Hepatic Malignancies and FDG PET/CT

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Contents

Malignancies of the liver can be primary which include hepatocellular cancers (HCC) predominantly in adults and hepatoblastomas seen in children or secondaries—commonest from colorectal primary.

This article shall discuss the utility of FDG PET/CT in management of primary hepatic tumors and metastatic disease from colorectal malignancies.

6.1 Hepatocellular Carcinoma

Hepatocellular carcinoma is a disease which frequently occurs in the patients with chronic liver disease – secondary to injury caused by either hepatitis or alcoholic intake.

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6.1.1 Staging

The outcome of these tumors depends on the stage of the disease at presentation; larger tumors and metastatic disease have poorer outcomes. Staging of HCC is generally done using a triple-phase contrast-enhanced computed tomography (CT) scan or magnetic resonance imaging (MRI) of the abdominal region for local evaluation, and metastatic work-up includes bone scan and a CT chest.

Fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT) extrapolates the Warburg effect, increasing glucose utilization by malignant tissue which is identified by overexpression of GLUT receptor on tumor sites. However, HCC cells show varied glucose receptor expression and hence the uptake of fluorodeoxyglucose (FDG) is variable [1–3].

The sensitivity of FDG PET or PET/CT for identifying primary HCC ranges from 50 to 65% as seen in various studies [2, 4, 5] (Figs. 6.1 and 6.2).

HCC with metastases have a poor prognosis with limited treatment options, while locally advanced HCC in the absence of extrahepatic spread could be offered aggressive local therapies; thus, accurate staging helps triage patients. FDG PET has been useful in the detection of distant metastases of HCC and fares better than conventional imaging modalities for detection of bony involvement while showing similar detection rates for lung and nodal disease [6, 7] (Fig. 6.3).

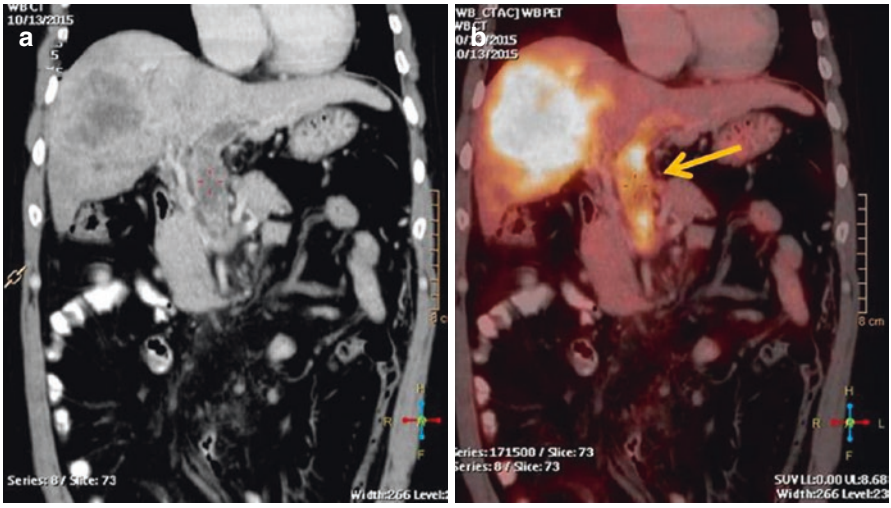

Fig. 6.1 Patient with HCC involving the right lobe of the liver as seen by the irregular hypodense lesion on the coronal section of CECT images (**a**) involving seg IV/VIII/VII and V and presence of right portal vein (PV) thrombosis, extending to MPV and SMV. FDG PET/CT done for staging shows intense FDG uptake in the primary mass (**b**) involving the lesion in right lobe of the liver with linear uptake (*arrow*) correlating with the tumor thrombus in the portal vein

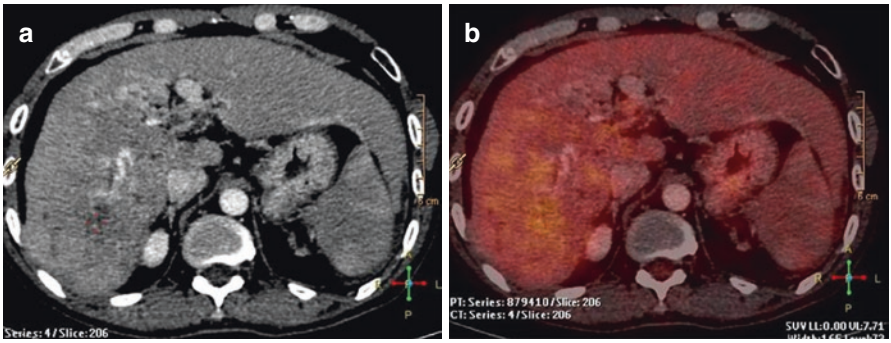

Fig. 6.2 12 × 9 × 9 cm mass in the right lobe of the liver with thrombosis of the right and main portal vein as seen on the transaxial CECT images (**a**). The correlative transaxial images of the FDG PET/CT study show no significant FDG uptake in the liver lesion (**b**) suggestive of a tumor with good biology

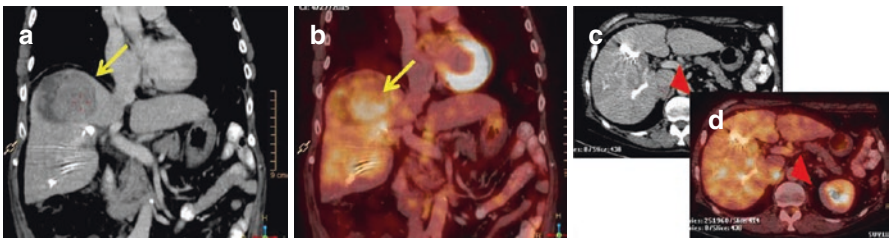

Fig. 6.3 A case of intermediate HCC involving the right lobe of the liver treated with TACE and planned for TARE. FDG PET/CT images show FDG uptake in the residual disease within the large heterogeneous lesion in the right lobe of the liver (*arrow* in **a**, **b**). Also noted is the FDG uptake in the metastatic nodule in the right adrenal gland on the transaxial and coronal-fused PET/CT images (*arrow head* in **c**, **d**)

A systemic review and meta-analysis evaluating FDG PET or PET/CT in extrahepatic metastases and recurrent disease included eight studies and showed pooled estimates of sensitivity, specificity, positive likelihood ratio, and negative likelihood ratio of FDG PET (PET/CT) in the detection of extrahepatic metastases at 76.6% (95% CI, 68.7–83.3%), 98.0% (95% CI, 92.8–99.8%), 14.68 (95% CI, 5.5–39.14), and 0.28 (95% CI, 0.20–0.40), respectively [8].

Few studies which tried to evaluate its role as a biologic marker identified that tumors with a higher density of glucose receptors tend to be aggressive; hence, tumors which show greater FDG uptake could represent a disease with a bad biology [3, 9].

Tumors with no FDG uptake have better outcomes [10], while among FDG-avid tumors, those with higher FDG uptake show poor outcomes as compared with tumors with lower FDG concentrations. Tumors with a greater FDG concentration also tend to show a shorter doubling time and present with higher stage of disease [11–13].

6.1.2 Treatment Response Assessment

Local targeted treatment (LRT) for HCC exploits the pathophysiology of dual blood supply of hepatic tumors. It blocks the predominant arterial blood supply leading to reduction in blood flow and cell death via either ischemia, thermal/coagulation, or radiation effect which do not result in tumor shrinkage [14, 15], but show necrosis and reduction in the enhancement pattern which are not accounted in RECIST 1 or RECIST 1.1 criteria. The newer guidelines have incorporated the enhancement criteria (mRECIST) and necrotic parameters in the response assessment of HCC [16–18].

Identifying enhancement features could be difficult due to benign posttreatment inflammatory changes, or a heterogeneous nature of the tumor environment and functional imaging like diffusion-weighted magnetic resonance (DWMRI) or FDG PET/CT is recommended.

Response assessment with FDG PET/CT is done either by visual assessment of the tumor site in the pre- and post-therapy scans in comparison with blood pool uptakes or by calculating the reduction of FDG uptake at the tumor site using various semiquantitative or quantitative methods, e.g., ratio of tumor SUV to the liver or mediastinum or SUV max. Studies show better survival and event-free rates in patients who depict significant reduction in the uptakes at the tumor site [19, 20]. When compared to conventional imaging methods like CECT, FDG PET/CT showed a higher sensitivity in identifying residual viable tissue which is generally seen as a focal eccentric uptake in the periphery [21, 22] (Fig. 6.4).

In a bid to standardize the response assessment of solid tumors using FDG PET/CT, the PERCIST criteria was suggested by Wahl et al., which is adapted from the anatomical-based RECIST 1.1 principle and measures the FDG standard uptake (lean) in up to five index lesions (up to two lesions per organ) with highest FDG uptake. The response is expressed as percentage change in peak standard uptake of sum of lesions of baseline and posttreatment scans [23] (Table 6.1).

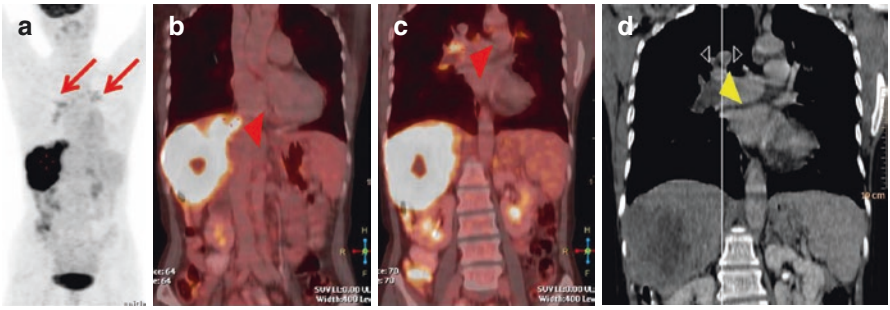

Fig. 6.4 Case of HCC involving the right lobe of the liver with portal thrombosis, patient was planned for trans arterial radioembolization and hence referred for a staging FDG PET/CT study. Intense FDG uptake was seen in the tumor involving a large part of the right lobe with uptake also seen in the portal vein thrombosis as seen on the MIP (**a**) and the coronal fused images (*arrow head* in **b**). Increased uptake is seen in the thoracic region bilaterally on the MIP image (*arrows* in **a**) which corresponds to filling defect seen in the pulmonary vein in the coronal-fused images (*arrow head* in **c**). The CECT of the thoracic region in the coronal image confirms the presence of bilateral pulmonary thrombosis (*arrow head* in **d**)

Table 6.1 Criterias for assesment of treatment response to conventional and targeted therapies (adapted from [24])

	RECIST 1.1	WHO	EASL	mRECIST	PERCIST
Complete response (CR)	Disappearance of all TL (up to 2 liver lesions)	Disappearance of all TL	Disappearance of all VL	Disappearance of all VL (up to 2 measurable liver lesions)	Disappearance of FDG uptake in the target lesions
Partial response (PR)	≥30% reduction in sum of greatest dimensional diameter of TL (compared to the baseline sum of diameter of TL)	≥50% reduction in the sum of products of bidimensional diameter of TL (as compared to the baseline sum of diameters)	≥50% reduction in the sum of products of bidimensional diameter of VL (as compared to the baseline sum of diameters)	≥30% reduction in sum of greatest dimensional diameter of VL (compared to the baseline sum of diameters)	Minimum reduction of 30% of SUV (lean) in measurable target lesion
Progressive disease (PD)	≥20% increase in the sum of diameter of TL (compared to the smallest sum of diameter of TL recorded since treatment started)	≥25% increase in the sum of diameter of TL (compared to the smallest sum of diameter of TL recorded since treatment started)	≥25% increase in the sum of diameter of VL (compared to the smallest sum of diameter of VL recorded since treatment started)	≥20% increase in the sum of diameter of VL (compared to the smallest sum of diameter of VL recorded since treatment started)	Increase of >30% of SUV (lean) or a new lesion identified on
Stable disease	Any case that do not qualify for PR or PD	Any case that do not qualify for PR or PD	Any case that do not qualify for PR or PD	Any case that do not qualify for PR or PD	Any case that do not qualify for PMR or PMD

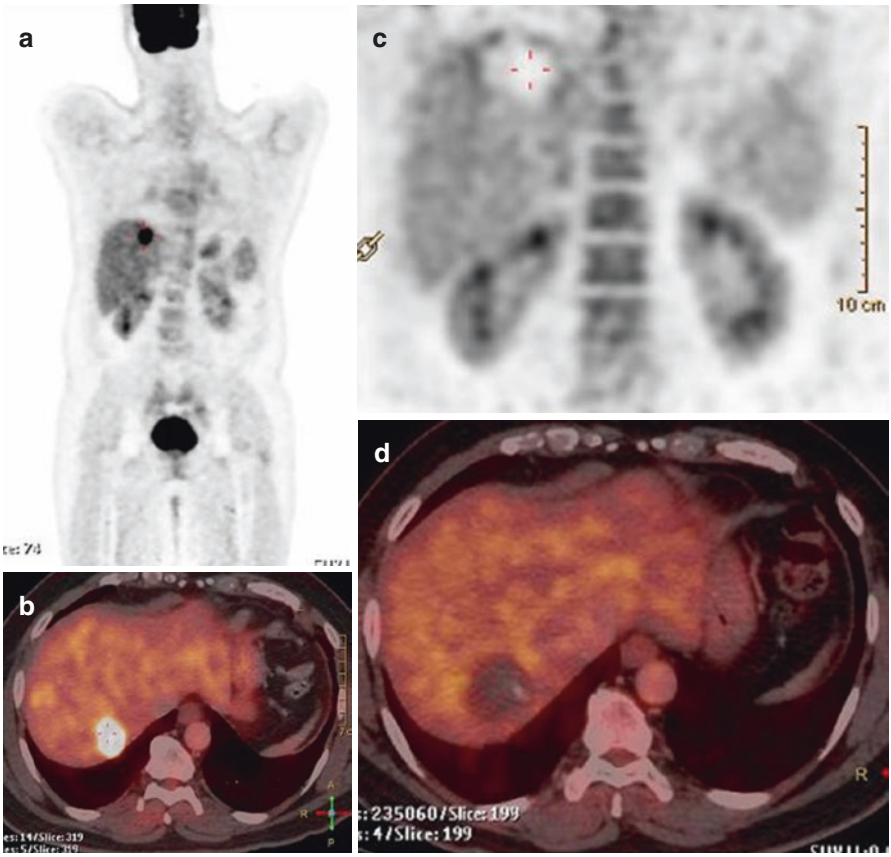

Fig. 6.5 Hepatic metastasis in a case of colon carcinoma, FDG PET/CT study done for restaging revealed a solitary liver lesion as seen in the whole body maximum intensity projection (MIP) (**a**) and well appreciated on the fused transaxial image (**b**). Post RFA FDG PET/CT study shows a photopenic area on the coronal PET image (**c**) which corresponds to the site of lesion with no uptake within or in the periphery as seen in the fused image (**d**) depicting completeness of the procedure

The ideal time to assess response would be at 3 months post therapy allowing for posttreatment-related changes to settle which could cause false-positive or equivocal readings.

Radiofrequency ablation is a localized treatment option for smaller tumors and those away from vessels. FDG PET/CT for this indication should be performed prior to initiation of inflammatory changes, i.e., within 6–12 h of procedure to avoid masking of the residual disease seen as a focal uptake in the periphery [25] (Fig. 6.5).

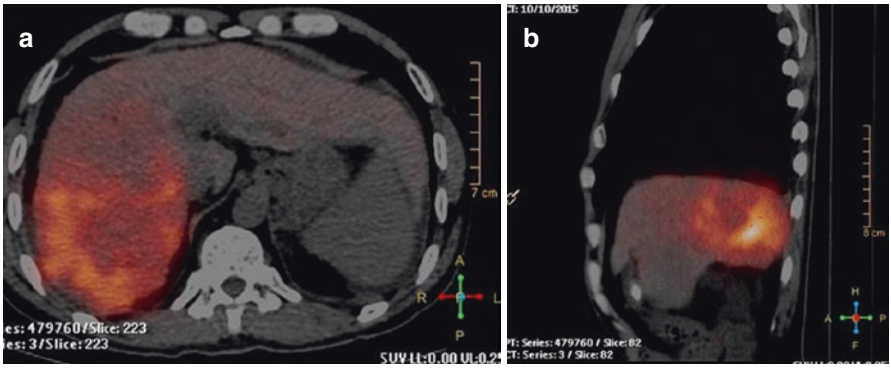

Fig. 6.6 Images acquired 3 h post 90 Yttrium therapy of patient in (**b**) reveal uptake at the primary tumor site in the right lobe—confirming delivery of the radiotracer into the hepatic lesion (**a**, transaxial and **b**, sagittal) and no tracer seen in rest of the liver parenchyma or elsewhere in abdomen—ruling out extravasation or leak of radiotracer

6.1.3 Utility of PET/CT in Evaluating Radioembolization of HCC

Post therapy scans in patients treated with 90 Yttrium tracers are evaluated with a bremsstrahlung imaging using the SPECT/CT scanner. Positron emissions from the Y90 radioisotope have been utilized to obtain an immediate post therapy PET/CT study. The advantage of this modality is the clear demarcation of region of radioisotope delivery and dosimetry to calculate actual dose delivered (Fig. 6.6). The presence of small extravasation of tracer into stomach or elsewhere is also identified which could have been missed on a pretreatment shunt evaluation dummy scan with colloids [26–28].

The posttreatment scan allows calculation of dose delivered to tumor which is a predictor of tumor response [29, 30] and to the normal liver which will help in identifying the dose leading to hepatic dysfunction.

6.1.4 Disease Recurrence

Early identification of local disease recurrence can be offered salvage treatment, and hence it is useful to identify extent of disease spread at restaging. FDG PET/CT has shown to be a helpful mechanism to identify sites of local or distant recurrence when a clinical suspicion is raised. FDG PET/CT showed an incremental value in patients with elevated tumor marker and negative imaging on CIMs and also better specificity and accuracy [31, 32] (Fig. 6.7).

A meta-analysis of eight studies discussed earlier showed a pooled estimate of sensitivity, specificity, and LR+ and LR− of FDG PET (PET/CT) in the detection of recurrent HCC to be 81.7% (95% CI, 71.6–89.4%), 88.9% (95% CI, 70.8–97.6%), 4.72 (95% CI, 2.21–10.07), and 0.19 (95% CI, 0.10–0.35), respectively [8].

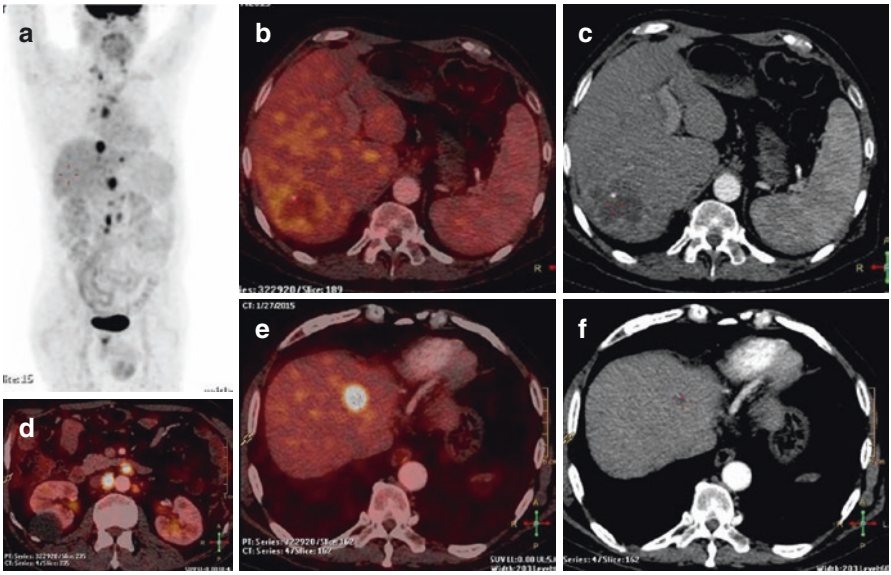

Fig. 6.7 Case of intermediate HCC treated with TACE had clinical suspicion of recurrence in view of elevated tumor marker. FDG PET/CT revealed absence of uptake in the primary site (**b**—CECT and **c**), focal FDG uptake seen in two lesions in the liver (**e**, **f**) and retroperitoneal nodes (**d**) and mediastinal and supraclavicular (**a**, *arrow*) metastatic nodal disease

6.2 Hepatoblastomas

Hepatoblastomas are glycogen-rich tumors and hence would have a high glucose receptor density leading to increased FDG uptake making it a suitable agent for staging these tumors; however, no significant literature is available pertaining to this [33]. Few studies which evaluated its role in restaging hepatoblastomas have found it to be a very specific test [34] and suggest an incremental value over conventional imaging (CT and MRI) in early recurrences [35] (Fig. 6.8).

Conclusion

Available literature suggests FDG PET/CT to be a prognostic factor while staging HCC and a good modality for assessing response to local therapies in intermediate HCC. There is not enough evidence to predict the role in hepatoblastomas.

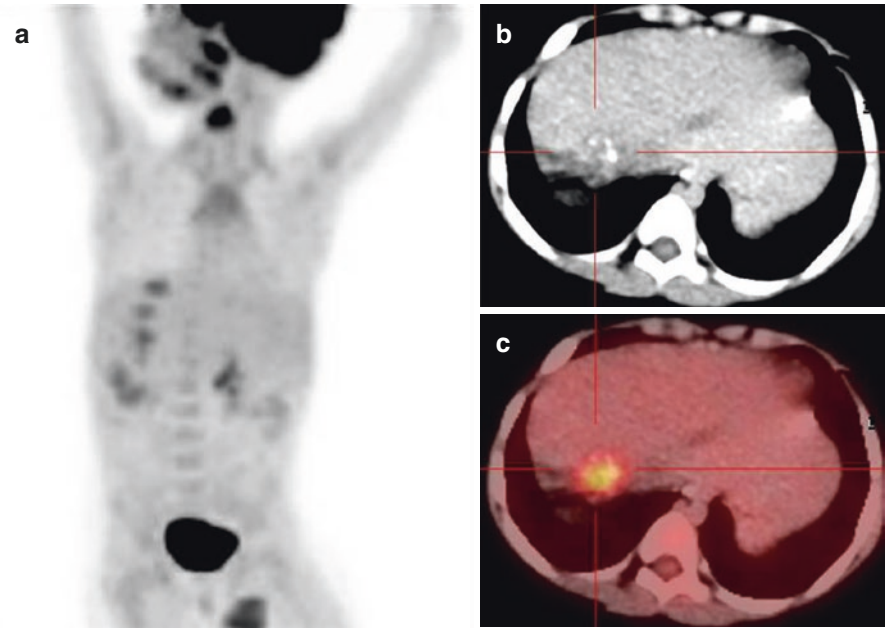

Fig. 6.8 Case of hepatoblastoma treated with chemotherapy followed by surgery and maintenance chemotherapy. On follow-up presented with elevated AFP level. Contrast CT scan did not reveal significant abnormality at the postoperative site or distant regions, a FDG PET/CT done revealed increased FDG uptake at the postoperative margins as seen on the MIP images (**a**) and on the fused transaxial PET/CT image (**c**) though no abnormality was seen on the correlative CT image (**b**). USG-guided biopsy confirmed recurrence on the diaphragmatic surface of the peritoneum overlying the liver

Key Points

- The sensitivity of FDG PET or PET/CT for identifying primary HCC ranges from 50 to 65% as seen in various studies.
- FDG PET has been useful in the detection of distant metastases of HCC.
- Tumors with no FDG uptake have better outcomes, while among FDG-avid tumors, those with higher FDG uptake show poor outcomes.
- FDG PET/CT showed a higher sensitivity in identifying residual viable tissue which is generally seen as a focal eccentric uptake in the periphery.
- The ideal time to assess response would be at 3 months post therapy allowing for posttreatment-related changes to settle which could cause false-positive or equivocal readings.
- FDG PET/CT is useful to identify sites of local or distant recurrence.
- FDG PET/CT showed an incremental value in patients with elevated tumor marker and negative imaging.

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