Complete Pathological Response in Stage IV Rectal Carcinoma: Proper Planning and Place is a Key

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ABSTRACT
Introduction: Liver metastasis is frequently encountered in patients with rectal cancer; it can be synchronous or metachronous. Some selected patients can be treated with curative intent using multimodality therapy under the care of a dedicated team in a comprehensive cancer center. However, the treatment is long and tiring for the treating team, the patient, and the relatives. Treatment is difficult to execute in a country like ours with a limited number of cancer centers. We present a patient from a remote village with stage IV disease, who completed all modalities of treatment with a favorable outcome.

Case Presentation: A fifty-five-year-old man from a remote village presented to us with a complaint of per rectal bleeding. He was diagnosed with rectal carcinoma with solitary liver metastases. He received multimodality treatment in the form of chemotherapy, radiotherapy, and surgery. He attained a complete pathological response at both primary and metastatic sites.

Conclusions: Good outcomes can be achieved in selected stage IV rectal cancer. This requires multimodality treatment and a proper plan, preferably in a comprehensive cancer center.

INTRODUCTION
Liver metastasis from colorectal cancer can be synchronous or metachronous. The incidence of synchronous liver metastases ranges from 14 to 17% [1]. It is estimated that 35–55% of patients with colorectal cancer will develop hepatic metastasis in the entire course of treatment [2]. Only 15–20% of patients are candidates for hepatectomy, so they can be put into curative intent treatment [3]. The survival of patients with colorectal liver metastases has increased due to early presentation, initiation of systemic therapies, facility of ablation, resection of the lesion, and multidisciplinary care. The multimodality approach is difficult to address in a country like ours with limited resources.

We present a case of rectal cancer with synchronous liver metastasis from a remote village in Nepal who completed all intended treatment plans and attained a complete pathological response. He was disease-free at a 24-month follow-up.

CASE PRESENTATION
A fifty-five-year-old diabetic and hypertensive gentleman with a BMI of 24 kg/m² from a remote village in Nepal presented to us with rectal bleeding for the last 6 months. Investigations revealed a well-differentiated rectal adenocarcinoma, 8 cm from the verge, and solitary 6 cm liver metastasis at segment VIII, and the carcinoembryonic antigen (CEA) level was 400 ng/mL. After the discussion in a multidisciplinary tumor meeting, we offered him systemic chemotherapy followed by a long course of chemoradiotherapy and surgery.

He was started on chemotherapy with a FOLFOX regimen (5-Fluorouracil 600 mg IV bolus D1, followed by infusion for 2 days, Oxaliplatin 85 mg/m² D1) every 2 weeks, and concurrent chemoradiotherapy (CTRT) was given after 3 months of systemic chemotherapy (3 cycles). Radiation was given using a Tele-Cobalt machine (2D planning) with a dose of 50 Gy in 25 fractions. Reassessment was done at 7 weeks using blood tests and imaging, which showed a reduced CEA level from...
400 to 2.43 ng/mL. A computed tomogram scan (CT scan) showed a reduced size of the liver and rectal lesion, and there was no other lesion elsewhere. A digital rectal examination showed growth at the tip of the finger.

He underwent open low anterior resection (LAR) with loop ileostomy, and intra-operative ultrasound followed by liver metastasectomy in a single setting. The waiting time after completion of neoadjuvant therapy was 9 weeks. The procedure was done under general anesthesia with central vascular access and epidural catheter placement for pain management. He was kept on a Lloyd Davies position with the upper limb tucked by the side of the body. LAR was done in a usual manner and stapled colorectal anastomosis was done using a circular stapler (CDH 29, Ethicon). The incision was from the symphysis pubis to Xiphisternum and extended to the right flank from just above the umbilicus. The total duration of surgery was 330 mins, blood loss was 300 mL, and there was no transfusion. He was discharged on the 10th day of surgery.

The histopathological finding was negative for residual tumor at both sites; rectum (Figure 1) and liver. The liver showed an extensive area of coagulative necrosis and acellular mucin, negative for viable tumor (Figure 2). All nodes were negative (0/16), and the margin was free. He received adjuvant with the FOLFOX regimen for 2 more months. The total duration of treatment was 11 months. We had to postpone his stoma reversal by 3 months due to the COVID pandemic. He recovered well after stoma reversal and was disease-free at 24 months.

DISCUSSION

Some patients with colorectal tumors present with only liver metastasis and are divided into groups based on the favorable surgical and oncological prognostic criteria. The favorable criteria are those lesions that can be easily resected without much morbidity, and adverse prognostic factors are node-positive disease with hepatic lesion > 1, the largest tumor > 5 cm, CEA > 200 ng/mL, the disease-free interval from primary to metastasis < 12 months, extrhepatic disease, and positive margin [4]. Surgical resection is the only treatment that offers a chance of cure and long-term survival, with 5- and 10-year survival rates of 40% and 25%, respectively [3]. Synchronous colorectal liver metastasis (CRLM) is defined if the lesion is detected concurrently or before primary cancer and has been shown to have less favorable biology, and post-resection 5-year survival was 39% compared with 48% in metachronous CRLM [5].

Our patient underwent surgery, chemotherapy, and radiotherapy during different phases of his treatment, which took eleven months, and it was very difficult for him, his relatives, and the treating team in terms of finances, multiple hospital visits, repeated admissions, accommodation, and travel. This kind of treatment is best done in a comprehensive cancer hospital under a multidisciplinary team (MDT) setting with medical oncology, radiation oncology, surgical oncology, and other allied faculties [6]. MDT discussions are a part of regular patient care in our hospital and are not practiced in most of the government hospitals, corporate private hospitals, and medical colleges of our country probably due to the non-availability of oncologists and lack of oncology departments and radiotherapy services. A prospective study showed MDT discussions are important. Despite 84% of clinicians being certain of their original plan before discussion, a change was
recommended in 36% of cases, 72% of which were major [7].

There are many factors to consider for the treatment of these patients in terms of dose and duration of radiotherapy, stages of surgery, chemotherapy regimen, and sequence of all these modalities. The role of radiotherapy (RT) is well established in non-metastatic rectal carcinoma, and preoperative rather than postoperative administration has been shown to reduce local recurrence and cancer-related mortality [8]. In the study by Fossum et al. including 93 patients, who underwent curative-intent surgery with metastasectomy, local recurrence was not observed in the neoadjuvant RT arm, and 12 patients (26%) developed local recurrence in the RT omission arm. Our patient has received pelvic RT after 3 months of systemic chemotherapy.

Current guidelines suggest oxaliplatin-based doublet chemotherapy with 5-Fluorouracil or Capecitabine as the neoadjuvant treatment of choice [9]. Molecular targeted therapy like epidermal growth factor receptor (EGFR)-inhibitor (Cetuximab) and anti-vascular endothelial growth factor (Bevacizumab) can be added to the regimen; both have shown a good response rate than chemotherapy alone, but the addition has not shown improved survival [10]. Targeted therapy was not used on our patient.

The factors to be considered for surgery are resectability of metastases, degree of resection, whether major (> 3 segments) or minor hepatectomy is required, whether it is symptomatic or not, and whether it needs any form of neoadjuvant therapy [11]. European guidelines recommend peri-operative therapy for most patients. However, Asians are keener toward doing upfront resection [9]. The benefits of neoadjuvant therapy are patient selection, downstaging, and conversion from non-resectable to resectable liver metastases [9].

Complete pathological response at primary is seen in 15–20% of the patients with locally advanced rectal carcinoma after neoadjuvant chemoradiotherapy [12]. Complete radiological disappearance of metastases can occur in 8% of patients after neoadjuvant chemotherapy, the phenomenon of disappearing liver metastases (DLM). At laparotomy local residual disease is still found in 11–67% of patients, and microscopic residual disease was found on 80% of specimens. Conservatively managed DLM resulted in 19–74% local recurrence, mostly within two years. There was a good imaging and biochemical response at primary and metastasis sites in our patient, but the lesion at both sites was visible and regressed.

Cancer is regarded as a nihilism by society, and stage IV cancer is regarded as a nihilism by the medical community as well which is not true in some solid organ cancers like rectal cancer. With proper planning and counseling, we can treat a patient with a favorable outcome as in our patient.

We encourage early referral of this category of the patient to the comprehensive cancer hospital for favorable outcomes.

CONCLUSIONS

Stage IV rectal carcinoma can be managed with a favorable outcome by multimodality therapy and proper planning.

DECLARATIONS

Ethics approval and consent to participate

Approval for publications was obtained from the department and hospital administration. Consent was taken from the patient and his son.

Competing of Interest

The author(s) declare no competing interest in this study.

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