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Case Report

Locally Advanced Rectal Cancer Invading the Gluteus Maximus Muscle Completely Responded to Total Neoadjuvant Therapy

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A 70-year-old male with anal pain and fever was diagnosed with rectal cancer perforation and abscess in the right gluteus maximus (GM) muscle. He underwent a transverse colon colostomy followed by preoperative capecitabine + oxaliplatin. Some local control was achieved but a residual abscess was observed in the right GM muscle. To secure circumferential resection margin by tumor reduction, he received chemoradiotherapy as total neoadjuvant therapy (TNT) and underwent laparoscopic abdominoperineal resection, D3 lymph node dissection, combined coccyx resection, and partial resection of the right GM muscle. The skin defect and pelvic dead space were filled with a right lateral vastus lateral great muscle flap. Histopathologically, the resected specimen showed no tumor cells in the primary tumor or lymph nodes, indicating a pathological complete response (pCR). This case suggests that TNT might improve the R0 resection and pCR rates and overall survival.

Key words: locally advanced rectal cancer, total neoadjuvant therapy, lateral vastus lateral great muscle flap

In western countries, the standard therapy for locally advanced rectal cancer (LARC) is preoperative chemoradiotherapy (CRT) followed by total mesorectal excision [1]. Although preoperative CRT has been shown to improve local control rates in LARC, its contribution to overall survival is limited. The concept of total neoadjuvant therapy (TNT), in which systemic chemotherapy is added to preoperative CRT, was proposed to further improve the prognosis of patients with LARC [2,3]. In Japan, although the standard treatment for LARC remains surgery followed by adjuvant chemotherapy [4], an increasing number of facilities are introducing multidisciplinary treatment. We report the case of a patient with LARC with right gluteus maximus muscle invasion in which TNT contributed to the patient's pathological complete response.

Case Presentation

A 70-year-old Japanese male visited the referring hospital with a complaint of fever and anal pain, and blood tests showed the elevated values WBC 12,800 /μL and CRP 10.3 mg/dL. Perirectal abscess due to perforation of lower rectal cancer was diagnosed based on the results of abdominal computed tomography and rectal endoscopy. The patient was immediately started on sulbactam/ampicillin and underwent a loop transverse colostomy. Percutaneous drainage was not performed because of the undeniable possibility of tumor extension into the abscess and the risk of tumor dissemination. After improvement of the perirectal abscess, the patient

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underwent a chemotherapy regimen consisting of five cycles of capecitabine plus oxaliplatin. He was then referred to our hospital for further treatment after the diagnosis of gluteal abscess. A rectal examination revealed an easily hemorrhagic, circumferential, elastic, hard mass immediately at the anal verge.

The hemoglobin value was 13.3 mg/dl, tumor markers were CEA 4.21 ng/mL and CA19-9 113.0 U/mL, and CA19-9 was elevated. Colonoscopy detected a circumferential, type 2 tumor in the rectum, extending 5 cm from the anal verge. A biopsy revealed a well differentiated tubular adenocarcinoma. Abdominal computed tomography showed marked wall thickening in the lower rectum, and invasion of the levator ani muscle with abscess formation caused by the perforation into the right gluteus maximus muscle (Fig. 1A). The lymph nodes in the mesorectum were enlarged. No distant metastasis was observed. MRI with T2-weighted imaging demonstrated a high-intensity mass in the lower rectum, and a continuous high-intensity area was observed from the mass to the right posterolateral wall, suggesting tumor perforation and extension beyond the rectal wall. The lesion was in close proximity to the coccygeal muscle, and abscess formation was seen in the right gluteus maximus muscle (Fig. 1B, C).

We conducted total neoadjuvant therapy (TNT) for LARC to secure a circumferential resection margin by tumor reduction, and the patient was treated with preoperative chemoradiotherapy: capecitabine 1,800 mg/body + total 50.4 Gy, boost irradiation 5.4 Gy to the primary lesion + gluteus maximus muscle (Fig. 2).

After the TNT, tumor markers were normalized to CEA 3.02 ng/mL and CA19-9 21.3 U/mL. Ulcerative changes were observed in the tumor area by colonoscopy. MRI revealed that the tumor had shrunk and the abscess had become indistinct.

The patient was preoperatively diagnosed as having a ycT4b (levator ani muscle) N0M0 Stage IIc tumor and underwent radical surgery 8 weeks after the completion of CRT. Subsequently, laparoscopic abdominoperineal resection with a combined resection of coccyx bone and right gluteus maximus muscle was performed (Fig. 3A). Perineal reconstruction with a right vastus lateralis muscle flap were performed after specimen removal (Fig. 3B, C). The loop transverse colon stoma was then

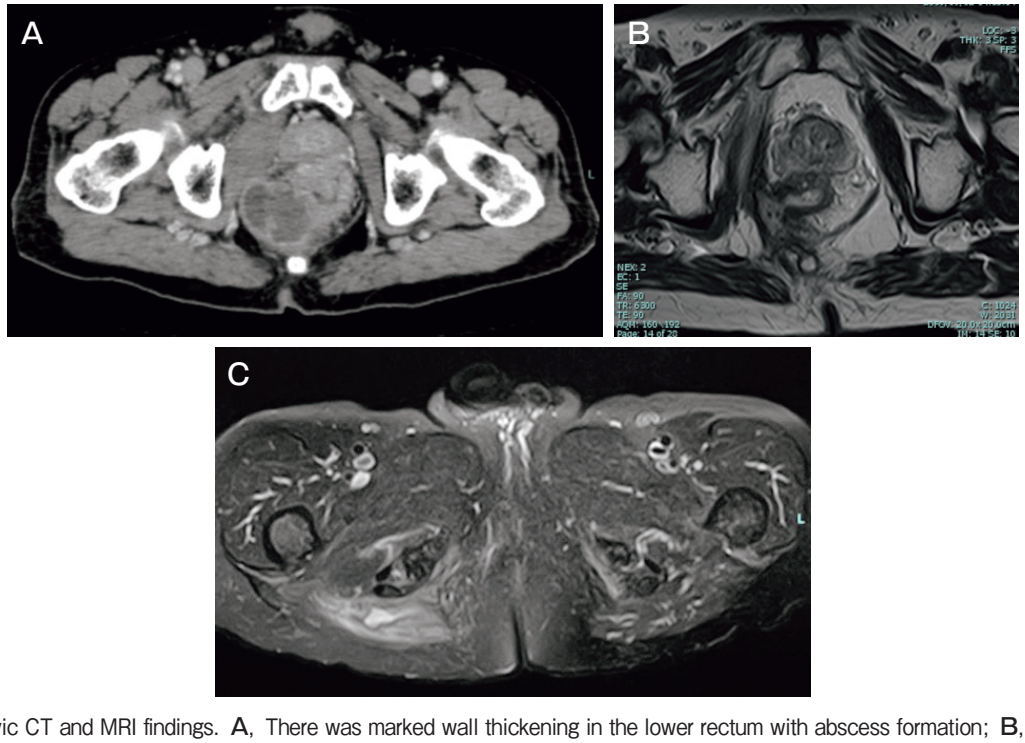

Fig. 1 Pelvic CT and MRI findings. A, There was marked wall thickening in the lower rectum with abscess formation; B, A continuous high-intensity area was observed from the right side of the lower rectum to the perirectal area; C, An abscess formation was identified in the right gluteus maximus muscle with a high-intensity mass.

closed, and a sigmoid colon stoma was newly created.

In the resected specimen, ulcer scarring was seen in the lower rectum, with the formation of a fibrous scar from the bottom of the ulcer to the gluteal muscles (Fig. 4). Macroscopically, the radial margin was negative for cancer. A histopathology examination identified no evidence of cancer at the ulcer site, and the fistulae and abscess formation had disappeared, leaving only fibrous scar tissue. The abscess of the gluteus maximus muscle also showed only fibrous scar tissue without cancer cells. The response to chemotherapy was Grade 3 with a complete response, pathologically. There were no lymph node metastases and the resection margins were negative, resulting in R0 resection.

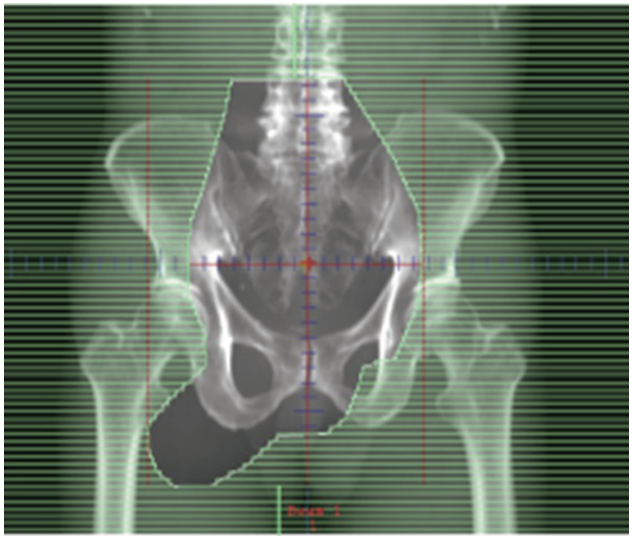

Fig. 2 Radiation dose distribution map. Dose distributions at treatment with external-beam radiation therapy: total 50.4 Gy, and 5.4 Gy for boost irradiation on the primary lesion plus the right gluteus maximus muscle.

The patient's postoperative course was good, and his neurogenic bladder dysfunction improved after a few days of urinary continence. After physical rehabilitation of his lower limbs, the patient was discharged on the 31st postoperative day. No postoperative adjuvant therapy was administered, and the patient is currently alive without recurrence 2 years after the surgery.

Discussion

The standard treatment for locally advanced rectal cancer (LARC) differs between western countries and Japan. In western countries, the standard treatment for LARC is preoperative chemoradiotherapy (CRT) followed by total mesorectal excision (TME) [1]. The con-

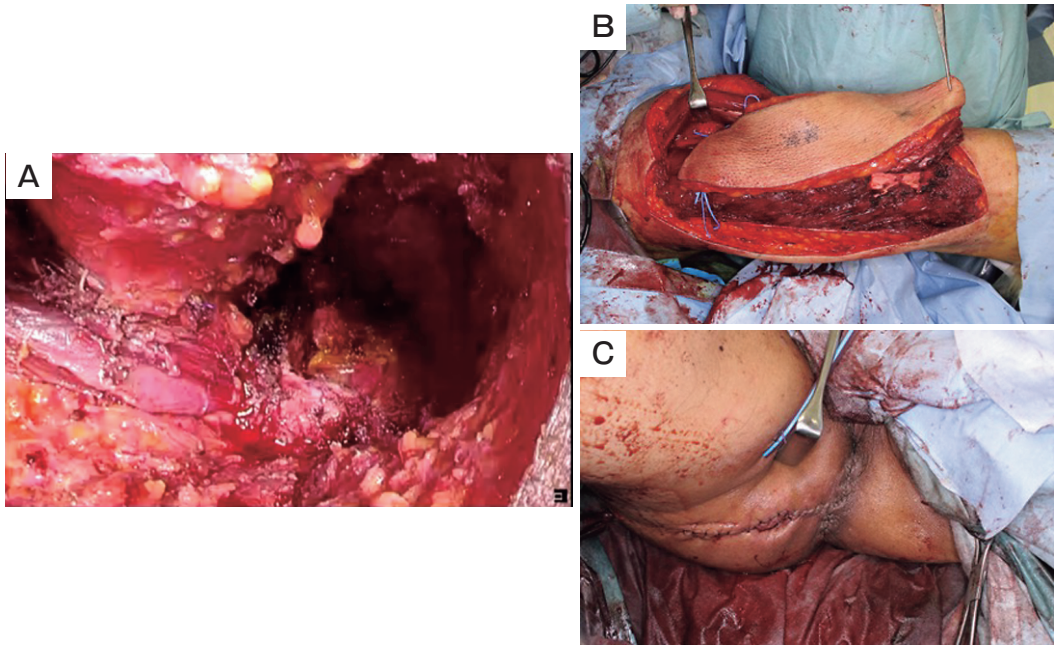

Fig. 3 Intraoperative findings. A, Abdominoperineal resection was performed with combined resection of coccyx bone and right gluteus maximus muscle; B, C, Perineal tissue defects were reconstructed with a right vastus lateralis muscle flap.

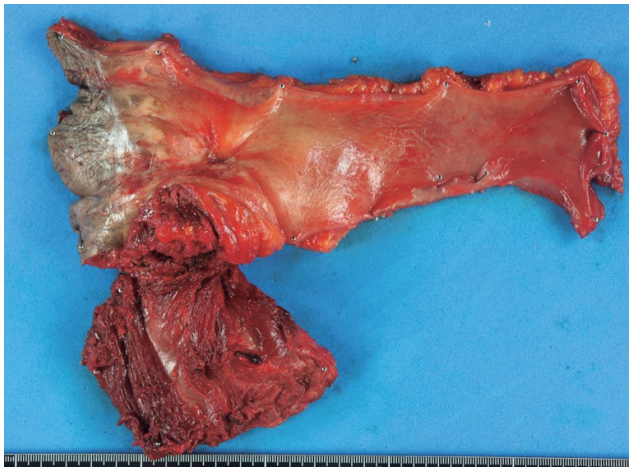

Fig. 4 Resected specimen extraction. Ulcer scarring was found in the lower rectum, with a fibrous scar formation from the bottom of the ulcer to the gluteal muscles.

cept of total neoadjuvant therapy (TNT), which improves the prognosis by adding potent systemic chemotherapy to preoperative CRT, was recently proposed [2,3]. In Japan, the standard treatment for LARC is TME plus postoperative chemotherapy [4], but an increasing number of institutions have recently introduced multidisciplinary treatment, including TNT [5]. In our present patient's case, the primary tumor was shrunk by capecitabine + oxaliplatin therapy, but there was a possibility of tumor extension within the abscess, and CRT was added based on the TNT concept aiming at further tumor shrinkage in order to ensure a circumferential resection margin. Ultimately, the patient responded to the CRT and underwent an R0 resection, and a pCR was obtained histopathologically.

Perineal wound infection in the defect after rectal cancer surgery with combined resection of other organs can be a problem. In the present case, a perineal reconstruction with a lateral vastus lateralis muscle flap was performed to prevent perineal wound infection, with a good postoperative outcome and clinical course. To determine the appropriate site for perineal reconstruction, it is important to consider the extent of resection and the route of reconstruction. The perineum is often reconstructed using thin muscle, the gluteus maximus, plus rectus abdominis skin flaps; compared to femoral skin flaps, rectus abdominis skin flaps have shown a lower incidence of total skin wound incision and pelvic abscess on the reconstructed side [6,7]. If there is a history of abdominal surgery or a history of colostomy, the femoral skin flap is the first choice. In the present case, because of the presence of a colostomy, a rectus abdominis myocutaneous valve was not used, and right lateral vastus skin valve reconstruction was simulated preoperatively because of the concomitant resection of the gluteal muscles.

TNT with chemotherapy in addition to preoperative CRT has been presented as an option in the U. S. National Comprehensive Cancer Network (NCCN) guidelines [8], and it has advantages such as an increased rate of chemotherapy, preoperative downstaging, and an earlier start of systemic treatment for micrometastases. The addition of chemotherapy before CRT is called induction chemotherapy, and the addition of chemotherapy after CRT and before surgery is called consolidation therapy; both of these significantly improved the local control rate compared to CRT alone [2,3,9,10]. Early adverse events of grade 2 or higher were seen in 34.3% of patients who underwent preoperative CRT, and the completion rate of preoperative CRT was reported to be 98.5% [11]. In the present case, the treatment with capecitabine + oxaliplatin resulted in Common Terminology Criteria for Adverse Events grade 3 thrombocytopenia, but the patient was able to complete capecitabine + radiotherapy.

The results of the 'watch-and-wait' approach, in which patients with a clinical complete response to preoperative CRT or TNT are followed up without surgery, were recently described [12-14]: approx. 70% of patients who achieve a pCR show no recurrence and have very good remote outcomes, and approx. 20-30% show local tumor re-growth. Although local tumor re-growth is observed, salvage surgery is reported to be feasible in most cases. Since there are no reports regarding the use of the watch-and-wait approach after successful TNT in cases of rectal cancer perforation, our current treatment strategy is to perform a radical resection after explaining the possibility of a pathologic CR to the patient. A number of randomized controlled trials are currently underway to clarify the optimal regimen of TNT and the indications for the watch-and-wait approach, the results of which are awaited.

Conclusion

We have described a case of a patient with LARC with right gluteus maximus muscle invasion who responded well to TNT and in whom a pathological

complete response was obtained. TNT might be a promising treatment to improve the prognosis of patients with LARC.

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