DIAGNOSTIC CHALLENGE: MULTIFOCAL NODULES IN FATTY LIVER DISEASE SIMULATING METASTASES

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Abstract

We present the case of a 32-year-old female with a history of rectal bleeding and severe anemia, who was found to have multiple liver lesions on imaging studies. Initially, the possibility of liver metastasis or multifocal nodular steatohepatitis was considered. However, biopsy findings confirmed multifocal nodular steatohepatitis. This case underscores the diagnostic challenges in differentiating benign and malignant liver lesions and highlights the role of advanced imaging and biopsy in arriving at a definitive diagnosis.

Keywords: *Liver Lesions, Multifocal Nodular Steatohepatitis, Liver Metastasis, Hepatocellular Carcinoma, Cholangiocarcinoma, Imaging, Biopsy, Anemia, Rectal Bleeding.*

Introduction

Liver lesions can arise from various causes, including benign conditions like steatosis and focal nodular hyperplasia, and malignant conditions like hepatocellular carcinoma (HCC), cholangiocarcinoma, or metastases(1). In cases presenting with nonspecific symptoms such as anemia and gastrointestinal bleeding, it can be challenging to establish the correct diagnosis based on imaging alone. This case focuses on a 32-year-old female with liver lesions, highlighting the differential diagnosis, and distinguishing between various liver mass etiologies.

Case Report

A 32-year-old female, with no significant past medical history, presented to the emergency department with complaints of bleeding per rectum for one month. She also reported increased fatigue, pallor, and generalized weakness. On physical examination, she appeared pale, with a hepatomegaly (liver span of 18 cm), and a nodular liver surface on palpation. The rest of the physical examination was unremarkable.

Laboratory Investigations:

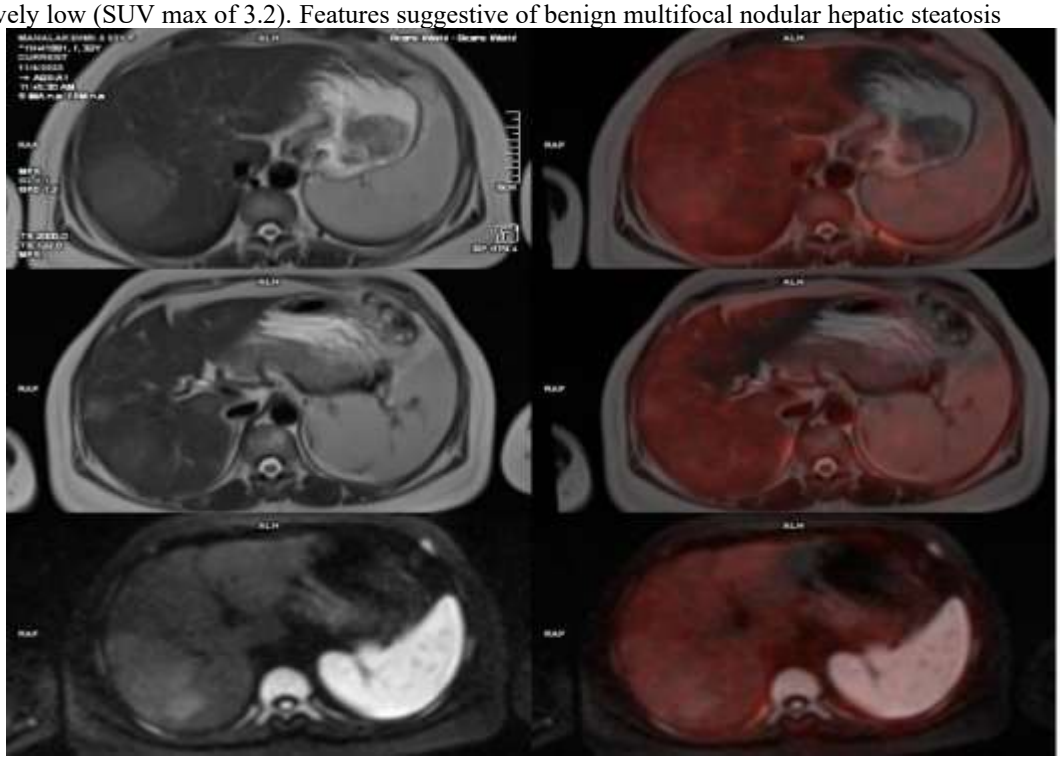
- Hemoglobin: 8 g/dL
- MCV: 65 fL (Microcytic Anemia)
- Total WBC count: 8000/mm³
- Platelet count: 5,00,000/mm³ (marked thrombocytosis)
- Ferritin: 10 ng/mL (low)

Colonoscopy: Given the history of rectal bleeding and severe anemia, a colonoscopy was performed, which revealed large hemorrhoids, without any other notable pathology. This excluded major colorectal pathology as the source of bleeding.

Liver Function Tests: Normal liver function tests were noted, suggesting no overt hepatic dysfunction.

Imaging Studies:

1. **Ultrasound Abdomen:** An ultrasound of the abdomen revealed multiple round, homogeneous nodules in both lobes of the liver, ranging from 2 to 3.5 cm in size. These nodules were isoechoic to the liver parenchyma with a clear hyper echoic rim, suggestive of well-defined lesions.
2. **CECT Abdomen:** Contrast-enhanced computed tomography (CECT) of the abdomen showed multiple hypodense lesions in both lobes of the liver. The largest lesion measured 6 x 4.8 cm. The lesions showed mild enhancement during the arterial phase, raising the possibility of either liver metastasis or multifocal nodular steatohepatitis.
3. **PET MRI:** A PET MRI scan showed multiple faintly FDG-avid, well-defined, iso-to-hypo-enhancing lesions in both liver lobes. The largest lesion, located in segments VII/VIII, measured 5.7 x 4.8 cm and had an SUV max of 5.1. There was no evidence of displaced hepatic vessels or biliary radicles. The MRI sequences revealed predominantly T1 hyperintensity and mildly T2 hyperintensity of the lesions, with no restricted diffusion. The background liver uptake was relatively low (SUV max of 3.2). Features suggestive of benign multifocal nodular hepatic steatosis



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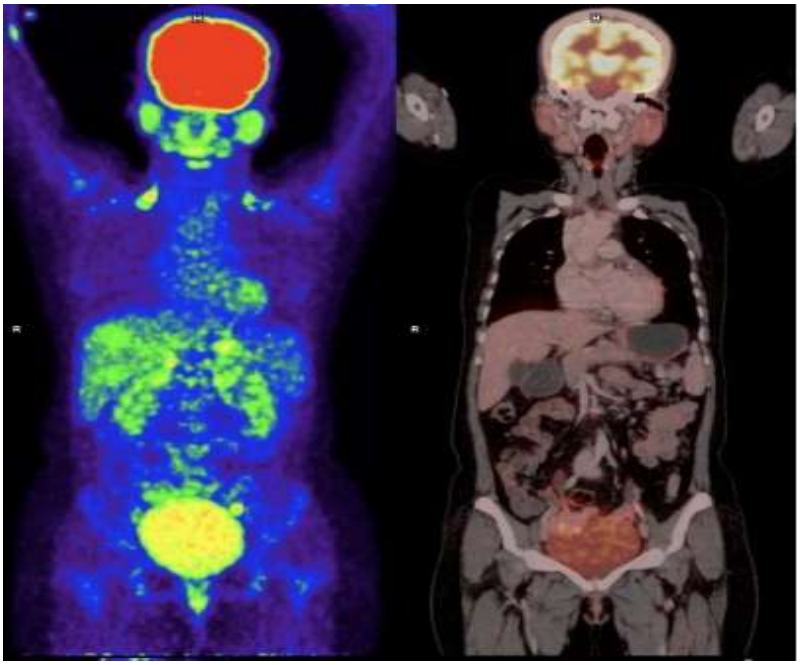

Figure 1: showing Multiple faintly FDG avid fairly well defined iso to hypo enhancing relatively hypo-dense lesions in both lobes of liver, largest lesion in segment VII / VIII measures 5.7 x 4.8 cms (SUV max 5.1) background uptake of liver 3.2. Correlative MRI shows predominantly T1 hyper-intense and mildly T2 hyper-intense lesions without restricted diffusion. - No other demonstrable FDG avid lesion or foci of restricted diffusion visualized in hepatic parenchyma

Liver Biopsy:
Liver biopsy reveals the presence of large fat vacuoles displacing hepatocyte nuclei peripherally, a hallmark of macrovesicular steatosis. Additionally, there is evidence of lobular inflammation characterized by scattered mononuclear infiltrates (lymphocytes and macrophages), occasionally accompanied by neutrophils. Hepatocytes exhibit ballooning degeneration, seen as enlarged cells with pale, rarefied cytoplasm and irregular borders. These histopathological features are classical for steatohepatitis.

Discussion
In the presented case, a 32-year-old woman with no significant medical history manifested with symptoms of iron-deficiency anemia secondary to rectal bleeding. However, the most striking finding was the incidental detection of multiple hepatic nodules, prompting an extensive imaging workup to rule out hepatic malignancy. Contrast-enhanced CT and PET-MRI findings initially raised suspicion for metastases or multifocal hepatocellular carcinoma (HCC). However, based on imaging patterns and preserved liver function, the lesions were eventually characterized as **multinodular steatohepatitis (MNS)**, a rare entity that may mimic malignant liver disease both clinically and radiologically.

Multinodular Steatohepatitis: A Diagnostic Mimicker
Multifocal or multinodular steatohepatitis is a histopathological and radiological variant of nonalcoholic steatohepatitis (NASH), characterized by hepatic fat infiltration, hepatocyte ballooning, and inflammatory activity distributed in a nodular pattern [1]. In most cases, MNS is associated with metabolic risk factors such as obesity, insulin resistance, or dyslipidemia, though patients may also be non-obese or non-diabetic, as seen in this case.Radiologically, MNS may present with multiple nodules ranging from 1–6 cm, often isointense or hyperintense on T1-weighted MRI and mildly hyperintense on T2-weighted imaging [2]. These lesions may enhance subtly in the arterial phase but usually lack the washout seen in HCC or metastasis. The absence of diffusion restriction and lack of vascular or biliary displacement further supports the benign nature of these nodules. However, when these imaging patterns overlap with those seen in malignancies, particularly in non-cirrhotic livers, the diagnostic dilemma becomes profound.

HCC vs MNS
Hepatocellular carcinoma typically develops in a cirrhotic liver, with hallmark imaging features including arterial phase hyperenhancement (APHE), washout on portal/delayed phases, and a capsule appearance on dynamic imaging [3]. These lesions are often FDG-avid, though poorly differentiated HCCs show greater uptake than well-differentiated ones [4].
In contrast, our patient had no signs of liver cirrhosis, preserved liver function, and relatively low FDG uptake (SUV max 5.1). The largest lesion (5.7 x 4.8 cm) lacked classical HCC features such as venous invasion, pseudocapsule, or satellite nodules. Furthermore, liver nodules in MNS often demonstrate stable imaging characteristics over time, unlike the progressive nature of HCC.
Liver Metastasis: Less Likely but Initially Suspected

Liver metastases are typically the most common malignant liver lesions and often appear as multiple, hypovascular lesions with peripheral rim enhancement on imaging [5]. FDG-PET is sensitive in detecting hepatic metastases from many primary tumors, particularly colorectal carcinoma, which was initially suspected in this patient due to rectal bleeding and anemia.
However, colonoscopy revealed only large hemorrhoids and no colonic pathology, ruling out a potential primary. The absence of a known malignancy elsewhere, and lack of significant FDG uptake in the lesions or other body sites, made metastasis less likely.

Cholangiocarcinoma: An Unlikely Differential
Intrahepatic cholangiocarcinoma (ICC) typically presents as a solitary mass with progressive biliary obstruction and irregular borders. It may show peripheral enhancement in the arterial phase and delayed centripetal fill-in on contrast-enhanced imaging [6].
Multifocal ICC is rare and usually presents in the context of chronic biliary disease. Our patient lacked any signs of jaundice, biliary dilation, or tumor thrombus. Moreover, the lesions showed no delayed enhancement, making this diagnosis unlikely.

PET-MRI: Advanced Tool but Still Limited
PET-MRI, as performed in this case, provides both metabolic and anatomical insights. The hepatic lesions displayed faint FDG uptake (SUV max 5.1), which is a gray zone. Benign hepatic lesions like FNH or steatohepatitis can show mild uptake, particularly in inflammatory states [7]. Importantly, the absence of diffusion restriction and lack of mass effect on vessels and biliary radicles favored a benign etiology.

Role of Thrombocytosis and Iron-Deficiency Anemia
While the hepatic findings dominated the imaging workup, the severe iron-deficiency anemia (Hb 8 g/dL, MCV 65 fL, Ferritin 10 ng/mL) pointed toward a chronic gastrointestinal blood loss. However, the source was confirmed as hemorrhoids on colonoscopy, dissociating the anemia from the liver findings.

Interestingly, the patient had **marked thrombocytosis (5,00,000/mm³)**. While commonly seen in reactive states (like anemia or inflammation), thrombocytosis has been associated with hepatic steatosis in non-cirrhotic patients, possibly due to inflammatory cytokine release [8].

Importance of Recognizing MNS
MNS remains underdiagnosed, and failure to differentiate it from malignancy may lead to unnecessary biopsies, invasive procedures, or even overtreatment. While histological confirmation remains the gold standard, close imaging follow-up and correlation with clinical and biochemical profiles are often sufficient to avoid invasive steps [9].
In this case, the preserved liver function, absence of systemic malignancy, and characteristic imaging helped in narrowing the differential. Recognition of this benign pattern prevented an unnecessary biopsy or surgical intervention.

Table 1: Imaging and Clinical Comparison of Common Multifocal Liver Lesions

Feature	Hepatocellular Carcinoma (HCC)	Liver Metastases	Cholangiocarcinoma (ICC)	Multinodular Steatohepatitis (MNS)
Liver Background	Cirrhotic	Normal or abnormal	Normal or chronic biliary disease	Usually steatotic, not cirrhotic
Enhancement Pattern	APHE + washout + capsule	Rim enhancement (hypovascular)	Delayed fill-in	Mild arterial enhancement, no washout
FDG Uptake (PET)	Variable (mod-high)	High (SUV >5)	High (SUV >5)	Mild (SUV ~5 or less)
T1/T2 MRI Signals	T1 hypointense, T2 hyperintense	Variable	T1 iso/hypo, T2 hyper	T1 hyper, T2 mildly hyper
Diffusion Restriction	Present	Present	Present	Absent
Liver Function	Often deranged	Usually preserved	Often impaired	Preserved
Common Associations	Cirrhosis, HBV/HCV	Known primary tumor	PSC, biliary tract disease	Metabolic syndrome, obesity
Need for Biopsy	Often not if classic imaging	Usually if no known primary	Yes	Avoid if confident on imaging

Conclusion
This case emphasizes the importance of recognizing **multinodular steatohepatitis (MNS)** as a benign hepatic entity that can closely mimic malignancies such as HCC or metastasis. Advanced imaging modalities, particularly PET-MRI, provide a high level of anatomical and metabolic detail, yet clinical correlation remains paramount. Avoiding over-investigation and unnecessary interventions hinges on radiologists being familiar with such mimics and adopting a comprehensive approach that includes imaging, clinical, and laboratory findings.

References
1. Brunt EM et al. Nonalcoholic Steatohepatitis: A Proposal for Grading and Staging. *Am J Gastroenterol*. 1999.
2. Grazioli L et al. Benign liver nodules: Imaging diagnosis. *Eur Radiol*. 2001.

3. Forner A et al. Diagnosis of HCC: EASL–EORTC Clinical Practice Guidelines. *J Hepatol*. 2012.
4. Delbeke D et al. FDG-PET in hepatocellular carcinoma. *J Nucl Med*. 2003.
5. Kinkel K et al. Detection of hepatic metastases from colorectal cancer. *Radiology*. 2002.
6. Kim TK et al. Intrahepatic Cholangiocarcinoma: Radiologic-pathologic correlation. *Radiographics*. 2015.
7. Barger RL et al. FDG-PET/CT of benign hepatic lesions. *Clin Nucl Med*. 2011.
8. Sookoian S et al. Platelet count in NAFLD: A marker of hepatic inflammation? *Clin Sci (Lond)*. 2010.
9. Ichikawa T et al. Imaging of fatty liver disease: review and future directions. *J Hepatol*. 2011.