18-Fluoro-deoxyglucose uptake in inflammatory hepatic adenoma: A case report

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Abstract
Positron emission tomography computed tomography (PET-CT) using 18-Fluoro-deoxyglucose (18FDG) is an imaging modality that reflects cellular glucose metabolism. Most cancers show an uptake of 18FDG and benign tumors do not usually behave in such a way. The authors report herein the case of a 38-year-old female patient with a past medical history of cervical intraepithelial neoplasia and pheochromocytoma, in whom a liver lesion had been detected with PET-CT. The tumor was laparoscopically resected and the diagnosis of inflammatory hepatic adenoma was confirmed. This is the first description of an inflammatory hepatic adenoma with an 18FDG up-take.

Key words: Liver surgery; Liver tumor; Liver cancer; Benign tumor; Laparoscopy; Prognosis

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Core tip: In cancer therapy, the use of 18-Fluoro-deoxyglucose (18FDG) positron emission tomography computed tomography as a staging or prognostic tool, is increasing. This is also the case for primary or secondary
Hepatocellular adenomas (HCAs) are rare benign hepatic tumors that are more frequent in women and have been associated with oral contraceptive use\(^1\). The risk of malignant transformation of HCAs is small but non-negligible\(^2\). The commonest complication of HCAs is bleeding, an occurrence which has been linked to multiple factors such as the size of the adenoma, pregnancy, visualization of lesional arteries, left lateral lobe location and exophytic growth. Due to these risks, recent guidelines have recommended the resection of adenomas that present: A diameter larger than 50 mm, signs of hepatocarcinoma or focal dysplasia, activated β-catenin mutation, high level of serum alphafoetoprotein, hepatocellular adenomas developing in male gender or hepatocellular adenomas developing in a glycogen storage disease\(^3\). The resection is regularly performed as laparoscopic hepatectomy\(^4\).

Positron emission tomography computed tomography (PET-CT) using 18-Fluoro-deoxyglucose (\(^18\)FDG) is an imaging modality that is based on an enhancement of glucose consumption, a distinguishing feature of most cancers that is in part related to the over-expression of GLUT-1 glucose transporters and increased hexokinase activity. The use of PET-CT in primary or secondary liver cancer is increasing\(^5\). As HCAs are benign lesions, they are not assumed to be \(^18\)FDG-avid, except in some rare cases. To the best of their knowledge, the authors described herein the first report of \(^18\)FDG uptake by an inflammatory HCA (I-HCA), and reviewed the literature for other reports of \(^18\)FDG uptake in other types of liver adenoma.

**DISCUSSION**

This report describes the occurrence of a 50-mm I-HCA that was highly avid for \(^18\)FDG at PET-CT. The exact nature of this I-HCA was confirmed by surgical resection. To the best of the authors’ knowledge, this is the first report of \(^18\)FDG uptake by an I-HCA. HCAs are classified into four types, according to their genetic and histologic features (Table 1): HNF1\(α\) inactivated HCA (H-HCA), β-catenin mutated HCA (β-HCA), I-HCA and unclassified HCA\(^7,8\). The actual risk of malignancy of all HCAs is evaluated at 4.2%\(^9,10\). The β-HCA subtype is associated with the highest risk of malignant transformation and must be resected (Table 1). After literature review, the authors found 22 other HCA cases with \(^18\)FDG uptake in PET-CT\(^9,11\) (Table 2), and none of them was the inflammatory type. Eighteen of them have a description of the histological findings with steatosis. Twelve reported a final diagnosis, which was either HNF1\(α\) or hepatic adenomatosis.

The uptake of \(^18\)FDG results from the increased metabolism of the cell. The intracellular FDG accumulation is proportional to the amount of glucose utilization\(^12\) and most cancers do have increased cellular activity.
The differential diagnosis of benign 18\textsuperscript{FDG} avid hepatic lesions might include focal steatosis, infectious, parasitic or inflammatory processes \textit{(e.g., hepatic abscess, cryptococcal infection, hepatic tuberculosis)} and hepatic adenoma\textsuperscript{[21,22]}. Focal fatty infiltration has been reported to be PET-avid\textsuperscript{[23]}. In fact, as a response to fat accumulation, a subacute inflammatory hepatic reaction with infiltration of activated Kupffer cells may occur, resulting in a higher SUV\textsubscript{max} than adjacent normal liver parenchyma. As said above, five cases of hepatic adenoma showed fatty changes but none of them were of the inflammatory type. Only one had a few inflammatory infiltrates. Maybe the fatty change itself was sufficient enough to induce a PET-avid response, without obvious inflammatory infiltrate in histological examination. It is also possible, as suggested by Nakashima \textit{et al}\textsuperscript{[14]}, that the high expression of glucose transporters might be responsible for the increased uptake. Indeed, one study demonstrated that in H-HCA the
LFABP gene ablation significantly increased the in-vitro expression of GLUT-2 but not that of GLUT-1 [24]. Another study demonstrated that HNF1α-inactivated HCAs activate glycolysis due to a strong up-regulation of glucokinase [25]. These two components are features of most cancers (rise of GLUT-1 and hexokinase activity) with features of H-HCA (rise of GLUT-2 and glucokinase). However, due to the few reports published in literature, no conclusion can be made on the risk of cancer development in HCA with uptake of 18FDG. Prospective and large series are needed to confirm the role of PET-CT in HCA evaluation and prognosis.

### Table 1  Classification of hepatocellular adenomas

| HCA subtype         | Abbreviation | Proportion | Markers          | Malignant transformation |
|---------------------|--------------|------------|------------------|--------------------------|
| HNF1α inactivated   | H-HCA        | 35%-40%    | LFABP            | Rare                     |
| β-catenin activated | β-HCA        | 10%        | β-catenin'/GS' activated | Yes                     |
| Inflammatory        | I-HCA        | 50%        | CRP*             | No                       |
| Unclassified        | U-HCA        | 5%         | None             | No                       |

HCA: Hepatocellular adenoma.

### Table 2  Cases of 18-fluoro-deoxyglucose-avid hepatocellular adenomas reported in literature

| Ref. | Gender | Age (yr) | Size (mm) | SUVmax | Diagnosis                  |
|------|--------|----------|-----------|--------|----------------------------|
| [7]  | Female | 41       | 10        | NA     | HCA                        |
| [8]  | Female | 37       | 33        | 5      | H-HCA                      |
| [9]  | NA     | 44       | 30        | 6.2    | H-HCA                      |
| [10] | Female | 52       | NA        | 4.09-9.8 | Hepatic adenomatosis     |
| [11] | Female | 65       | 30        | NA     | Necrotic HCA               |
| [12] | Male   | 69       | 40        | 10.4   | H-HCA                      |
| [13] | 4 cases| NA       | 73 ± 15   | 6 ± 0.5 | HCA                        |
| [14] | Female | 34       | 20-30     | 3.9    | HCA                        |
| [15] | Male   | 73       | 25        | 11.9   | Fatty liver                |
| [16] | Female | 44       | 23        | 7.9    | H-HCA                      |
| [17] | 9 cases| 49 ± 16  | 27 ± 15   | 8.2 ± 4.3 | H-HCA                  |
| This case | Female | 38 | 50 | 9.3 | I-HCA |

HCA: Hepatocellular adenoma; 18FDG: 18-fluoro-deoxyglucose; H-HCA: HNF1α inactivated HCA; I-HCA: Inflammatory HCA; NA: Not available.

**Clinical diagnosis**
This tumor was asymptomatic and described at follow-up imaging after surgical resection of a pheochromocytoma.

**Differential diagnosis**
Adenoma, hepatocellular carcinoma, other primary or metastatic hepatic tumors.

**Laboratory diagnosis**
Blood tumor markers, and particularly alphafoetoprotein, were negative.

**Imaging diagnosis**
Magnetic resonance imaging was compatible with hepatocellular adenoma, but the lesion was 18-fluoro-deoxyglucose (18FDG) avid at positron emission tomography computed tomography (PET-CT).

**Pathological diagnosis**
Percutaneous biopsy and surgical specimen confirmed inflammatory hepatocellular adenoma (I-HCA).

**Treatment**
Laparoscopic liver R0 resection.

**Related reports**
To the authors’ knowledge, this case is the first report of a PET-CT FDG-avid I-HCA.

**Term explanation**
Hepatocellular adenomas are benign liver lesions whose imaging diagnosis could be uncertain.

**Experiences and lessons**
PET-CT positivity is not necessary linked to cancerous degeneration in liver adenomas.
This paper reported a case of PET-avid hepatocellular adenomas and reviews related literature to show variety case of PET-avid HCA.

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