Neoadjuvant volumetric modulated arc radiochemotherapy with a simultaneous integrated boost technique for the treatment of locally advanced rectal cancer

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Abstract

Background: Locally advanced rectal cancer (LARC) includes cancers which are extending through the rectal wall and/or regional lymph nodes are involved. Preoperative chemoradiotherapy with radiation doses up to 45-50 Gy and radical transabdominal surgery are considered as best treatment options in such cases, but dose escalation to the gross tumor using simultaneous integrated boost technique has been introduced recently.

Aim: We present a case of locally advanced rectal cancer treated with simultaneous integrated boost, capecitabine and surgical intervention. The main aim of this case is to show that a combination of simultaneous integrated boost technique and chemotherapy with capecitabine is associated with clinical and pathological complete response and the ability of sphincter preservation without increased risk of acute toxicity.

Conclusion: This case reports advantages of simultaneous integrated boost technique for the treatment of LARC, which is expressed in clinical and pathological complete responses after the treatment and possibility to achieve sphincter preservation, without radiation associated severe acute toxicity. (TCM-GMJ March 2019; 4(1):P20-P24)

Keywords: Simultaneous integrated boost technique; Locally advanced rectal cancer; Neoadjuvant chemoradiation.

Introduction

Locally advanced rectal cancer (LARC) includes cancers which are extending through the rectal wall and/or regional lymph nodes are involved. At present preoperative chemoradiotherapy (CRT) followed by radical transabdominal surgery and postoperative chemotherapy is preferred as the best treatment option for the treatment of LARC (1). Radical pelvic radiotherapy up to 45-50 Gy in 25-28 fractions have become established as the standard treatment (2) but simultaneous integrated boost (SIB) techniques have also been considered (3). Simultaneous integrated boost is excellent technique to deliver higher doses up to 60 Gy to the cancer tissue, while irradiating the rest of the rectum and regional lymph node stations with the standard doses. According to several trials, SIB technique leads to better down-staging, increases number of R0 resections and reports better oncological outcome with the same rates of acute toxicity (4,5). Based on these clinical data we present a case report of the patient with LARC, who received high-dose radiotherapy by using SIB technique, showed a complete pathological and clinical response and underwent radical surgery with sphincter-preservation.

Case Presentation

53-year-old man visited the hospital in May 2017 because of diarrhoea, which had started a year before. Patient had also complained of haematochezia and rectal pain for last 3 months. Complete blood cell counts, and biochemistry test results were within normal ranges. The serum carcinoembryonic antigen level was 12.33 ng/mL (normal range 0-5.0 ng/mL) and carbohydrate antigen 19-9 was 111.5 U/ml (normal range 0-37 U/ml). Pelvic and abdominal MRI revealed tumour with distal end located 4.5 cm from anal verge, with craniocaudal length 7.5 cm and perirectal fat infiltration. MRI scan also showed 8 enlarged mesorectal lymph nodes, with short axis diameter 5-9 mm, irregular border contour and heterogeneous signal intensity (Fig. 1). Peripheral zone of the prostate gland appeared to have slightly heterogeneous signal intensity. Prostate specific antigen was 1.41 ng/ml (normal range 0-4 ng/ml). Colonoscopy revealed an ulcerating mass with the distal end located 5 cm from the anal verge and pathological examination showed a poorly-differentiated adenocarcinoma. Chest CT was without any pathological changes. No distant metastasis was detected. The pretreatment clinical stage was determined to be T3N2bM0 (IIIC) according to the American Joint Committee on Cancer staging, 7th ed. This clinical case was presented to our institutional multidisciplinary team meeting and it was decided to start the treatment with neoadjuvant CRT. Radiotherapy was performed by using simultaneous integrated boost technique: 46 Gy to the elective volume and 57.5 Gy as a boost to the rectal tumour in 23 fractions. This treatment plan was approved by the institutional ethical committee. The patient signed an informed consent. The treatment was conducted according to the Declaration of Helsinki’s “Ethical Principles for Medical Research Involving Human Subjects.”
Patient was immobilized, simulated and treated in the supine position. Simulation was performed with Siemens Somatom AS CT with slice thickness of 3 mm and was instructed to achieve stable conditions of bladder and rectal filling (Fig. 2). Target volume and organs at risk (OAR) were delineated on the SomaVision 13.7 (Varian Medical Systems). The gross tumour volume (GTV) was determined by a combination of findings on physical exam, endoscopy and MRI. The primary clinical target volume (CTVp) included GTV plus pararectal area. PTV primarily included CTVp plus 5 mm. The CTV nodes included the internal and external iliac, pre-sacral and peri-rectal lymph node stations (Fig 3). The PTV node was generated with a 5 mm symmetrical margin around the CTV node. The small bowel, bladder and femoral heads were defined as organs at risk.

Patient was treated with VMAT technique on the Truebeam linac with 6 MV photons and Millennium MLC (120 leaves) (Varian Medical Systems, Palo Alto, CA). Patient set-up was daily checked by using cone beam computed tomography image. Plan evaluation was performed with dose-volume histogram parameters for target structures as well as for OARs (Fig 4). Chemotherapy was administered concurrently with RT, using capcitabine 825 mg/m² twice daily (6,7). During the treatment, patient complained of the acute toxicity, such as radiation dermatitis, mild diarrhoea, nausea and fatigue, which subsided with conservative management.

Pelvic MRI and colonoscopy were performed 6 weeks after completion of preoperative treatment. This investigation showed rectal wall thickness due to the radiation induced changes, no enlarged lymph nodes were detected (Fig 5). No intraluminal mass was observed during colonoscopy. It was considered as complete clinical response to the neoadjuvant treatment. Patient underwent radical transabdominal surgery 8 weeks after finishing neoadjuvant CRT. It was possible to perform sphincter preservation, but radiation induced fibrosis was more expressed compared to standard doses of radiotherapy, such as 45-50 Gy. Pathological examination after radical surgery revealed complete pathological response. 15 months after treatment, the patient is alive with no evidence of disease and no severe complications.

Discussion

New treatment modalities, such as volumetric modulated arc therapy makes it possible to increase the dose conformity and decrease treatment time. The efficacy of VMAT is also confirmed in case of prostate (8), gastric (9) and oesophageal (10) cancer. In our case, we were focused on evaluation of clinical and pathological down-staging, perioperative surgical complication rate, early toxicity and quality of life. It was important to assess if the possibility of sphincter-preservation and the degree of fibrosis would increase after using dose escalation. Sphincter preservation is very important for the patient, since it significantly improves the quality of life. First, it is necessary to accurately detect the tumours that have more potential for sphincter preservation. There are several criteria: tumour location, tumour stage >pT3 and non-mucinous and signet ring cell are independent factors for sphincter-preservation (11). Radiation-induced fibrosis is a long-term side effect of external beam radiation therapy, it results in a multitude of symptoms that significantly impact quality of life. Several factors increase the risk of fibrosis. The primary treatment-related factors are the total dose of radiotherapy and dose per fraction, the volume of tissue treated, and the time course of treatment delivery. More specifically, the degree of fibrosis directly correlates with increased radiation dose and hypofractionation (fewer fractions require greater doses), increased field size, and prolongation of therapy (12). Other treatment-related factors known to play a role include concurrent use of chemotherapy as well as incorporation of surgical management pre- or post-radiotherapy (13).

Conclusion

This case reports advantages of SIB-VMAT technique for the treatment of LARC, which is expressed in clinical and pathological complete responses after the treatment and possibility to achieve sphincter preservation. Volumetric modulated arc therapy with simultaneous integrated boost make it possible to increase dose on the tumour tissue, while preventing dose spread on the healthy tissue. SIB-VMAT technique may increase the quality of radiation induced fibrosis due to dose escalation but decreases the treatment time without increased risk of radiation induced severe acute toxicities.

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References

Figure 1. Pretreatment MRI

Figure 2. CT simulation in the supine position with full bladder and empty bowel.

Figure 3. CTVp included GTV and pararectal area, CTVn -internal and external iliac, presacral and perirectal lymph node stations.
Figure 4. Dose-Volume Histogram: PTV-boost (red right), PTVp/n (red left), spinal canal (dark yellow), small bowel (purple), right femoral head (orange), left femoral head (pink), bladder (yellow).

Figure 5. Posttreatment MRI 6 weeks after finishing neoadjuvant CRT.

9. Zhang T, Liang ZW, Han J, Bi JP, Yang ZY, Ma H. Double-arc volumetric


