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FDG-Avid Focal Liver Reaction from Proton Therapy in a Patient with Primary Esophageal Adenocarcinoma

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Abstract

25-year-old man with IgA deficiency treated with two months of chemotherapy and proton therapy for gastroesophageal junction adenocarcinoma. Restaging PET/CT 18 days post-therapy demonstrated two new foci of increased FDG uptake in the left hepatic lobe, which were favored to represent radiation injury as opposed to new metastases. Follow-up MRI with contrast two weeks later demonstrated hypoenhancement and T1/T2 hypointensity in the liver, without restricted diffusion, which correlated with the dominant FDG-avid focus. The hepatic lesions resolved on subsequent FDG PET/CT and MRI studies, confirming the diagnosis of acute radiation injury.

Keywords

PET CT; proton therapy; external beam radiation; liver radiation injury; FDG; gastroesophageal adenocarcinoma; focal liver reaction

Focal liver parenchymal damage after proton beam radiotherapy, or focal liver reaction (FLR) presents a clinical and diagnostic challenge. Clinical response and complex benign liver changes may appear similar, particularly on CT (1–3). On CT, hyperdense halo and lack of enhancement may indicate response (4–6). Standard size and enhancement parameters can be unreliable in irradiated liver (7–10). FLR was described as early as 1965 with radiation hepatitis in patients with gynecological cancer treated with whole-abdomen external beam radiation (11). Few others have been documented, including a case identified on MRI and two others on PET (12, 13, 18–20).

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FLR has two phases: acute (< 3 mo) and chronic (> 3 – 6 mo). Histopathologic changes in the acute phase include sinusoidal congestion, hyperemia, and diffuse fatty infiltration corresponding to radiological hypodensity (13). Chronic phase changes include marked hepatocellular regeneration and partial-to-complete resolution of imaging abnormalities. Portal tract fibrosis and structural disorganization appearing as a non-segmental bandlike lesion are also characteristic (6, 13, 15–17). Several postulated hypotheses include venous occlusion, tissue congestion, progressive fibrin deposition, and hemosiderin-laden macrophage accumulation (12). The findings in this report follow the normal pattern of hepatocellular regeneration in liver parenchyma during the chronic phase (13).

References

1. Sanuki-Fujimoto N, Takeda A, Ohashi T, et al. CT evaluations of focal liver reactions following stereotactic body radiotherapy for small hepatocellular carcinoma with cirrhosis: relationship between imaging appearance and baseline liver function. *Brit J Radiol*. 2010; 83:1063–1071. [PubMed: 21088090]
2. Chiou SY, Lee RC, Chi KH, et al. The triple-phase CT image appearance of post-irradiated livers. *Acta Radiol*. 2001; 42:526–531. [PubMed: 11552892]
3. Park MJ, Kim SY, Yoon SM, et al. Stereotactic body radiotherapy-induced arterial hypervascularity of non-tumorous hepatic parenchyma in patients with hepatocellular carcinoma: potential pitfalls in tumor response evaluation on multiphase computed tomography. *PloS One*. 2014; 9:e90327. [PubMed: 24587326]
4. Brook OR, Thornton E, Mendiratta-Lala M, et al. CT imaging findings after stereotactic radiotherapy for liver tumors. *Gastroent Res Prac*. 2015; 2015
5. Price TR, Perkins SM, Sandrasegaran K, et al. Evaluation of response after stereotactic body radiotherapy for hepatocellular carcinoma. *Cancer*. 2012; 118:3191–3198. [PubMed: 22025126]
6. Herfarth KK, Hof H, Bahner ML, et al. Assessment of focal liver reaction by multiphasic CT after stereotactic single-dose radiotherapy of liver tumors. *Int J Radiat Oncol*. 2003; 57:444–451.
7. Forner A, Ayuso C, Varela M, et al. Evaluation of tumor response after locoregional therapies in hepatocellular carcinoma. *Cancer*. 2009; 115:616–623. [PubMed: 19117042]
8. Sharma MR, Maitland ML, Ratain MJ. RECIST: no longer the sharpest tool in the oncology clinical trials toolbox—point. *Cancer Res*. 2012; 72:5145–5149. [PubMed: 22952219]
9. Lock M, Malayeri AA, Mian OY, et al. Computed tomography imaging assessment of postexternal beam radiation changes of the liver. *Future Oncol*. 2016; 12:2729–2739. [PubMed: 27576360]
10. Ingold JA, Reed GB, Kaplan HS, et al. Radiation hepatitis. *Am J Roentgenol*. 1965; 93:200–208.
11. Takamatsu S, Yamamoto K, Maeda Y, et al. Evaluation of Focal Liver Reaction after Proton Beam Therapy for Hepatocellular Carcinoma Examined Using Gd-EOB-DTPA Enhanced Hepatic Magnetic Resonance Imaging. *PloS One*. 2016; 11:e0167155. [PubMed: 27907063]
12. Maturen KE, Feng MU, Wasnik AP, et al. Imaging effects of radiation therapy in the abdomen and pelvis: evaluating “innocent bystander” tissues. *Radiographics*. 2013; 4(33):599–619.
13. Lewin, K., Millis, RR. Human radiation hepatitis. A morphologic study with emphasis on the late changes. Stanford Univ, CA; 1973 Jul 1.
14. Okumura T, Itai Y, Tsuji H, et al. Focused radiation hepatitis after Bragg-peak proton therapy for hepatocellular carcinoma: CT findings. *Journal Comput Assist Tomo*. 1994; 18:821–823.
15. Ahmadi T, Itai Y, Onaya H, et al. CT evaluation of hepatic injury following proton beam irradiation: appearance, enhancement, and 3D size reduction pattern. *Journal Comput Assist Tomo*. 1999; 23:655–663.
16. Cameron S, Schwartz A, Sultan S, Schaefer IM, Hermann R, Rave-Fränk M, Hess CF, Christiansen H, Ramadori G. Radiation-induced damage in different segments of the rat intestine after external beam irradiation of the liver. *Exp Molecular Pathol*. 2012; 92:243–258.

17. Yamasaki SA, Marn CS, Francis IR, et al. High-dose localized radiation therapy for treatment of hepatic malignant tumors: CT findings and their relation to radiation hepatitis. *AJR*. 1995; 165(1): 79–84. [PubMed: 7785638]
18. Iyer RB, Balachandran A, Bruzzi JF, et al. PET/CT and hepatic radiation injury in esophageal cancer patients. *Cancer Imaging*. 2007; 7:189–194. [PubMed: 18055293]
19. Wong JJ, Anthony MP, Lan Khong P. Hepatic radiation injury in distal esophageal carcinoma: a case report. *Clin Nucl Med*. 2012; 37:709–711. [PubMed: 22691523]
20. Nguyen D, Maheshwary R, Rajput A, et al. PET-CT Post–Hepatic Radiation Change in Gastroesophageal Adenocarcinoma. *Clin Nucl Med*. 2017; 42:e54–e55. [PubMed: 27749425]

FIGURE 1.

25-year-old man with history of IgA deficiency and biopsy-proven metastatic adenocarcinoma of the gastroesophageal junction treated with two months of neoadjuvant chemotherapy (weekly carboplatin plus paclitaxel) and proton therapy (5040 cGy in 180 cGy fractions to gross disease and 4500 cGy to at-risk lymph nodes). Treatment-related dysphagia, anorexia, and weight loss improved. Post-therapy restaging FDG PET/CT (**A–D**) performed 18 days after completion of proton therapy demonstrated two new foci of increased FDG avidity in the left hepatic lobe adjacent to the GE junction with maximum SUV of 11 (**B**, solid arrow) and 8 (**D**, empty arrow); no anatomic correlate was seen on noncontrast CT (**A**, **C**). This study also demonstrated FDG uptake in the patient's primary esophageal adenocarcinoma with maximum SUV of 7.3 (**B**, arrowhead), decreased from a maximum SUV of 8.5 on prior. The patient received additional chemotherapy (mFOLFOX), and follow-up FDG PET/CT (**E–H**) 8 months later demonstrated interval resolution of FDG-avid hepatic foci (**F**, **H**), consistent with hepatic radiation injury.

FIGURE 2.

Post-therapy abdominal MRI of GE adenocarcinoma. MRI images acquired one month after proton therapy (**A, B**) demonstrated a region of T1 hypointensity on pre-contrast images (**A**, solid arrow) without enhancement on post-contrast images (**B**, open arrow), which correlated with the dominant FDG-avid hepatic lesion (FIGURE 1B). T2-weighted images also demonstrated hypointensity without restricted diffusion on diffusion-weighted images. Findings resolved on follow-up MRI five months post-therapy (**C, D**) consistent with acute radiation injury.

FIGURE 3. Radiation dose distribution of proton therapy plan. Clinical target volume (orange) and planning target volume (yellow) are shown with color wash of radiation dose scaled from 1000 to 5400 cGy using two posteriorly oriented beams using double scattered proton therapy.