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# Role of Fluorine-18 Fluorodeoxyglucose Positron Emission Tomography in Detection of Portal Vein Tumor Thrombosis in Hepatocellular Carcinoma

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**ABSTRACT**

A 56 year old gentleman with no known comorbidities presented with pain abdomen for 1 month. Triphasic CECT abdomen showed features of cirrhosis with surface irregularities, fissural widening and volume redistribution changes in the liver. Segment VII of liver showed an arterial enhancing lesion measuring 4.2 x 3.5cm showing washout in delayed phase. In view of BCLC A stage with Child Pugh B7, ablation was planned. Before proceeding with ablation, in view of very high alpha-fetoprotein (AFP) level of 9836 ng/mL, he was advised for metastatic evaluation with 18F-FDG PET-CT. The PET scan showed abnormal heterogeneous increased FDG uptake in segment VII of liver (SUV Max 4.7) with arterial enhancement and washout suggestive of metabolically active hepatocellular carcinoma. Also seen was an abnormal linear increased FDG uptake in right branch of portal vein (SUV Max 4.8) which was suggestive of portal vein invasion. In view of portal vein tumor thrombus, ablation procedure was deferred for the patient. Role of PET scan in HCC with vascular invasion is not yet defined. Poor specificity of FDG PET is the major hindrance in establishing PET scan as diagnostic tool for vascular invasion. In small segment invasion when CECT is not able to differentiate between tumour versus bland thrombus PET scan may be significant tool to differentiate between bland thrombus and tumour thrombus. Vascular invasion confirmation have treatment related and prognostic significance. There is a need for a prospective study evaluating the prognostic significance of PET scan based diagnosis of vascular invasion.

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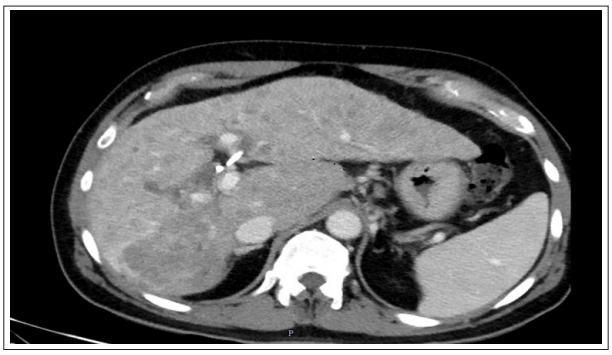
## Introduction

We report a case of hepatocellular carcinoma (HCC) diagnosed and staged as BCLC A on triphasic Contrast Enhanced Computed Tomography (CECT), with subsequently done Fluorine-18 Fluorodeoxyglucose Positron Emission Tomography (18F-FDG-PET) showing portal vein tumor thrombosis, thus upstaging to BCLC C.

## Case History

A 56 year old gentleman with no known comorbidities presented with pain abdomen for 1 month. Initial investigations revealed chronic liver disease, hepatitis (HBsAg positive) and elevated inflammatory markers. Triphasic CECT abdomen showed features of cirrhosis with surface irregularities, fissural widening and volume redistribution changes in the liver. Segment VII of liver showed an arterial enhancing lesion measuring 4.2 x 3.5cm showing washout in delayed phase. Multiple tiny hypodense nodules were also seen scattered in both lobes of liver, likely to represent regenerative nodules. There was no portal vein thrombosis Figure 1. In view of elevated inflammatory markers, was started on broad spectrum antibiotics and tenofovir, the patient developed severe abdominal pain with vomiting. Repeat triphasic CECT abdomen done showed features of pancreatitis with biliary sludge, and no portal vein thrombosis. He underwent stenting of bile duct, with improvement in liver function and performance status. In view of BCLC A stage with Child Pugh B7, ablation was planned. Before proceeding with ablation, in view of very high alpha-fetoprotein (AFP) level of 9836 ng/mL, he was advised for metastatic evaluation with 18F-FDG PET-CT. The PET scan showed abnormal heterogeneous increased FDG uptake in segment VII of liver (SUV Max 4.7) with arterial enhancement and washout suggestive of metabolically active hepatocellular carcinoma. Also seen was an abnormal linear increased FDG uptake in right branch of portal vein (SUV Max 4.8) which was suggestive of portal vein invasion Figure 2. There was no abnormal increased FDG uptake in multiple hypodense liver nodules scattered in both lobes suggestive of dysplastic nodules. No nodal or distant metastasis were identified. In view of portal vein tumor thrombus, ablation procedure was deferred for the patient.



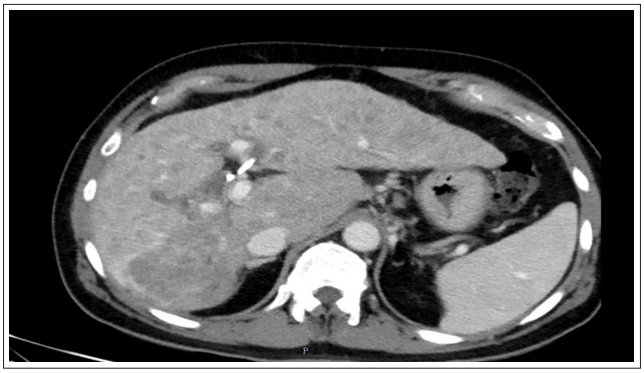


**Figure 1:** Triple Phase CT Scan with Contrast (arterial phase) not Showing the Portal Vein Invasion

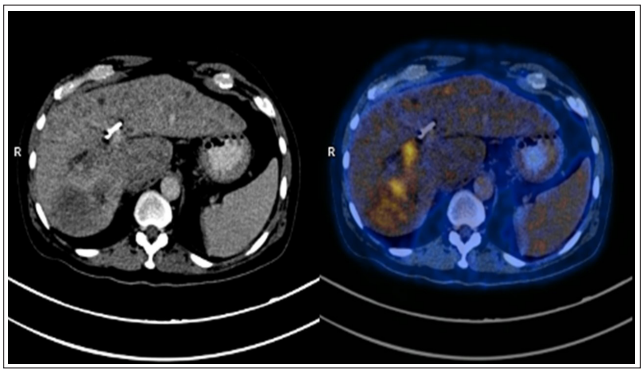


**Figure 2a:** FDG PET Scan Showing Avidity (SUV max 4.8) in the Right Branch of Portal Vein (Axial)

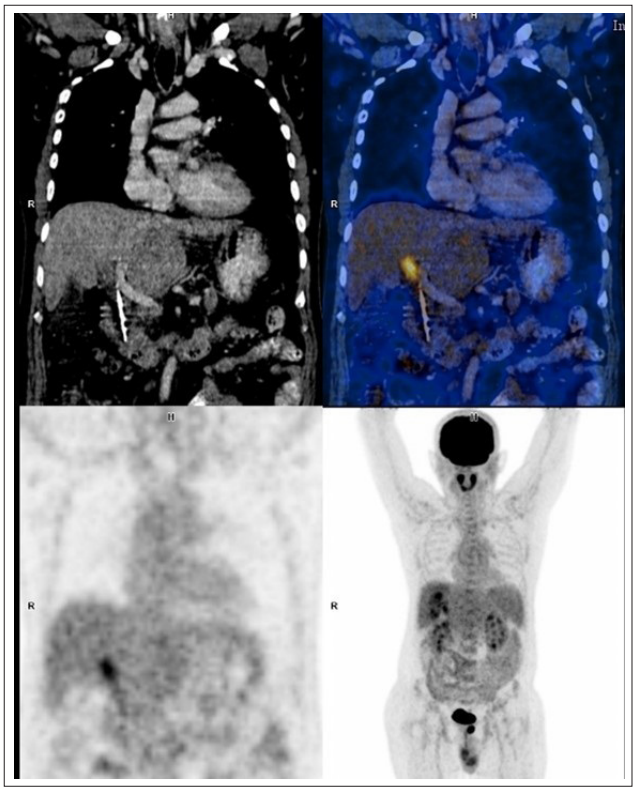


**Figure 2b:** FDG PET Scan Showing Avidity (SUV max 4.8) in the Right Branch of Portal Vein (Coronal)

## Discussion

Hepatocellular carcinoma is one of the challenging cancer for treatment. Early cases have excellent survival, but a large proportion of patient presents with vascular invasion or poor liver function and these patients have poor survival function. The crude incidence rate of liver cancer in the world in 2020 was 11.6 per 100000 population [1]. It is ranked as third among cancer deaths in the world. HCC is the most common primary cancer in liver and the most common causes include Hepatitis B and C virus infection and alcohol use [2]. However, in recent years non-alcoholic steatosis (NASH) induced hepatocellular carcinoma is on the rise. Outcome after treatment varies with associated co-morbidies, vascular invasion, extent of lesion and liver function. In early stage, median survival is about 60 months with resection or ablation. Single lesion with preserved liver function is best treated with resection. Patients with underlying liver dysfunction who are otherwise good candidates for resection as per Milan criteria (single lesion ≤ 5cm or upto three nodules ≤ 3cm) benefit from liver transplantation. Situations where surgery can get delayed, ablation or transarterial chemoembolization (TACE) can used to bridge the gap [3,4]. In intermediate stage, TACE can improve survival by few months (median survival is 20 months compared to 16 months without treatment). Targeted therapies such as sorafenib, lenvatinib or regorafenib increase survival in advanced HCC with a median survival of 11 months [4,5].

### HCC with Vascular Invasion

Early stage suitable for surgery, ablation or transplant are associated with good 5 year survival of 40 – 70% [6]. Advanced HCC associated with chronic liver disease is usually symptomatic and is associated with a 5 year survival of 0 – 10 % [6]. Vascular invasion (portal vein tumor thrombus) in HCC is a poor prognostic factor, hence in case of vascular invasion recommended guidelines suggest only palliative treatment and liver transplantation is contraindicated [4]. In clinical practice vascular invasion is observed in about one third cases (35-50%). Hence, vascular invasion in HCC presents with a pertinent clinical dilemma. In these patient cohort, median survival is usually between 2.7 and 4 months in absence of therapy, but a small proportion of patients survive up to 5 years or more, thus depicting an extremely variable scenario. The median time to radiologic progression in an advanced HCC including extrahepatic disease in 51% and PVTT in 38% treated with sorafenib in SHARP trial was 5.5 months with only 2% of patients achieving partial response [4]. In ASIA PACIFIC trial which included 34% PVT patients and 68% patients with extrahepatic disease the median survival was only 6.5 months [3,4]. Major reason of variable prognosis in portal vein thrombosis may be related with the appropriate diagnosis of vascular invasion.

### Diagnosing Vascular Invasion

Sensitivity and specificity of different diagnostic modalities are mentioned in table 1.

Diagnosis of portal vein invasion is done by 'filling' defect in portal vein in radiological evaluation. Triphasic CECT is considered the investigation of choice for diagnosis of HCC and is thus widely practised. EASL defined non-invasive diagnostic criteria of HCC based on imaging is presence of arterial hypervascular pattern in nodules > 2cm. The AASLD noninvasive criteria include arterial hypervascularization and subsequent contrast washout in portal and late phases after vascular contrast agent administration [7-9]. PVTT in Triphasic CECT appears as a 'filling defect' of the vessel and peripheral enhancement of wall of the vein. Arterial enhancement with rapid washout, neovascularity of thrombus or direct invasion by adjacent lesion can differentiate a portal vein tumor thrombus from a benign thrombus. The sensitivity of CECT in detecting portal vein thrombus is moderate with reported rates ranging from 70-87.5% (10). Differentiating tumour thrombus

from benign thrombus sometimes is a challenge. Irregular or 'patchy' contrast enhancement in portal vein thrombus suggests tumour thrombus. On the other hand, no or minimal enhancement of thrombus suggests 'bland' thrombus or benign thrombus. This issue is more pronounced when only a small region of portal vein or its tributaries are thrombosed. Hence, diagnosing early portal vein thrombus times is overlooked as bland thrombus and also in occasions small segment bland thrombus is considered as vascular invasion and treated with palliative intent. Appropriate diagnosis of portal vein invasion have significant therapeutic and prognostic implications.

CE MRI also may be used to characterise thrombus [11]. Partial patency in a thrombosed vessel can be confirmed by USG Doppler, with a flow pattern different from that of a intra-thrombus flow pattern [7-11]. Identifying the presence and extent of PVTT is important in deciding management plan. PVT may be benign or malignant [12,13]. Malignant PVT is considered a contraindication for TACE and transplant, whereas transplant can be considered in benign PVT. The Liver Cancer Study Group of Japan (LCSGJ) has classified PVTT into four grades, depending on distal to second order, second order, first order, and main trunk of portal vein or contralateral branch involvement [14]. The vessel could be completely or partially occluded by the thrombus, with a rim enhancement by either dilated vasa vasorum in case of complete occlusion or patent part of portal vein showing contrast enhancement.

**PET-CT in Portal Vein Tumor Thrombosis**

Biological imaging may help in differentiating early portal vein invasion from bland thrombus. However, hepatocytes are rapidly proliferating cells and these cells have huge glucose uptake. Hence, utility of FDG PET in differentiating HCC thrombus from active hepatocytes are a real concern. Biological imaging utilising the glucose metabolic activity of tumor cells is a confirmatory finding of PVTT [15,16]. Metabolic abnormalities may precede the morphologic changes observed using triphasic CECT. PET-CT has a positive predictive value of 91.7% [11]. PET CT can differentiate malignant from benign thrombus, with a SUVmax threshold of 3.35[15]. However, the specificity of FDG PET in diagnosing HCC with vascular invasion is quite low [16-18]. Choline PET have higher sensitivity and specificity compared to FDG PET in vascular invasion, though there is no prospective study confirming superiority of choline PET guided treatment in improving survival function in PVTT. Diagnostic abilities of various imaging modalities for portal vein thrombosis are summarised in Table 1.

**Table1: Sensitivity & specificity of different imaging modality in hepatocellular carcinoma**

| IMAGING MODALITY | SENSITIVITY | SPECIFICITY | REMARKS | REFERENCES |
|---|---|---|---|---|
| Ultrasound- colour Doppler | 20-93% | 92-99% | In ultrasound scan, thrombus is seen as hypo or isoechoic material occupying the lumen of a mildly dilated vein in acute PVT or hyperechoic material in chronic PVT after clot organization. The specificity of intra-thrombal pulsatile flow in Doppler for the diagnosis of malignant PVT is high if the character of this flow is clearly different from that of the hepatic artery and a patent segment of the PV. | 7-9 |
| Triphasic CECT | 70.5-87.5% | 95-100% | Triphasic CT findings of PVT are filling defect partially or totally occluding the vessel lumen and rim enhancement of the vessel wall. Neovascularity of thrombus, arterial enhancement with rapid washout, direct invasion by adjacent hepatic mass may be seen. | 10,14,15 |
| CE-MRI | 70-100% | 95- 98% | T2-weighted hyperintensity of the PVT and restricted diffusion within the PVT seen as an increased signal in diffusion weighted images and a decreased signal in apparent diffusion coefficient maps. | 10-12 |
| 18-FDG PET-CT | 91.5-93.6% | 64-80% | Increased activity associated with thrombus in CT | 16-18 |

CECT: Contrast Enhanced Computed Tomography; CE-MRI: Contrast Enhanced Magnetic Resonance Imaging; 18-FDG PET-CT: 18-Fluoro Deoxy Glucose Positron Emission Tomography Computed Tomograph

In this patient, triple phase CT scan showed a 'non-contrast uptake filling defect' in right branch of portal vein. CT scan could not differentiate between bland thrombus and tumour thrombus. PET -CT scan showed tumor adjacent to the right branch of portal vein and presence of linear uptake into the vessel suggesting active disease in the portal vein and hence diagnosed as portal vein tumor thrombosis. Patient was treated with palliative intent and not considered for radical surgery (transplant). PET scan may be useful in these situation with small segment filling defect with small volume primary disease [16]. However, histopathological proof of portal vein thrombosis is not available for confirmation. Specificity of PET-CT in portal vein thrombosis is reportedly lesser compared to triphasic CECT [13]. However in equipoise scenarios, additional information from PET-CT could help in decision making regarding further treatment plan for such patients [17-18].

**Implication of Vascular Invasion on Treatment**

The variability in outcome in PVTT depends on extent of involvement, type of branch involved, partial or complete obstruction of vessel, extrahepatic spread, liver function status of patient, and response to treatment. EASL 2018 guidelines recommend sorafenib as standard practice in HCC with vascular invasion, and also consider resection in research setting for segmental or secondary order branch involvement [3]. Other options available include TARE and TACE in very selected patients [3,4]. Radiotherapeutic treatment of HCC with PVTT also could result in response and improved outcome. The median OS in PVTT responders was 13.8 months, compared with 6.3 months in PVTT non-responders in study by Im et al [5]. The median survival time in primary tumor responders was 15.0 months, which was longer than the 6.8 months in primary tumor non-responders. In recent years, with stereotactic radiosurgery (SBRT) targeting the portal

vein thrombus and adjacent tissue have shown to improve survival in responders. PET scan is also useful in response assessment and prognostication by identifying 'responders'.

In summary, role of PET scan in HCC with vascular invasion is not yet defined. Poor specificity of FDG PET is the major hindrance in establishing PET scan as diagnostic tool for vascular invasion. However, in small segment invasion when CECT is not able to differentiate between tumour versus bland thrombus PET scan may be significant tool to differentiate between bland thrombus and tumour thrombus. Choline PET may be more specific in diagnosing vascular invasion. Vascular invasion diagnosis have treatment related and prognostic significance. There is a need for a prospective study evaluating the prognostic significance of PET scan based diagnosis of vascular invasion.

**References**

1. Sung H, Ferlay J, Siegel RL, Mathieu Laversanne, Isabelle Soerjomataram et al. (2021) Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: a cancer journal for clinicians 71: 209-249
2. Akinyemiju T, Abera S, Ahmed M, Noore Alam, Mulubirhan Assefa Alemayohu et al. (2017) The burden of primary liver cancer and underlying etiologies from 1990 to 2015 at the global, regional, and national level: results from the global burden of disease study 2015. JAMA oncology 3:1683-1691.
3. Cerrito L, Annicchiarico BE, Iezzi R, Antonio Gasbarrini, Maurizio Pompili et al. (2019)Treatment of hepatocellular carcinoma in patients with portal vein tumor thrombosis: Beyond the known frontiers. World J Gastroenterol 25: 4360-4382
4. Cheng AL, Kang YK, Chen Z, Chao-Jung Tsao, ShukuiQin et al. (2009) Efficacy and safety of sorafenib in patients in the double-blind, placebo-controlled trial. Lancet Oncol 10:25-34
5. Im JH, Yoon SM, Park HC, Jong Hoon Kim, Jeong Il Yu et al. (2017) Radiotherapeutic strategies for hepatocellular carcinoma with portal vein tumour thrombosis in a hepatitis B endemic area. Liver Int 37: 90-100
6. Marrero JA, Kulik LM, Sirlin CB, Andrew X Zhu, Richard S Finn et al. (2018) Diagnosis, staging, and management of hepatocellular carcinoma: 2018 practice guidance by the American Association for the Study of Liver Diseases. Hepatology 68: 723-750
7. Tessler FN, Gehring BJ, Gomes AS et al. (1991) Diagnosis of portal vein thrombosis: value of color Doppler imaging. AJR. Am J Roentgenol 157: 293-296.
8. Sacerdoti D, Serianni G, Gaiani S, M Bolognesi, G Bombonato et al. (2007) Thrombosis of the portal venous system. J Ultrasound 10: 12-21
9. Ricci P, Cantisani V, Biancari F, F M Drud, M Coniglio et al. (2000) Contrast-enhanced color Doppler US in malignant portal vein thrombosis. Acta radiologica 41: 470-473
10. Bae JS, Lee JM, Yoon JH, Siwon Jang, Jin Wook Chung et al. (2020) How to best detect portal vein tumor thrombosis in patients with hepatocellular carcinoma meeting the Milan criteria: gadoxetic acid-enhanced MRI versus contrast-enhanced CT. Liver cancer 9: 293-307
11. Shah TU, Semelka RC, Voultsinos V, Jorge Elias, Ersan Altun et al. (2006) Accuracy of magnetic resonance imaging for preoperative detection of portal vein thrombosis in liver transplant candidates. Liver transpl 12: 1682-1688
12. Kim JH, Lee JM, Yoon JH, Dong Ho Lee, Kyung Bun Lee et al. (2016) Portal vein thrombosis in patients with hepatocellular carcinoma: diagnostic accuracy of gadoxetic acid–enhanced MR imaging. Radiology 279: 773-783
13. Teama AH, Elbarbary AA, Elhawary KE, Wafaa A.Abusekina et al. (2015) Color Doppler US and tri-phasic CT in differentiating benign from malignant portal vein thrombosis (PVT). The Egyptian Journal of Radiology and Nuclear Medicine 46: 847-857
14. Tarantino L, Francica G, Sordelli I, Esposito F, Giorgio A et al. (2006) Diagnosis of benign and malignant portal vein thrombosis in cirrhotic patients with hepatocellular carcinoma: color Doppler US, contrast-enhanced US, and fine-needle biopsy. Abdominal imaging 31: 537-544
15. Tublin ME, Dodd 3rd GD, Baron RL (1997) Benign and malignant portal vein thrombosis: differentiation by CT characteristics. AJR. American J Roentgenol 168:719-723
16. Nguyen XC, Nguyen DS, Ngo VT, Simone Maurea et al. (2015) FDG-Avid Portal Vein Tumor Thrombosis from Hepatocellular Carcinoma in Contrast-Enhanced FDG PET/CT. Asia Ocean J Nucl Med Biol 3: 10-17
17. Wu B, Zhang Y, Tan H (2019) Value of 18F-FDG PET/CT in the diagnosis of portal vein tumor thrombus in patients with hepatocellular carcinoma. Abdom Radiol (NY) 44: 2430-2435
18. Hu S, Zhang J, Cheng C (2014) The role of 18F-FDG PET/CT in differentiating malignant from benign portal vein thrombosis. Abdom Imaging 39:1221-1227.