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Case Report

Radiopathologic findings of multifocal nodular hepatic steatosis ☆,☆☆

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ABSTRACT

Multifocal nodular hepatic steatosis (MFNHS) is a rare benign clinical entity mimicking metastatic disease. This study is designed to describe the imaging and histopathologic findings and clinical course of patients with MFNHS. In this retrospective study during 2005 and 2023, 10 patients with an imaging and pathologic diagnosis of MFNHS were included. The imaging and histopathology findings were reviewed in each case. The follow-up images were reviewed to assess the clinical course of the disease. The mean age was 50.0 ± 10.5 years, and the male-to-female ratio was 4:6. Three patients had a past medical history of cancer. All patients were found to have lesions suspicious of malignancy on either ultrasound (US) or computed tomography (CT) requiring further workup. Six patients underwent magnetic resonance imaging (MRI), and 4 patients underwent an image-guided biopsy which resulted in hepatic steatosis. During the follow-up period, the majority of patients (71.5%) remained unchanged or improved, while 2 patients (28.5%) progressed. MRI is a reliable modality in detecting and characterizing MFNHS and should be considered to further assess multiple hepatic lesions in cases where the clinical suspicion is not high for metastasis.

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Introduction

Hepatic steatosis is a relatively common disease process with estimates as high as 25% of the global population [1,2].

Risk factors are multiple and include obesity, viral hepatitis, hemochromatosis, and certain chemotherapeutics [1,3]. Hepatic steatosis typically appears as diffuse fatty infiltration of the hepatic parenchyma but can occasionally present as single or multiple nodular lesions [4], the latter termed multifo-

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Table 1 – Patients' demographic and clinical characteristics.

Patients	Age (y)	Sex	BMI (Kg/m ²)	Medical history	Surgical history
Case 1	36	Female	29.5	Hypertension Transplant with transplant rejection Autoimmune hepatitis	Liver transplant
Case 2	44	Female	18.6	Gastric cancer Pancreatitis Diabetes	Gastrectomy Left Partial Hepatectomy
Case 3	52	Female	31.9	Multiple myeloma Obesity Diabetes Hypertension	Sleeve Gastrectomy Hysterectomy
Case 4	71	Male	30.2	Obesity	-
Case 5	59	Male	27.4	Hepatitis C	-
Case 6	51	Female	31.3	Hypertension Fibromyalgia Lupus Carcinoid tumor of sigmoid colon Pulmonary fibrosis Sjogren's disease	Hysterectomy Oophorectomy (L)
Case 7	58	Male	25.2	Porokeratosis	Vasectomy
Case 8	40	Female	19.4	Chronic Pancreatitis Endometriosis GERD Irritable bowel syndrome Thyroid disease Raynaud disease	Appendectomy Cholecystectomy Total Pancreatectomy Islet cell transplant
Case 9	42	Male	27.7	Severe MVA Bronchiectasis Neuromuscular disorder Digestive disorder GERD	Abdominal surgery Exploratory laparotomy with bowel resection Abdominal wall surgery Hernia repair
Case 10	48	Female	43.6	Fibromyalgia Kidney stones GERD Hypertension Thyroid disease Diabetes (II)	Appendectomy Cholecystectomy Cesarean section Cystoscopy stent & stone removal Tubal ligation

cal nodular hepatic steatosis (MFNHS). These lesions are incidentally found on ultrasound (US) or computed tomography (CT) and are often difficult to distinguish from malignancy, prompting biopsy for definitive diagnosis which is costly and potentially distressing to patients [2,5]. This disease process is mostly described in single-patient case reports. This case series study is designed to describe the imaging findings of MFNHS in 10 patients; 4 of them underwent image-guided biopsy providing radiologic-pathologic correlation.

Cases

In this retrospective study during 2005 and 2023, all the patients with an imaging and pathologic diagnosis of MFNHS were included. The imaging and histopathology findings were reviewed in each case.

A total of 10 patients (Male: female = 4:6) with a mean age of 50.0 ± 10.5 years were included in this study. Table 1 lists the background demographic and clinical data of the patients.

The average BMI in this series was 28.5 ± 7.0 Kg/m². One of the patients had a history of liver transplantation. Three patients had a history of malignancy, and one patient had a history of chronic hepatitis C.

Table 2 summarizes the imaging and clinical data of the patients in this study. In all patients, imaging was performed for other reasons and MFNHS was suspected incidentally. CT (90%) was the most common imaging modality used in the workup of the patients, followed by magnetic resonance imaging (MRI) (60%) and ultrasound (40%).

US was the initial imaging in 4 (40%) patients. The ultrasound findings included multifocal areas of increased echogenicity, some of which demonstrated posterior acoustic enhancement (Fig. 1). All lesions found on US imaging were further assessed using CT and MRI. The MFNHS lesions were found as small non-enhancing lesions on contrast-enhanced imaging. CT was the only modality performed in 4 patients. In these patients the lesions demonstrated fat density based on the Hounsfield Unit, confirming the diagnosis of fat-containing lesions (Fig. 1). When CT was not confirmatory, a contrast-enhanced MRI was performed which demonstrated

Table 2 – Patients' imaging evaluation and clinical outcomes.

	Ultrasound	CT	MRI	Biopsy	Outcome	Follow up (mo)
Case 1	Yes	Yes	Yes	Yes	Improved	100.3
Case 2	No	Yes	Yes	Yes	Improved	214.6
Case 3	No	Yes	Yes	No	Unchanged	3.6
Case 4	Yes	Yes	Yes	Yes	-	Lost follow up
Case 5	Yes	Yes	Yes	Yes	Progressed	163.1
Case 6	Yes	No	Yes	No	-	Lost follow up
Case 7	No	Yes	No	No	-	Lost follow up
Case 8	No	Yes	No	No	Progressed	6.3
Case 9	No	Yes	No	No	Improved	22.4
Case 10	No	Yes	No	No	Progressed	53.8

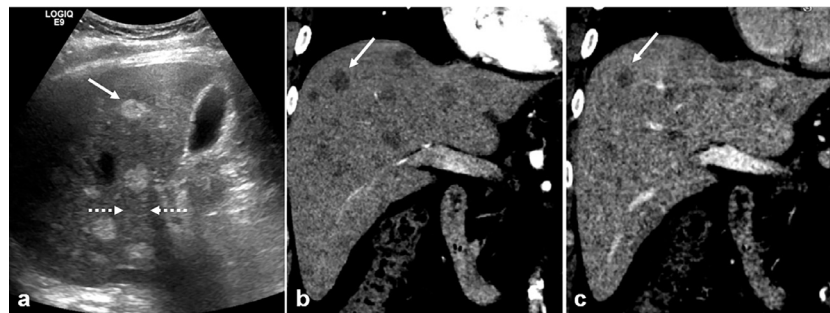


Fig. 1 – (A) Transverse US image showing multiple hyperechoic round well-defined lesions (solid arrow) with posterior acoustic enhancement (dotted arrows). (B) Coronal CT image in the arterial phase, and the portal venous phase (C) showing multiple non-enhancing round hypodensities throughout the hepatic parenchyma.

multiple, not-enhancing pseudolesions showing a high signal on T1 and T2-weighted images and signal dropout on the out-of-phase images compared to in-phase images (Fig. 2). There was no restricted diffusion. In one patient (case #5) due to the high suspicion for malignancy, and the background liver disease additional investigative imaging was carried out. This included a nuclear medicine liver-spleen scan showing geographic areas decreased Tc-99m sulfur colloid uptake, and a positron emission tomography/CT scan (PET-CT) showing no hypermetabolic liver lesions (Fig. 3). Biopsy and histopathology assessments were performed in 4 patients which revealed focal macrovesicular steatosis and microsteatosis in some cases (Fig. 4).

In this series, 3 patients (30%) were lost during follow up and 7 patients (70%) were followed for a median of 54 months (range: 6.3-215 months). During the follow-up period, 3 patients (43.0%) improved with a decreased number and size of lesions, while 2 patients (28.5%) remained unchanged, and 2 patients (28.5%) progressed.

Discussion

Hepatic steatosis is often diffuse in nature but can present as focal singular or multifocal nodular pseudo-lesions [6,7]. The reported cases of MFNHS are typically involving middle-aged females [3]. The patients in this study included both males and females with differing underlying medical comorbidities.

Patients are often asymptomatic with normal laboratory findings work, including LFTs [2,4,5], and are found incidentally on imaging done for other clinical indications [8]. The multinodular presentation of MFNHS on imaging can easily be misidentified as primary or secondary hepatic malignancies, leading to additional diagnostic workup and undue patient distress. Four out of 10 patients in this series underwent an image-guided biopsy before further imaging characterization by MRI. In patients without a history of primary malignancy, the clinical suspicion for metastasis is low, and further assessment with more advanced imaging is warranted. In patients with a primary malignancy, metastasis would be in the differential diagnoses and attention to clinical presentations, the patient's medical history and imaging characteristics may be helpful to consider advanced imaging before ordering a biopsy.

The location of the lesions on imaging may be helpful. The nodules may be seen in known geographic distributions; near the falciform ligament or in segment IV of the liver in the gallbladder bed [1]. However, in certain cases, it can be seen distributed throughout the hepatic parenchyma either as geographic and ill-defined or nodular and well-defined. In contrast to malignancy, MFNHS does not present with mass effect or invasion of hepatic vasculature [2]. The lesions present the characteristics of microscopic fat on imaging. On ultrasound, MFNHS presents as multiple focal hyperechoic lesions without mass effect or posterior acoustic enhancement. The lesions may be seen on CT images as multiple non-enhancing hypodense geographic or nodular lesions scattered throughout the hepatic parenchyma. On MRI, MFNHS may present

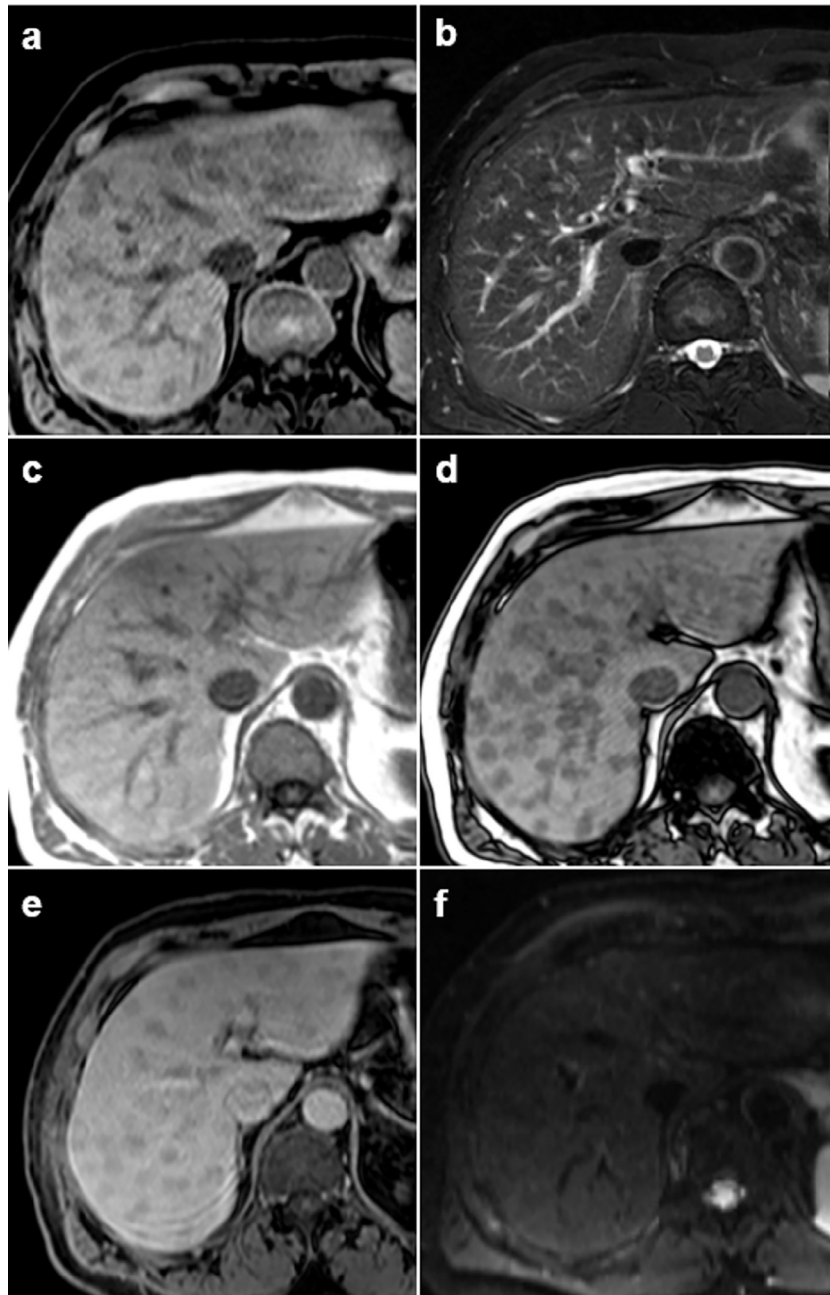


Fig. 2 – Unenhanced T1 (A) and T2 (B) weighted images showing multiple round lesions throughout the liver demonstrating low signal intensity on T1 and iso to mildly high signal intensity on T2-weighted images. The lesions show signal dropout on the out-phase image (D) compared to the in-phase image (C) and do not enhance or restrict diffusion on contrast-enhanced (E) and diffusion-weighted images (F).

as non-enhancing geographic or nodular lesions of variable T1/T2 hyperintensity which do not restrict diffusion [5,9–11]. Importantly, these lesions do not invade the surrounding vasculature or biliary system. Given their lipid content, these lesions demonstrate variable degrees of hypointense signal on the fat-suppressed sequences in addition to signal dropout on out-of-phase imaging.

Histopathology study is often diagnostic of benign fatty lesions. On pathology, MFNHS presents as circumscribed

non-encapsulated focal infiltrates composed of macroscopic fat. There is no vascular involvement, and the surrounding parenchyma displays variable amounts of inflammation and fibrosis [8,12]. The natural history of MFNHS is quite variable. In this series, the majority of patients remained unchanged or improved during the follow-up period while a smaller portion of patients progressed during the study time, similar to other studies [1,2,4]. Importantly, none of the lesions demonstrate malignant degeneration.

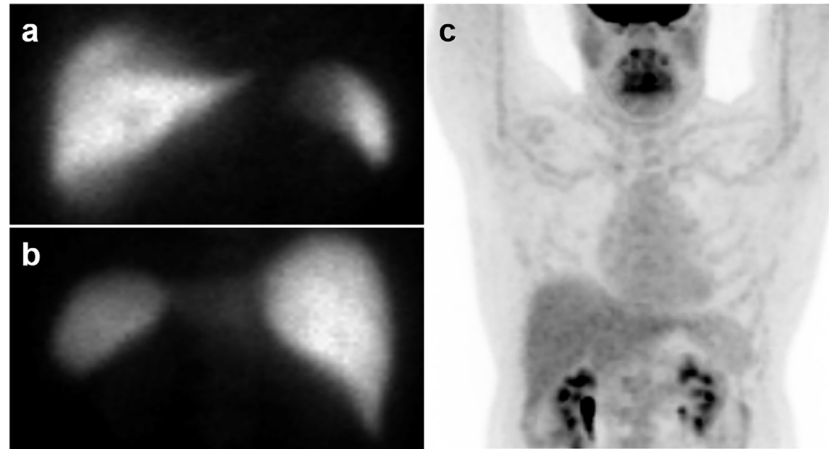


Fig. 3 – Anterior (A) and posterior (B) views of the nuclear medicine Liver-Spleen scan showing geographic areas of decreased colloid uptake. Scout PET image showing no hypermetabolic lesion within the liver.

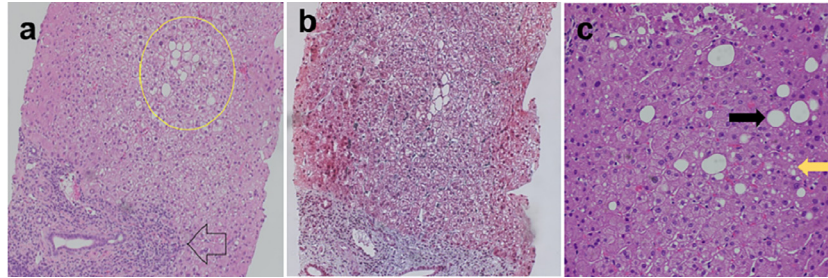


Fig. 4 – Histopathology exam in patient 1. (A) H&E at 10x magnification demonstrates benign hepatic tissue with small areas of focal, mild, steatosis (yellow circle). There is stage II periportal fibrosis and mild inflammation of the portal tracts (arrow). (B) A trichrome special stain of the same biopsy at 10x magnification highlights the periportal fibrosis without any additional pathologic findings. There are no vascular lesions identified in the submitted tissues. (C) 20x magnification of the biopsy demonstrating both the focal macrovesicular steatosis (black arrow) and some clinically insignificant microsteatosis (yellow arrow).

In summary, as the prevalence of steatosis continues to increase, radiologists are likely to encounter MFNHS in their practice and should be knowledgeable of its typical imaging characteristics and management. Ultrasound and CT findings are often nonspecific in diagnosing MFNHS and are often suspicious for malignancy which prompts unnecessary biopsies. MRI is a reliable modality in detecting and characterizing MFNHS.

Patient consent

This retrospective study was approved by the IRB and it was exempted of obtaining a written, informed consent.

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