False-positive $^{18}$F fluorodeoxyglucose positron emission tomography-avid benign hepatic tumor: Previously unreported in a male patient

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Abstract

We report a case of $^{18}$F fluorodeoxyglucose (FDG) positron emission tomography (PET)–computed tomography-avid histologically confirmed inflammatory hepatic adenoma in a 77-year-old male patient without any history of steroid, alcohol use. This is the first case report of inflammatory hepatic adenoma in a male patient documented in the published literature showing uptake on $^{18}$F-FDG PET. Previous single case report of $^{18}$F-FDG PET-avid hepatic adenoma in a male patient was of hepatocyte nuclear factor-1-α subtype.

Key words: Adenoma; FDG-PET; hepatic; inflammatory; male

Introduction

Hepatic adenoma is the most common benign tumor seen in women of reproductive age group who are on oral contraceptives. It is a rare tumor in male and seen in patients with a history of anabolic steroids intake. Positron emission tomography (PET) using $^{18}$F-fluorodeoxyglucose ($^{18}$F-FDG) for the diagnosis of hepatic adenoma is useful in hepatocyte nuclear factor (HNF)-1-α and inflammatory subtypes of hepatic adenoma. Inflammatory subtype of hepatic adenoma is rare in males. The purpose of this case is to present a case of FDG-PET-avid inflammatory hepatic adenoma in a male patient without any history of drug abuse or any other comorbid condition.

Case Report

A 77-year-old male patient presented to the outpatient department with chief complaints of heaviness and upper abdominal discomfort, generalized weakness, and weight loss since last 7 months. The patient was subjected to ultrasound examination and blood examination. His hemoglobin was 12.7 g/dl. Anti-HB core was nonreactive and hepatitis C virus-RNA was not detected in plasma. Minimally deranged liver function tests were seen in the form of mild elevation of total serum bilirubin – 1.9 mg/dl (N: 0.3–1.2 mg/dl), aspartate aminotransferase/serum glutamic-oxaloacetic transaminase – 49 IU/L (N: 5–40 IU/L). Ultrasound upper abdomen was done, which revealed a large hyperechoic
lesion with a hypoechoic halo in the right lobe of liver [Figure 1]. The liver architecture was noncirrhotic. Serum alpha fetoprotein was normal. No history of diabetes, alcohol abuse, and steroid usage was present.

Thereafter, patient was advised contrast-enhanced magnetic resonance imaging (MRI) to further characterize the lesion. Contrast-enhanced MRI with hepatobiliary-specific contrast was done, which revealed a solitary well-encapsulated lesion measuring $9 \times 8 \times 8.6$ cm$^3$ in segment VII of liver. The lesion showed heterogeneous signal on T2-weighted images. On postcontrast scans, the lesion showed contrast pooling in portal phase with persistent areas of contrast pooling and subtle washout in delayed phase. On hepatobiliary phase, the lesion showed predominant hypointense signal with subtle areas of contrast retention within the lesion [Figure 2]. Computed tomography (CT)–PET was also done, which revealed the liver lesion to be FDG-avid with a standardized uptake value (SUVmax) of 9.7 [Figure 3].

Liver biopsy was done from the lesion, which showed 1–3 cell thick cord of hepatocytes, few of them binucleated with interspersed areas of sinusoidal dilatation, peliosis, and telangiectasia. Few unpaired tortuous arteries were seen at the periphery. No steatosis was seen. Immunohistochemistry showed strong positive SAA, glypican-3 negative, CD34 diffuse staining in sinusoidal lining, strongly positive glutamine synthase. β-catenin normal membranous staining in atypical hepatocytes was seen; however, no nuclear or cytoplasmic expression was seen; CD45 and CD68 positivity; CK7 but not CK19 staining of few atypical hepatocytes; but no well-formed ductules [Figures 4 and 5]. Inflammatory cells near ductular reactive cells were not appreciated in this biopsy sample; however, this is a small sample to make definitive comment. The final diagnosis was inflammatory hepatic adenoma showing telangiectasia.

Figure 1: Ultrasound shows a large hyperechoic lesion (arrows) with a hypoechoic halo in the right lobe of liver

Figure 2 (A-F): Abdominal MRI. (A) T1-weighted image (WI) showing well-defined hypointense lesion with hyperintense layering; (B) heterogeneously hyperintense on T2-WI; (C) subtle enhancement in arterial phase; (D) contrast pooling in portal venous phase; (E) which persists in delayed phase; and (F) which appears predominantly hypointense in hepatobiliary phase

The patient was advised surgery, but the patient refused to undergo any surgical procedure and is currently on follow-up.
Discussion

Hepatocellular adenoma (HCA) is the second most common benign liver neoplasm and seen predominantly in women of reproductive age group. PET-avid hepatic lesions are usually suggestive of malignancy. PET-avid hepatic adenoma in male is extremely rare and has been described mostly in females in the form of case reports in the literature. To our knowledge, this is the first case report of histopathologically proven PET-avid inflammatory hepatic adenoma in a male patient. Previous case reports or case series in the literature either have shown PET-avid adenomas in female patient mostly with HNF-1-α mutation or with no detail pathological analysis.\(^{[1-8]}\) Single case report of HNF-1-α mutated PET-avid HCA has been reported in a male who had a history of testosterone usage for a year.\(^{[1]}\)

![Figure 3 (A and B): 18F-FDG PET-CT showing the liver lesion to be FDG-avid with a standardized uptake value (SUVmax) of 9.7](image)

Bioulac-Sage et al.\(^{[9]}\) have classified HCA into four subtypes: inflammatory, HNF-1-α inactivated, β-catenin activated, and unclassified type. Inflammatory hepatic adenomas (I-HCA) are the commonest, accounting for 40–55% of HCAs. It is more common in females and history of oral contraceptive usage is present in >90% cases. This subtype is extremely rare in males. It is associated with obesity, alcohol abuse, and inflammatory syndrome. Inflammatory HCAs have an increased risk of bleeding (up to 30%) but risk of malignant transformation is very less (5–9%). Clinically, the patient may have fever, leukocytosis, and elevated serum C-reactive protein. Histologically, these are characterized by marked sinusoidal dilatation, polymorphous inflammatory infiltrates, peliosis, thickened tortuous arteries, and prominent ductular reaction.\(^{[10]}\) Steatosis within this variant is less common. Previously, these adenomas were misclassified as “telangiectatic focal nodular hyperplasias.” On imaging, I-HCAs manifest as hypervascular hepatic masses with persistent enhancement in the portal venous and delayed phases. They are markedly hyperintense on T2-weighted images corresponding to areas of sinusoidal dilatation.\(^{[11]}\)

HNF-1-α mutated HCAs account for 35–50% of the subtypes and is exclusively seen in women. It has a strong association with oral contraceptive use. HNF-HCAs are characterized by marked intralveolar steatosis. Fat accumulation within the lesion is due to stimulation of lipogenesis by suppression

![Figure 4 (A-E): Liver biopsy slides. (A) 1–2-cell thick hepatocyte cords, multifocal sinusoidal dilatation, peliosis (arrows); (B) thick hepatocyte cords, peliosis, and telangiectasia with patchy mixed inflammation (circle); (C) marked peliosis (thin arrows) surrounding thin hepatocyte cords (thick arrows), minimal cytologic atypia, and no mitosis; (D) preserved reticulin framework, thin hepatocyte cords (thin arrows), peliotic spaces (thick arrows) (reticulin silver stain); (E) hepatocytes showing cytoplasmic staining (arrows) with antibody against acute-phase inflammatory reactant – serum amyloid-associated protein](image)
of gluconeogenesis, activation of glycolysis, and promotion of fatty acid biosynthesis. The downregulation of fatty acid binding protein-1 leads to “faulty” transport of fatty acids and to intralesional deposition of fat. The patients tend to develop familial adenomatosis and diabetes mellitus due to germ-line mutations of HNF-1-α gene. No risk of malignant transformation is seen and these subtypes may show intralesional hemorrhage. Histologically, excessive lipid accumulation within the tumor hepatocytes is documented with no inflammatory infiltrates or peliosis. On imaging, the characteristic finding of this subtype is diffuse intralesional steatosis or macroscopic fat that is classically demonstrated as diffuse signal dropout on out-of-phase T1-weighted gradient echo-imaging or macroscopic fat-attenuation areas on CT. On contrast-enhanced CT or MRI, moderate arterial enhancement which does not persist onto the portal venous and delayed phases is seen.

β-catenin-mutated HCAs account for small subset (10–18%). These tumors primarily affect patients with glycogen storage disease and on androgen treatment and have a greater propensity than the other subtypes of HCAs to undergo malignant transformation to hepatocellular carcinoma. This is the subtype more commonly seen in males. Histologically, no significant peliosis or steatosis is seen. Immunohistochemistry shows strong diffuse overexpression of glutamine synthetase and nuclear β-catenin staining. On imaging, they strongly mimic hepatocellular carcinoma (HCC) and show arterial enhancement and washout in portal venous phase.

Unclassified variants of HCA are poorly understood and lack specific pathological and imaging features. No gender predilection is, however, seen.

FDG-PET is used in liver imaging to differentiate benign and malignant lesions, surveillance staging, and monitoring in cancer patients although there are pitfalls associated with its use. Moderate physiological FDG uptake is noted in the liver. The overall sensitivity of FDG PET-CT in detecting well-differentiated, low-grade, and small HCC is low. False-positive FDG-avid liver lesions include focal steatosis, hepatic adenomatosis (HNF-1-α and inflammatory subtype), infectious or inflammatory processes such as abscess, hepatic tuberculosis. Currently, surgical resection is recommended for HCAs more than 5 cm, adenomas which do not regress after stopping the offending drugs, HCAs with malignant change, or evidence of β-catenin activation as demonstrated on biopsy, and all HCAs in male patients. Intervention radiological techniques such as transarterial embolization and radiofrequency ablation have also been found to be safe and effective in treating HCAs.

Conclusion

Hepatic adenomas are benign lesions with unique tumor biology, pathology, and radiological imaging features. When there is discordance between the clinical, biochemical, PET findings with classical radiological imaging findings.
as seen in our case, possibility of inflammatory adenoma should be kept in the list of differential diagnosis.

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Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient has given the consent for the images and other clinical information to be reported in the journal. The patient understands that name and initial will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Conflicts of interest
There are no conflicts of interest.

References