Complete Radiologic and Metabolic Response of Colorectal Liver Metastasis After Neoadjuvant Chemotherapy: To Resect or Not?

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Abstract Resection of liver metastasis has led to improved survival in selected patients with colorectal cancer. Neoadjuvant chemotherapy in this setting has many advantages. Positron emission tomography scan (PET) is useful in monitoring the response of the liver metastases to chemotherapy. Neoadjuvant chemotherapy can cause a complete response of the liver metastasis in some patients. We report a complete radiological and metabolic response of a liver metastasis following neoadjuvant chemotherapy and discuss the therapeutic implications and options in such a situation.

Keywords Colorectal liver metastasis · Neoadjuvant chemotherapy · Complete response · PET-CT

Introduction

Surgical resection of colorectal liver metastases offers a potential for cure, with 5-year survival rates of 24–58 % in selected patients [1]. However, only 10–25 % of liver metastases are resectable [2]. Advances in systemic therapies have enabled downsizing the colorectal liver metastases and bring them within the purview of surgery. Fluoro deoxy glucose-positron emission tomography (FDG-PET) scan is useful in staging recurrent disease and in assessing the response to neoadjuvant chemotherapy. We report a case of complete radiological and metabolic response of the liver metastases after neoadjuvant chemotherapy and discuss the therapeutic implications.

Case Report

A 66 year old gentleman was diagnosed with adenocarcinoma of sigmoid colon with a pre-operative serum CEA value of 7.7 ng/ml. He underwent anterior resection with en bloc resection of the tumour with an adherent segment of proximal ileum and a part of the anterior parietal wall. Post-operative histopathology was suggestive of adenocarcinoma grade 2, pT4aN0 (stage IIb). After detailed discussion with the patient, he was kept under regular follow up. A routine surveillance CT scan done 14 months after surgery revealed a suspicious hypo dense lesion in segment 8 of the liver with a normal serum CEA value (1.65 ng/ml). FDG PET-CT revealed two lesions, one each in segment 5 and 8 of the liver, with largest measuring 3×2.6 cm in segment 5 with a standard uptake value (SUV) of 8.5, with no evidence of extra-hepatic disease. He received neoadjuvant XELOX chemotherapy and PET-CT done after 2 cycles of chemotherapy revealed an 8.9 mm sized residual lesion in segment 5 with reduction in SUV to 5. There was a complete radiologic and metabolic response of the second metastasis in segment 8 (Fig. 1). The patient underwent a laparotomy. Intra-operative ultrasound revealed a residual lesion 1.5×1.5 cm in segment 5 & a small 5 mm size non-homogeneous area with micro calcification in segment 8. He underwent anatomical resection of segment 5. A non-anatomical resection of the abnormal area in segment 8 identified by ultrasound was performed although there was a complete metabolic and radiological response pre-operatively. Post-operative histopathology was suggestive of viable tumour (metastatic adenocarcinoma) measuring 0.8 cm & 1 cm in segment 8 and 5 respectively with resected margins being free of tumour.

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Fig. 1 *Top row:* CT and PET-CT images showing metastasis in segment 8 of the liver before chemotherapy; *Bottom row:* CT and PET-CT of the same patient after chemotherapy showing complete radiological and metabolic response of the segment 8 lesion

Discussion

In patients with liver metastasis from colorectal cancer, chemotherapy with 5 Fluoro-uracil in combination with either oxaliplatin or irinotecan can result in up to 50 % tumor response rates [3], and can result in resection of 7–40 % of initially unresectable liver metastases. Complete radiologic response (defined as complete disappearance of the target lesion on imaging) of the liver metastasis following chemotherapy can occur in 5 to 38 % of patients depending on the type and duration of chemotherapy and the imaging modality used to assess response [4, 5].

A complete response on imaging does not always correlate to a complete pathological response. During surgery, a residual tumor has been reported to be detected in 11–45 % of patients in whom pre-operative imaging showed disappearance of the liver metastasis [4, 5]. Microscopic residual disease has been found in these sites in 25–65 % of patients following resection [4, 5].

Although complete metabolic response in the liver metastasis can occur in up to 75 % of patients receiving neoadjuvant chemotherapy on follow-up PET scans [6], persistent microscopic or macroscopic residual disease or early recurrence in-situ can have been observed in up to 83 % of these lesions [7]. While the sensitivity of FDG PET-CT scan in detecting colorectal liver metastases is 93.3 %, it comes down to 49 % after neoadjuvant chemotherapy [8].

Decrease in size of the metastasis in response to neoadjuvant chemotherapy is one of the explanations for this reduced sensitivity. PET scan has a limited spatial resolution and lesions less than 1 cm are often not picked up. Another possible reason can be the altered cellular metabolism in response to chemotherapy. Chemotherapeutic agents can decrease the activity of glycolytic enzyme hexokinase causing altered tumour glucose metabolism, resulting in reduced FDG uptake [9]. Lastly, there may be heterogeneous uptake of FDG by tumour following chemotherapy –there may be central necrosis & only a thin peripheral rim which may be FDG avid causing underestimation of FDG uptake [10].

A meta-analysis of various imaging modalities showed that the pooled sensitivity of MRI in detecting liver metastasis after neoadjuvant chemotherapy was 85.7 %, compared to 69.9 % with a CT scan and 51.7 % with a PET-CT scan [11]. It has been suggested that patients with a disappearing liver metastasis on CT should undergo an MRI scan [4, 11].

In-situ recurrence of liver metastasis has been reported to occur in 38–74 % of patients if the site of a disappearing liver metastasis following neoadjuvant chemotherapy was not resected [4]. In one series, the 3-year intrahepatic recurrence-free survival rates were significantly lower for patients with untreated disappearing liver metastasis when compared to those patients in whom all initial disease was treated (16 % vs 35 %, $p=0.04$) [12]. However, this may not impact the overall survival [5].

The multi-disciplinary consensus statement of the European Society of Medical Oncology on colorectal cancer recommends that resection of liver metastasis after a course of neoadjuvant chemotherapy should ideally be performed before complete disappearance of the metastasis. This requires close monitoring with imaging and a multi-disciplinary discussion [13]. In case of complete disappearance of the metastasis, if an anatomical resection can be performed, it should be carried out based on the initial site of the metastasis. If the initial site of the metastasis precludes an anatomical resection, then other options suggested include more systemic therapy, hepatic artery infusion therapy or delaying the resection until relapse occurs [13]. Some authors have suggested a chemotherapy break to determine if the complete response is a durable one [5].

Conclusion

A complete radiological or metabolic response of a liver metastasis following neoadjuvant chemotherapy does not necessarily mean a complete pathological response. Such patients should be closely monitored by a multi-disciplinary team. In case of a complete radiological response, it is advisable to resect the site of the original metastasis if technically feasible since it may harbour residual disease.

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