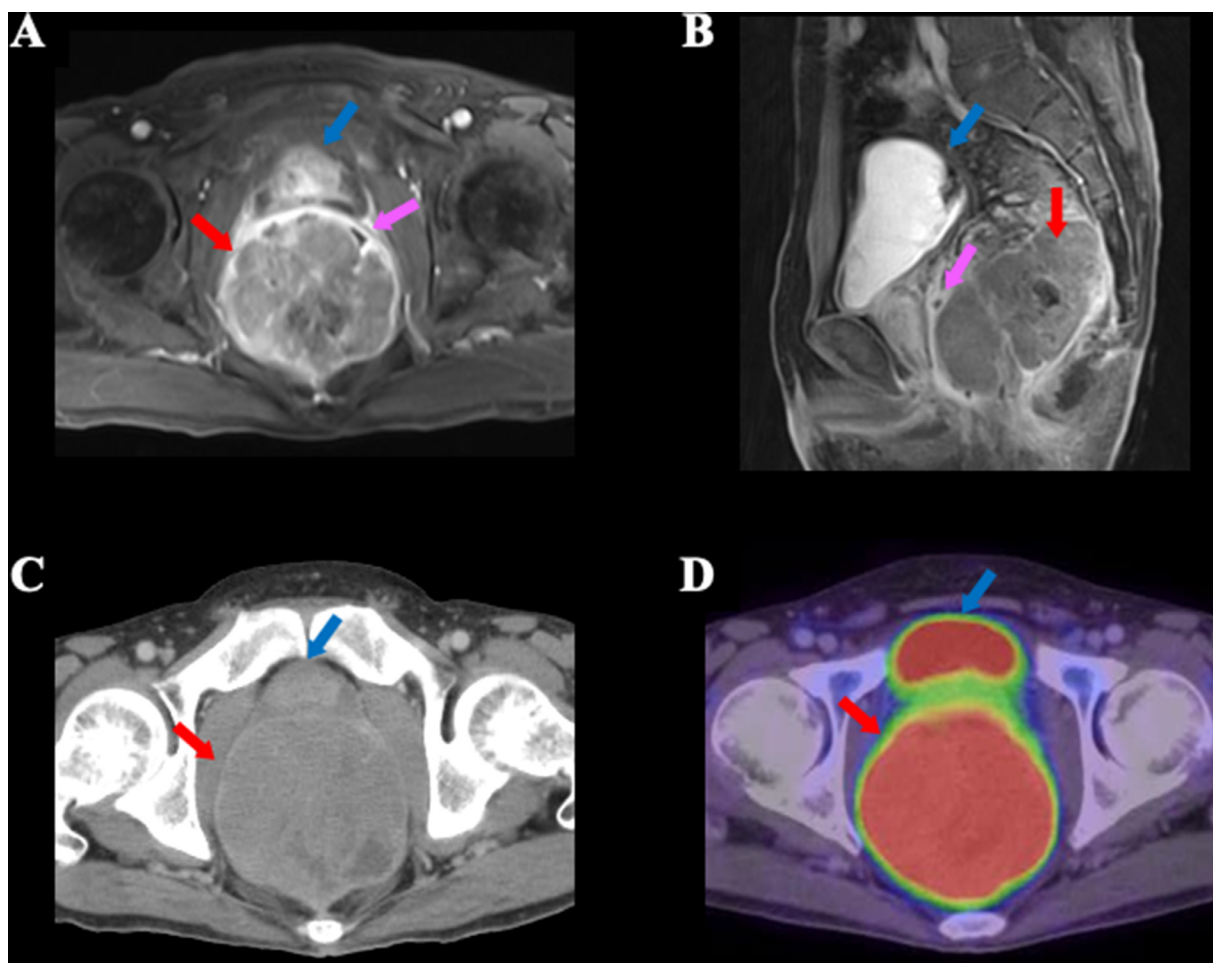
Fig. 1 Magnetic resonance imaging (MRI), contrast-enhanced computed tomography (CT), and fluorodeoxyglucose (FDG)-positron emission tomography (PET) showing postoperative pelvic recurrence of rectal cancer, with the tumor compressing a wide area of the rectum before the initiation of carbon ion radiation therapy. The tumor was located on the pelvic floor with contrast enhancement and abnormal FDG uptake. The size of the tumor was $90 \times 80 \times 75$ mm. (a) Axial MRI of the gadolinium-enhanced T1-weighted image. Red arrow shows the rectum; (b) sagittal MRI of the gadolinium-enhanced T1-weighted image; (c) axial contrast-enhanced CT image; and (d) axial FDG-PET. Blue, magenta, and red arrow shows the bladder, rectum, and tumor, respectively.

up. Grade 1 dysuria developed as a late toxicity. The patient remains alive and has survived without evidence of local recurrence, distant metastasis, or late toxicities for 5 years (Figs. 3 and 4).

Discussion

We presented a case of postoperative pelvic recurrence of rectal cancer with a large tumor infiltrating and compressing a wide area of the rectum that achieved positive clinical outcomes after C-ion RT. Generally, a pelvic recurrence of rectal cancer is considered difficult to cure using x-ray RT because its large hypoxic cell components are radioresistant.[12] However, C-ion RT can overcome hypoxia[13] and shows a drastic therapeutic outcome that is similar to that observed in the present case.

Regarding toxicity, rectal perforation is the most feared toxicity. A previous study of uterine cancer showed that the tolerable dose to the GI tract is 60 Gy (RBE).[14,15] In the present case, although the DVH parameters of D_{max} to the rectum exceeded 60 Gy (RBE), the patient did not develop rectal perforation. One of the reasons why no colorectal toxicities occurred is that excrement did not pass through the rectum owing to the colostomy, and the irradiated rectal wall was not exposed to the stimulus of excrement. This is one possibility, as the safety of performing a colostomy before C-ion RT and administering >60 Gy (RBE) to the rectum has not been confirmed in clinical trials. However, our experience with the present case suggested that when tumor infiltration or GI tract compression occurs, performing a colostomy before C-ion RT can be a safer approach. We believe that further investigation is warranted to include an accumulated
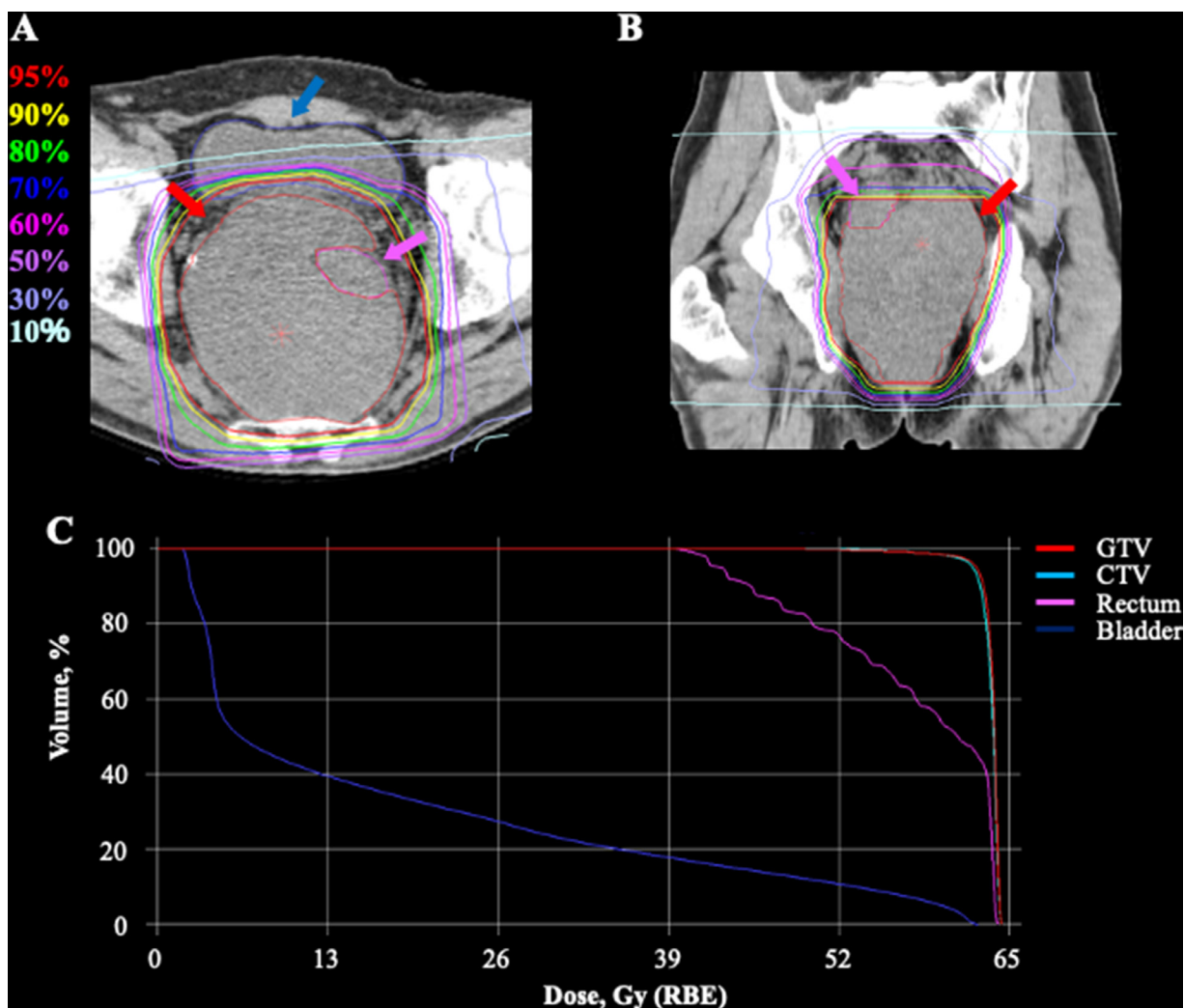
Fig. 2 Dose distribution of carbon ion radiation therapy. (a) Axial image; (b) coronal image; and (c) dose−volume histogram of the gross tumor volume (red), clinical target volume (light blue), rectum (magenta), and bladder (blue). The area within the red outline is the gross tumor volume, the magenta outline is the rectum, and the blue outline is the bladder. The blue, magenta, and red arrow show the bladder, rectum, and tumor, respectively. Highlights show the 95% (red), 90% (yellow), 80% (green), 70% (dark blue), 60% (magenta), 50% (purple), 30% (blue), and 10% (light blue) isodose curves (100% was 64.0 Gy; relative biologic effectiveness).

Table 1   Dose-volume histogram parameters of the targets and organs

	Volume, cm^3	D_{98}, Gy (RBE)	D_{95}, Gy (RBE)	V_{60}, %
Gross tumor volume	477.3	60.5	62.5	98.2
Clinical target volume	592.0	60.4	62.1	20.8
Planning target volume	719.2	57.2	60.9	17.2

	D_{max}, Gy (RBE)	D_{1cc}, Gy (RBE)	D_{2cc}, Gy (RBE)	D_{mean}, Gy (RBE)	V_{60}, cm^3
Rectum	64.1	63.9	63.8	57.5	10.3
Bladder	62.6	61.9	61.6	17.6	6.5

Abbreviations: D_{xcc} = minimum dose of most exposed small volume in x cm^3 of organ; D_{9x} = percentage of minimum dose that covered 9x%; D_{max} = maximum dose of organ; D_{mean} = mean dose of organ; RBE = relative biologic effectiveness; V_{60} = volume of target that received >60 Gy (RBE).
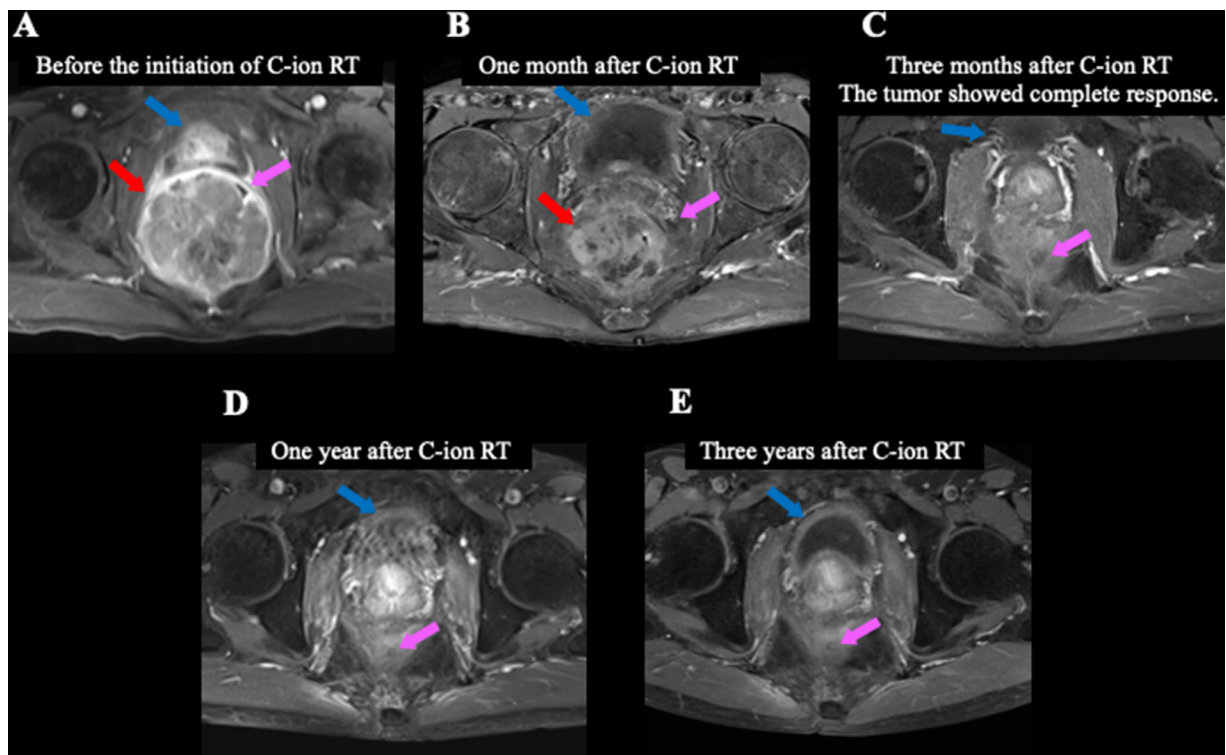
Fig. 3 Treatment response of carbon ion radiation therapy (C-ion RT) assessed by magnetic resonance imaging. (a) Before the initiation of C-ion RT; (b) 1 month after C-ion RT; (c) 3 months after C-ion RT with the tumor showing complete response; (d) 1 year after C-ion RT; and (e) 3 years after C-ion RT. The blue, magenta, and red arrow show the bladder, rectum, and tumor, respectively.

number of patients with tumor compression or involvement of the GI tract who have had a colostomy before C-ion RT, and analyze the safety and changes in a tolerable dose of C-ion RT.

If patients with a pelvic recurrence of colorectal cancer are unsuitable for surgery or refuse chemotherapy, RT might be an appropriate candidate. SBRT is a suitable treatment modality; however, previous reports on SBRT
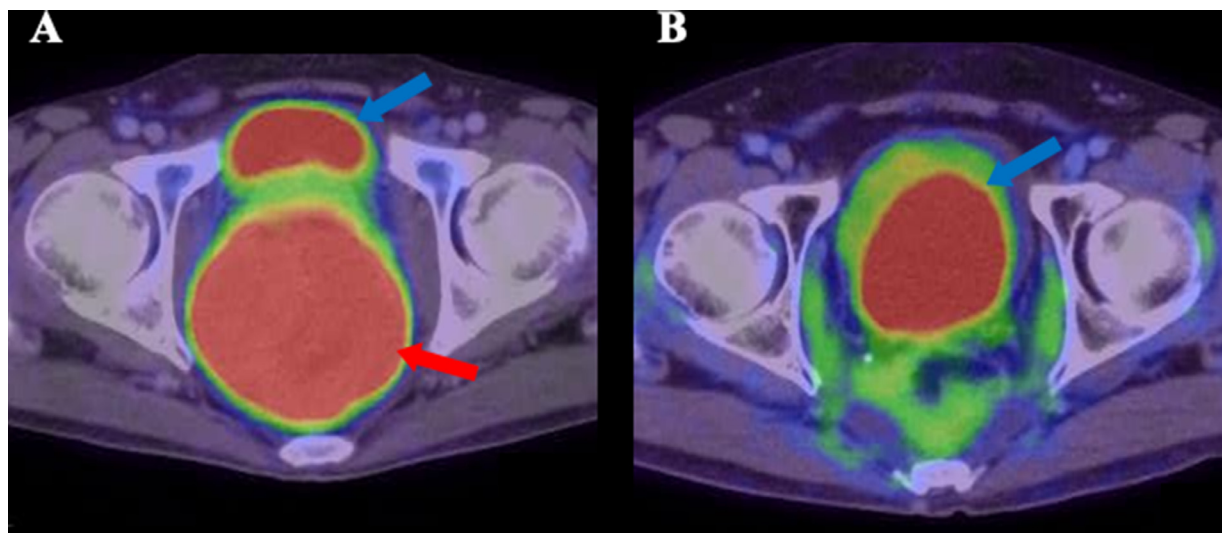

Fig. 4 Treatment response of carbon ion radiation therapy (C-ion RT) assessed by fluorodeoxyglucose-positron emission tomography. (a) Before the initiation of C-ion RT; and (b) 5 years after C-ion RT. The blue and red arrow show the bladder and tumor, respectively.

have been performed for a tumor size up to 8 cm or 122 cm^3.[3,4] Additionally, recurrent tumors infiltrating or compressing the GI tract or recurrence at the anastomosis site or the residual colon are usually excluded from SBRT because of severe possible toxicities to the GI tract.[4] In the present case, SBRT was not indicated due to the large size and volume of the tumor (9 cm and 477.1 cm^3, respectively), as well as infiltration and compression to the rectum. Therefore, conventional x-ray RT, including intensity modulated RT, which is considered a safer treatment than SBRT, is usually indicated; however, its therapeutic efficacy is poor, with a 3-year local control rate of 19%.[16] In a previous study, clinical results of C-ion RT reported treatment of tumors size up to 14 cm in diameter,[5] and even large tumors can be treated by C-ion RT. In the present case, we performed C-ion RT for a large tumor, and received survival benefits from the therapy for local control.

A limitation of this study is that this is a case of a tumor, infiltrating or compressing rectum that is usually not clinically indicated for C-ion RT owing to the high risk of severe rectal toxicities. This case was treated with a clear understanding of the high risks of severe toxicities, such as rectal perforation, bleeding, and abscess that might be difficult to salvage and may be fatal.

Conclusions

We achieved drastic outcomes without severe toxicities using C-ion RT for a patient who presented with a pelvic recurrence of rectal cancer, with a large tumor, infiltrating and compressing the rectum, located on the pelvic floor.

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