



Organ preservation in rectal cancer patients following complete clinical response to neoadjuvant chemoradiotherapy: Long-term results in three patients

Neoadjuvan kemoradyoterapi sonrası klinik tam cevap veren rektum kanseri hastalarında organın korunması: Üç hastanın uzun dönem sonuçları

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ABSTRACT

Rectal cancer patients following complete clinical response to neoadjuvant chemoradiotherapy (CRT) can be followed up without surgery. Those patients in particular who needed abdominoperineal resection before CRT choose the follow-up protocol, should they be given the necessary information. The purpose of this study was to demonstrate the long-term follow-up results of patients following neoadjuvant CRT without surgery.

Key Words: Rectal cancer, neoadjuvant chemoradiotherapy, clinical complete response, wait-and-see protocol

ÖZET

Rektum kanserinde neoadjuvan kemoradyoterapi (KRT) sonrası klinik olarak tam yanıt veren hastalar ameliyat edilmeden izlenebilirler. Özellikle KRT öncesi değerlendirmede abdominoperineal rezeksiyon gereken hastalar, kendilerine gerekli bilgi verildikten sonra takip edilmeyi tercih etmektedirler. Bu çalışmada, neoadjuvan KRT sonrası ameliyat edilmeden takibe alınan hastaların uzun süreli takip sonuçları bildirilmiştir.

Anahtar Kelimeler: Rektum kanseri, neoadjuvan kemoradyoterapi, klinik tam yanıt, bekle ve gör protokolü

INTRODUCTION

Neoadjuvant chemoradiotherapy (CRT) for rectal cancer patients is the mainstay of its management and yields a complete tumor response in 10%-30% of patients (1-3). These patients can be followed up without surgery. The present study demonstrates the long-term outcomes of three patients with cT2-3/N+ rectal cancer who progressed to a clinical complete response following neoadjuvant CRT. Radiotherapy consisted of a total of 5040 cGy delivered in 28 fractions of 180 cGy, 5 times weekly. During the first and fifth weeks of radiotherapy, 5-fluorouracil was given at a dose of 1000 mg/m². Patients were re-evaluated 8 weeks after the completion of CRT using clinical, endoscopic, and endosonographic studies, including a biopsy of the tumor bed. Patients were staged as ycT0N0M0 when a complete clinical response was considered. They were included in observation group without surgery that was checked every 3 months for a period of 2 years and 6 months subsequently. All patients are alive, with no evidence of tumor recurrence or distant metastasis.

CASE PRESENTATIONS

Case 1

A 31-year-old female nurse was admitted with rectal bleeding in January 2010. She had been diagnosed with adenocarcinoma histopathologically. The tumor was located 3 cm proximally and anteriorly from the anal verge and was staged as cT2N+ with an endorectal ultrasound (ERUS) (Figure 1). The tumor was 3 cm in diameter, and the carcinoembryonic antigen (CEA) level was 0.7 ng/mL. Neoadjuvant CRT was delivered to the patient. The patient was re-evaluated 8 weeks after the completion of radiation. There was no tumor endoscopically, which was staged as ycT0N0 with ERUS (Figure 2, 3). A transanal full-thickness biopsy of the tumor bed revealed no signs of the tumor. The patient was provided with complete information about her illness, and she chose to wait without surgery. The chemotherapy protocol was completed during the waiting period. The complete tumor response was sustained at 50 months.

Case 2

A 56-year-old woman was diagnosed as having rectal adenocarcinoma in June 2011. The tumor was 4 cm in diameter and located posteriorly in the lower part of the rectum. The tumor stage was cT3N0 with ERUS. The CEA level was normal, and the BMI was 36. She was given neoadjuvant CRT. After completion of the CRT, the patient was completely tumor-free. An endoscopic biopsy of the tumor bed revealed no signs of the tumor, and she decided to go without surgery. She was given 4 cycles of chemotherapy

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Received / Geliş Tarihi: 03.07.2014

Accepted / Kabul Tarihi: 29.07.2014

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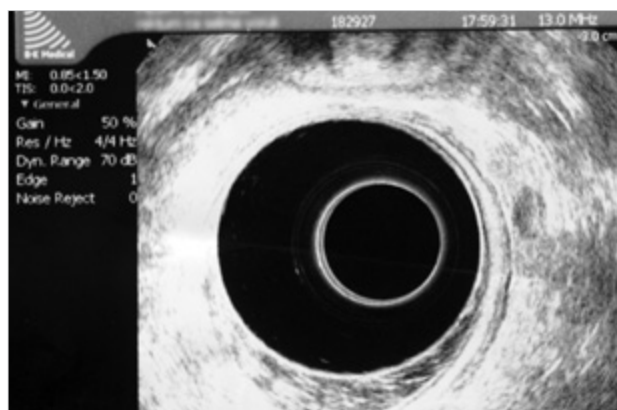


Figure 1. ERUS of the first patient, staged cT2N+
ERUS: endorectal ultrasound



Figure 2. ERUS of the first patient after chemoradiotherapy, staged ycT0N0
ERUS: endorectal ultrasound

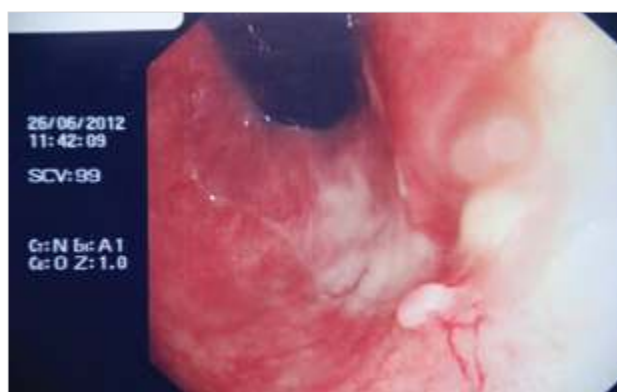


Figure 3. Endoscopic appearance of the tumor bed

during the follow-up period. She has been living without any problems for 34 months.

Case 3

A 49-year-old woman who refused surgery from the outset was admitted for a second opinion. She had a history of neoadjuvant chemotherapy because of cT3N0 rectal cancer. She had also received chemotherapy after CRT. A physical examination and endoscopy revealed that there was an ulcer scar at the tumor bed, located posteriorly in the lower part of the rectum. After being provided with complete information, the patient chose a waiting protocol without surgery. She has been tumor-free for 25 months.

DISCUSSION

Neoadjuvant CRT for rectal cancer patients has a number of potential advantages, including a complete clinical or pathological response. A complete pathological response is defined as the absence of tumor on histological examination of the specimen after surgery. The definition of a clinical response is considered there being no signs of the tumor by a digital rectal examination and endoscopy. These patients can be candidates for nonoperative management and follow-up without surgery. For this reason, the definition of a complete clinical response (cCR) is of utmost important. Habr-Gama et al. (4) described cCR as a whitening of the mucosa and telangiectasia with mucosal integrity. There should be no ulceration, residual nodules, or stenosis at the tumor site. Biopsy or transanal local excision can accurately assess the tumor response after CRT. We performed one transanal excision and one biopsy of the tumor bed. There were no signs of tumor in either case. The third patient refused a biopsy and surgery. All of the patients decided to go without surgery, since they would have needed an abdominoperineal excision before the CRT.

An endorectal ultrasound can accurately define the depth of the tumor invasion with high sensitivity and specificity rates (90% and 85%, respectively) (5). However, re-staging after neoadjuvant therapy is a challenge because of radiation-induced fibrosis, edema, inflammation, and necrosis. The sensitivity and specificity rates drop to 40% and 75%, respectively (6). Furthermore, there is some inaccuracy in determining the circumferential margin.

Magnetic resonance imaging is the gold standard for the local staging of rectal cancer before CRT, but the role of MRI for the selection of cCR patients is questionable (7). A pooled analysis of 33 studies that reported on restaging with MRIs revealed that the overall sensitivity and specificity were 50% and 91%, respectively (8). Conventional MRIs cannot differentiate between fibrosis and tumors. New functional magnetic resonance technology has the potential to improve the identification of a complete clinical response.

Lymph node status after CRT was found to be an independent predictor of survival. Neither of the modalities mentioned here can accurately determine malignant lymph nodes without surgery. Positron emission tomography is valuable for predicting the response of rectal carcinoma to neoadjuvant therapy. A meta-analysis reported 78% sensitivity and 66% specificity for the prediction of response (9).

Because neoadjuvant CRT may lead to a complete clinical response, the clinical assessment of post-CRT staging is of utmost important. There were no survival benefits from surgery over the observation group in the cCR patients (10). The mean follow-up of our three patients was 36 months without recurrence. The studies indicate that recurrence during the observation period may occur within 12 to 18 months. Local recurrence can be salvaged with surgery.

CONCLUSION

Organ preservation in rectal cancer following a complete clinical response to neoadjuvant CRT can be possible in a select group of patients. These patients should be followed up closely during the observation period. Clearly, prospective random-

ized studies are necessary, but it is not easy to convince tumor-free candidates to be in a surgery group.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Conflict of Interest: No conflict of interest was declared by the author.

Financial Disclosure: The author declared that this study has received no financial support.

Hasta Onamı: Yazılı hasta onamı bu çalışmaya katılan hastalardan alınmıştır.

Hakem Değerlendirmesi: Dış bağımsız.

Çıkar Çatışması: Yazar çıkar çatışması bildirmemiştir.

Finansal Destek: Yazar bu çalışma için finansal destek almadığını beyan etmiştir.

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