

Hepatic adenoma mimicking a metastatic lesion on computed tomography-positron emission tomography scan

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Author contributions: Lim D and Lee SY wrote the manuscript and provided the images; Lim KH provided pathological expertise and the histological slide; Lee SY and Chan CY were involved in the management of the case and the critical review of the manuscript; all authors have read and approved the final manuscript.

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Received: April 2, 2013 Revised: May 15, 2013

Accepted: June 1, 2013

Published online: July 21, 2013

Abstract

Positron emission tomography (PET) using ^{18}F -fluorodeoxyglucose (^{18}F -FDG) is an imaging modality which reflects cellular glucose metabolism. Most malignant cells accumulate and trap ^{18}F -FDG, allowing the visualisation of increased uptake. It is hence widely used to differentiate malignant from benign lesions. "False positive" findings of hepatic lesions have been described in certain instances such as hepatic abscesses, but are rare in cases involving hepatocellular adenomas. To our knowledge, there have been only 7 reports in the English literature documenting PET-avid hepatocellular adenomas; 6 of the 7 reports were published in the last 3 years with the first report by Patel *et al.* We report the

case of a 44-year-old Chinese female patient with a history of cervical adenocarcinoma, referred for a hepatic lesion noted on a surveillance computed tomography (CT) scan. A subsequent CT-PET performed showed a hypermetabolic lesion (standardized uptake value 7.9) in segment IVb of the liver. After discussion at a multi-disciplinary hepato-pancreato-biliary conference, the consensus was that of a metastatic lesion from her previous cervical adenocarcinoma, and a resection of the hepatic lesion was performed. Histology revealed features consistent with a hepatocyte nuclear factor-1 α inactivated steatotic hepatocellular adenoma.

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Key words: Hepatic adenoma; Positron emission tomography; ^{18}F -fluorodeoxyglucose; Hepatocellular adenoma; Hepatocyte nuclear factor-1 α

Core tip: This case illustrates a unique example of a false-positive finding on the computed tomography-positron emission tomography (CT-PET) due to a hepatic adenoma mimicking a metastatic lesion in the liver. It serves to highlight that not all CT-PET findings are associated with malignancy. In equivocal cases where CT-PET findings are discordant with other imaging modalities and/or clinical/biochemical features, further evaluation with different imaging modalities or novel PET tracers may be considered. This is especially pertinent in this day and age, where the PET scan is widely used in clinical practise to differentiate benign from malignant lesions, as well as a modality in cancer surveillance and staging.

Lim D, Lee SY, Lim KH, Chan CY. Hepatic adenoma mimicking a metastatic lesion on computed tomography-positron emission tomography scan. *World J Gastroenterol* 2013; 19(27): 4432-4436 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v19/i27/4432.htm> DOI: <http://dx.doi.org/10.3748/wjg.v19.i27.4432>

INTRODUCTION

Positron emission tomography (PET) using ^{18}F -fluorodeoxyglucose (^{18}F -FDG) is an imaging modality which reflects cellular glucose metabolism. In most malignant cells, the relatively low level of glucose-6-phosphate leads to accumulation and trapping of ^{18}F -FDG intracellularly, which in turns results in its visualization. As such, the PET scan is widely used for differentiating benign from malignant lesions, as well as a modality in cancer surveillance and staging. With regards to lesions in the liver, computed tomography (CT)-PET imaging classically shows increased uptake for moderately/poorly-differentiated hepatocellular carcinoma (HCC) and extra hepatic metastatic disease^[1]. False-positive results have generally been described in hepatic abscesses, and false-negative results described in well-differentiated HCC^[2].

Hepatocellular adenoma (HCA), also known as hepatic adenoma, is a benign tumor of the liver and the second most common benign liver neoplasm after focal nodular hyperplasia^[3,4]. It occurs predominantly in women within their reproductive years with a male-to-female ratio of 1:8-10^[5,6]. The estimated incidence is about 1 per million in women who have never used oral contraceptives (OCP), up to a significantly higher incidence of 30-40/million in long-term OCP users^[3,4].

“False positive” findings in PET/CT are rare in HCA. To our knowledge, there have been only 7 reports in the English literature documenting PET-avid HCAs; 6 of the 7 reports were published in the last 3 years with the first report in 1997 by Patel *et al*^[7-13].

CASE REPORT

A 44-year-old female patient, with a history of International Federation of Gynecology and Obstetrics stage IB2 cervical adenocarcinoma was referred to our hepatopancreato-biliary (HPB) service for further management of a hepatic lesion noted on her surveillance CT scan (Figure 1). Her cervical adenocarcinoma was treated with a radical hysterectomy 6 mo prior to this presentation. The hepatic lesion measured 2.3 cm \times 1.8 cm and was located in segment IVb of the liver. A CT-PET was performed to further delineate the nature of the hepatic lesion and exclude extrahepatic metastases; the liver lesion appeared hypermetabolic with a standardized uptake value (SUV_{max}) of 7.9 (Figure 2). This was discussed at a multi-disciplinary HPB tumor conference and the consensus was that it was a solitary metastasis from the cervical adenocarcinoma without evidence of extrahepatic disease. In view of the patient's previous surgery and the need for a lymphadenectomy, a decision was made for open surgical resection of the liver lesion with a perihilar lymphadenectomy.

On presentation, the patient was asymptomatic and recovered well from her hysterectomy. Clinical examination was largely unremarkable. Laboratory results and tumor biomarkers were within normal ranges [liver function test, complete blood count, carcinoembryonic antigen,



Figure 1 Surveillance computed tomography scan showing hypodense lesion in segment IVb of liver. Cross-sectional image of the hypodense lesion in segment IVb of the liver (arrow).

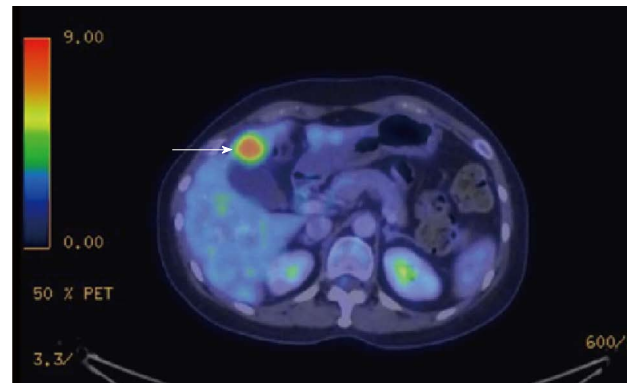


Figure 2 Computed tomography-positron emission tomography scan revealing the positron emission tomography avid lesion in segment IVb of the liver. Cross-sectional image of the positron emission tomography avid lesion in segment IVb of the liver (standardized uptake value 7.9) (arrow).

α -fetoprotein, carbohydrate antigen (CA) 19-9, CA125]. Her hepatitis B and C virology markers were negative. She had no family history of liver cancer or OCP usage.

After exploration to exclude any peritoneal metastases, an open resection of this segment IVb hepatic lesion, cholecystectomy and perihilar lymphadenectomy was performed. A 3 cm \times 2.5 cm segment IVb lesion was removed with clear margins. The patient recovered uneventfully.

Histology revealed a well demarcated lesion composed of bland uniform hepatocytes displaying clear vacuolated macrovesicular fat globules predominantly. No bile ducts, entrapped portal tracts or ectatic vessels were identified. No central scar was seen. Reticulin staining showed normal trabeculae without expanded thickened areas. Glypican-3 was negative. Overall features were consistent with a hepatocyte nuclear factor-1 α (HNF-1 α) steatotic adenoma (Figure 3). All lymph nodes excised were also negative for malignancy.

DISCUSSION

This case illustrates a unique example of a false-positive

finding on the CT-PET due to a HCA mimicking a metastatic lesion in the liver. Hepatic adenomas can be classified by their molecular phenotypes into four main groups: HNF-1 α inactivation, β -catenin activating, inflammatory and unclassified^[14,15]. The presence of the diffuse steatotic appearance and histological features in this case was consistent with a HNF-1 α inactivated HCA. Radiological features of HNF-1 α inactivated adenomas on Magnetic resonance imaging (MRI) include a diffuse signal dropout on T1-weighted chemical shift sequence, isosignal or slight hypersignal on T2-weighted images and moderate enhancement in the arterial phase, with no persistent enhancement in the portal venous and delayed phases. These appearances have been shown to have a high sensitivity and specificity for the diagnosis of steatotic adenomas^[16,17].

There is an increasing importance in the role of FDG-PET in the evaluation of liver lesions to distinguish between benign and malignant. Its uses also include the surveillance, staging and monitoring of therapy for patients with cancer e.g. colorectal cancer. However, some of the limitations of PET/CT in evaluation of liver lesions are emerging^[18,19]. The overall sensitivity of FDG PET/CT in detecting HCC is low with a reported range of 50%-65%, contributed mainly by the poor sensitivity in low-grade HCC^[20,21].

The liver can have an unpredictable ¹⁸F-FDG uptake^[19]. Glucose-6-phosphatase enzyme and glucose transporter activity have a wide variation in HCC. As a further confounder, the liver is the major producer of non-dietary glucose and a major regulator of glucose homeostasis. This limitation of PET/CT in HCC handicaps the usefulness of PET/CT in the evaluation of HCA, as one of the major concerns of HCA is its malignant potential and it harboring a foci of HCC within^[6].

This case highlights that not all “hot” hepatic lesions on the PET are associated with malignancy. Benign examples of high FDG activity in the liver include focal steatosis, hepatic adenomatosis (*e.g.*, inflammatory subtype) and infectious or inflammatory processes in the liver (*e.g.*, liver abscess, hepatic tuberculosis). These can consequently lead to “false-positive” PET results^[10,19,22,23]. Due to the limitations of CT/PET as an imaging modality, it is not possible to distinguish a PET-avid HCA from a liver abscess or a hepatic tuberculoma solely from its features on CT/PET. Other information is required to make such a distinction, such as clinical history and laboratory investigations. For example, patients with liver abscess may have signs and symptoms of infection such as fever/chills and pain; liver function test may be mildly abnormal with leukocytosis and inflammatory makers such as C-reactive protein and erythrocyte sedimentation rate may be elevated. Patients with HCA will not have such signs/symptoms of infection but may have a history of OCP usage and tend to be females in the reproductive age group. There is no evidence in the literature to suggest that CT/PET alone can distinguish PET-avid HCA from a liver abscess/tuberculoma.

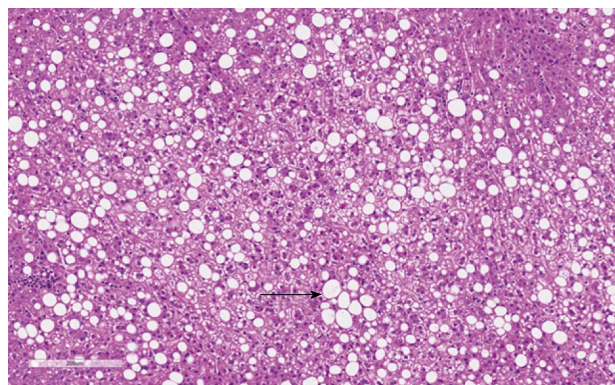


Figure 3 Representative histological slide of the hepatic adenoma. Medium power HE of the hepatic adenoma shows trabeculae with normal thickness composed of hepatocytes with moderate to severe steatotic changes (arrow) and bland uniform nuclei. No large cell or small cell change is identified. Notably, bile ducts, entrapped portal tracts or ectatic vessels were absent. There is a circumscribed border without a thick capsule (HE, $\times 200$).

Comparing our case to existing case reports of PET-avid HCAs in the literature, only 3 out of the 7 previous cases provided a detailed description of the histological findings^[7-13]. Similar to our case, these 3 cases showed predominantly fatty change^[8,9,11]. Of these 3 cases, only one report further classified the lesion as a HNF-1 α hepatic adenoma^[8].

Several hypotheses can explain the positive radiotracer uptake in such situations. In infections or inflammation, increased FDG uptake in lesions can be explained by the presence of inflammatory cells, which result in enhanced glucose metabolism or increased cell density^[24-26]. However, pathological examination of the HCA in our patient revealed no evidence of inflammation. Also, none of the reported PET-avid HCAs in the literature included any of the inflammatory HCA subtype.

Radiotracer activity can increase at an early stage of malignant transformation and present as a “hot” lesion; activated β -catenin HCA has a higher malignant potential and may harbor small foci of HCC. In both our patient and the cases in the literature, none of the PET-avid HCAs were activated β -catenin mutated.

Focal fatty infiltration of the liver has been reported to be PET-avid. As a response to fat accumulation, a subacute inflammatory hepatic reaction with infiltration of activated Kupffer cells occur, resulting in a higher SUV_{max} than adjacent normal liver parenchyma^[27,28]. Fat necrosis has been reported to have increased FDG uptake in benign lesions as well^[29]. In the literature, 3 cases reported prominent fatty change but there was no mention of any inflammatory infiltrate (including our case), perhaps the fatty change itself was sufficient to evoke a PET-avid response without significant histological evidence of inflammatory infiltrate.

Lastly, hypervascularity of a HCA can induce an accumulation of glucose by the relative local increased blood flow to the lesion without a sufficient “washout”. This hypothesis was suggested for HCA without any

evidence of inflammation, fatty content or malignant change^[11].

In conclusion, hepatocellular adenomas are a heterogeneous group of liver benign neoplasms that are characterized by varied genetic and molecular abnormalities, pathology, tumor biology and radiological features. Positron emission tomography is increasingly utilized in cancer surveillance and work-up. This case highlights that “false-positives” can arise in case of benign liver lesions such as HCA. In equivocal cases where CT-PET findings are discordant with other imaging modalities, and/or clinical/biochemical features, further evaluation with different imaging modalities (*e.g.*, contrast enhanced sonography or MRI with liver-specific contrast) or novel PET tracers (*e.g.*, ¹¹C-acetate or ¹⁸F-fluorocholine PET) should be considered^[1,30-33].

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P-Reviewer Gao C S-Editor Gou SX
L-Editor A E-Editor Zhang DN





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ISSN 1007-9327

