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Multifocal nodular hepatic steatosis: A rare benign disorder that mimics Metastatic Liver Disease

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Abstract: *Hepatic steatosis is a frequent benign liver condition. Rarely, it adopts a multifocal nodular pattern mimicking multiple liver metastases. A correct diagnosis is crucial to address prognosis and eventual treatment. We present the case of a 57-year-old male with an incidental finding of multiple hypodense liver lesions suggestive of liver metastases, with an unknown primary malignancy. He was extensively investigated with radiological imaging, endoscopy, and liver biopsy. Histopathology confirmed the diagnosis of multifocal nodular fatty infiltration. The peculiarity of this case was the association of multiple focal nodular liver lesions with hepatic steatosis, and atypical imaging findings that required histological confirmation. Multifocal nodular fatty infiltration of the liver entails a challenging problem that should be included as a differential diagnosis when dealing with healthy patients with an incidental finding of multiple liver lesions.*

Keywords- *hepatic steatosis, fatty liver, multifocal nodular liver lesions, liver metastases, unknown primary*

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I. Introduction

Hepatic steatosis is a benign condition characterised by diffuse or focal fatty infiltration of the liver parenchyma. It can be idiopathic or secondary to diabetes mellitus, obesity, alcohol use, hepatitis, or parenteral nutrition.[1] Fatty infiltration of the liver usually has a diffuse pattern in the parenchyma, with diffuse increased echogenicity on ultrasound scan (USS), reduced density on computed tomography (CT) and T1-hyperintense texture on magnetic resonance imaging (MRI).[2, 3, 4] Rarely, however, fatty infiltration may appear as multiple nodular areas separated by normal liver tissue producing a pseudotumor appearance. This may pose a diagnostic dilemma as its imaging appearance mimics metastatic liver disease. Advanced imaging techniques and a complete clinical assessment are the key to the diagnosis of this rare entity. We present the case of a patient referred for possible liver metastases of unknown origin.

II. Case Report

A 57-year-old male was referred to our institution for an incidental finding of multiple hepatic lesions found on computed tomography (CT) scan of the chest for work up of left lower lung consolidation. Based on the radiological findings, metastatic liver disease was suspected. On presentation he was asymptomatic and denied any respiratory, gastrointestinal, or hepatobiliary symptoms. He denied recent weight loss or signs of active infection. He had no history of malignancy or recent trips abroad and no significant family history. His past medical history included hypertension, asthma, and moderate alcohol consumption (two standard drinks/day). Physical examination was unremarkable aside from an elevated body mass index (BMI) of $27 kg/m^2$.

Routine blood tests were normal aside from mildly deranged liver function with increased alanine aminotransferase (ALT) and aspartate transaminase (AST) of 113U/L and 130U/L respectively. Tumour markers, including carcinoembryonic antigen (CEA), alpha-fetoprotein (α-FP), carbohydrate antigen 19-9 (CA 19-9) and cancer antigen 125 (CA 125) were all within normal limits.

He underwent a thorough diagnostic workup with further radiological imaging, gastroscopy, and colonoscopy. A combination positron emission tomography-computed tomography (FDG PET/CT) scan of the chest, abdomen and pelvis showed multiple isolated hypodense foci scattered throughout the liver (Fig. 1 and Fig. 2). On post-contrast phases, the lesions had similar enhancement to adjacent liver parenchyma, without mass effect or invasion into adjacent vasculature. There was no evidence of a primary tumour or nodal disease.

Gastroscopy and colonoscopy were subsequently performed, and both were unremarkable aside from a sessile polyp in the descending colon which was excised- histopathology confirming tubular adenoma with low grade dysplasia.

After multidisciplinary discussion, the consensus was that there remained insufficient evidence to make a definite diagnosis and that further investigation was needed to exclude malignancy. Magnetic resonance imaging (MRI) of the liver with Primovist contrast was performed and showed a normal sized non cirrhotic liver demonstrating multiple circumscribed lesions throughout the liver parenchyma. No displacement nor invasion of hepatic vascular structures, diffusion restriction, or enhancement after contrast injection was observed. Signal drop on T1 out-of-phase sequence compared with in-phase sequence was seen, indicating the possibility of intracellular lipid content (Fig. 3). No lesions could be seen in fat-suppression images. An ultrasound guided liver biopsy was subsequently performed to confirm the histopathological diagnosis of multifocal nodular hepatic steatosis.

The patient was informed of the diagnosis and was enrolled in a surveillance program. During surveillance, a 6-month and 12-month follow up MRI liver was performed, showing stability of the hepatic steatosis. He has remained completely asymptomatic.

III. Discussion

Hepatic steatosis is a benign condition characterised by the accumulation of excessive fat in the liver. This condition affects ten to twenty-four percent of the general population and up to 75% of obese individuals.[1] Multinodular focal fatty infiltration is considered an uncommon and atypical manifestation of focal fatty liver. Due to its spherical shape and multifocal distribution, multinodular fatty infiltration does not meet the conventional imaging criteria generally used for the diagnosis of focal fatty liver.[5,6,7] Therefore, this multinodular variety of fatty infiltration has frequently been mistaken for metastatic disease and can be a diagnostic challenge for clinicians and radiologists alike.[7,8]

Hepatic steatosis can be diagnosed by three main imaging modalities: ultrasound, CT scan and MRI.[2,3] Ultrasound is relatively insensitive as it requires at least 30% fat to detect an increased echogenicity that is characteristic of steatosis.[9] CT imaging shows steatosis as having lower density than normal liver parenchyma but is also unable to detect lower fat quantities.[5] The differential diagnosis of CT-hypodense lesions should therefore include other benign and malignant conditions such as simple cysts, adenomas, abscesses, and lymphoma in addition to the possibility of liver metastasis.[3,8] It is therefore important for practitioners to consider clinical presentation, past medical history, previous malignancy, long-term medications, and family history in the evaluation of patients with multiple hypodense liver lesions. For instance, in a seriously ill patient who has a history of malignancy and/or abnormal blood test results, the diagnosis of malignant metastatic disease is more likely; on the contrary, in a young, fit, and asymptomatic patient who has normal blood test results and no significant past medical history, other possible diagnoses should therefore be considered.

In addition to complete clinical assessment, advanced imaging techniques such as MRI currently represents the most specific imaging modality for the diagnosis of fatty liver. [5, 7, 10] MRI can provide information on the histologic characteristics of liver lesions, with a very high specificity, especially for fat-containing lesions.[10] Out-of-phase T1-weighted gradient-echo imaging is a highly accurate technique to distinguish focal hepatic steatosis from neoplastic masses. Focal hepatic steatosis is isointense or hyperintense to liver parenchyma on in-phase images and loses signal homogenously on out-of-phase images, which is highly diagnostic for focal steatosis. [5] Diagnosis is also suggested by lack of mass effect on vessels, or the biliary system.

In line with previous studies, the combination of contrast enhanced CT imaging and in and out-of-phase MRI yields the most accurate differentiation between the diagnosis of liver metastases and multinodular focal fatty infiltration.[3, 4, 6] Although MRI has been proposed as a valid alternative to biopsy[10], we felt that the risk of misdiagnosis was significant enough that we could not rely solely on non-invasive imaging techniques alone. In future, with a higher index of suspicion on part of the radiologist or treating physician at the time of initial investigation, the combination of CT and MRI might be considered as the most appropriate modality to avoid unnecessary workup and anxiety in these patients. However, it must be emphasised that a percutaneous or laparoscopic liver biopsy might be needed in patients with inconclusive imaging results.

IV. Conclusion

The diagnosis of liver lesions may be a challenge for clinicians and radiologists. In our case, focal hepatic steatosis was diagnosed after an extensive workup for metastatic disease involving multiple invasive and non-invasive procedures. Focal steatosis presents a diagnostic dilemma as the need to exclude malignant aetiology often outweighs the risks of invasive procedures. Clinical presentation must be considered, as well as past medical history and family history. Our case demonstrates that the utilisation of CT and MRI imaging in evaluating liver masses can potentially decrease the cost and morbidity associated with invasive procedures such

as endoscopy and liver biopsy. However, biopsy can play a crucial role in confirming the diagnosis in doubtful cases. Multifocal nodular fatty infiltration of the liver should be considered in the differential diagnosis of multiple liver lesions, especially if the patient's clinical presentation is not consistent with advance malignant disease.

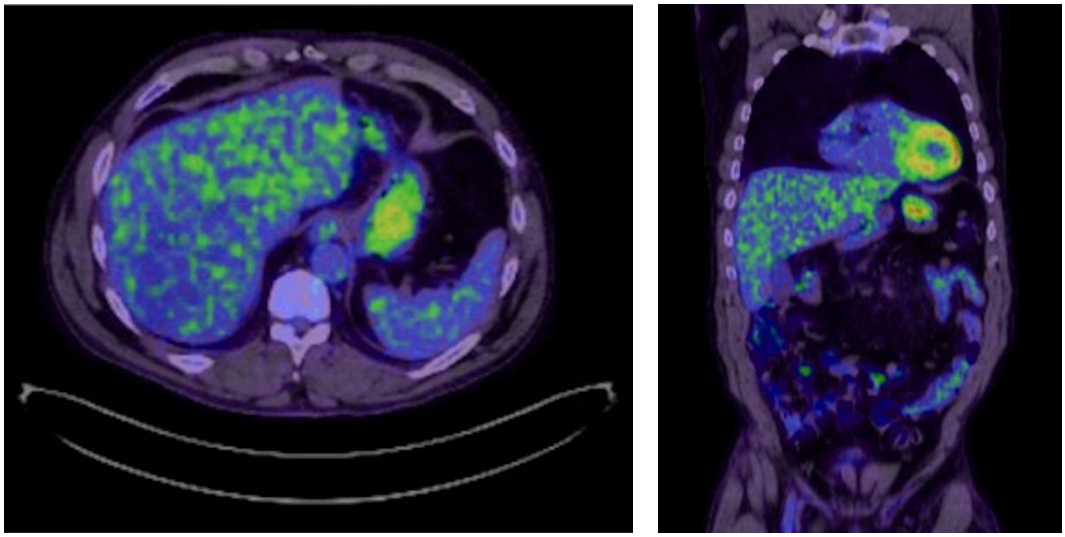

Fig 1. FDG PET/CT of chest, abdomen, pelvis showing no FDG avidity in the liver

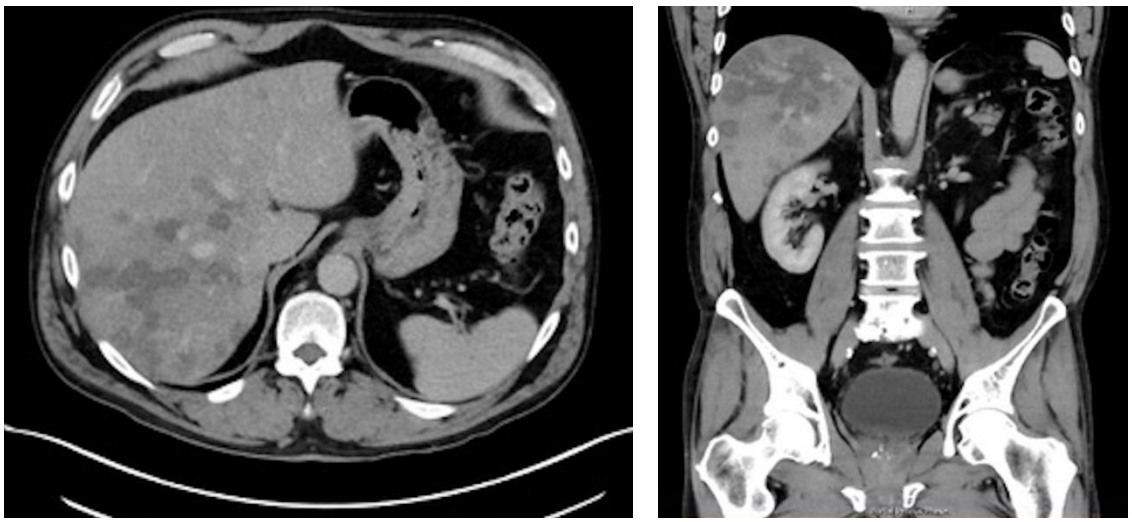

Fig. 2 Abdominal contrast-enhanced computed tomography scan showing multiple liver hypodense lesions

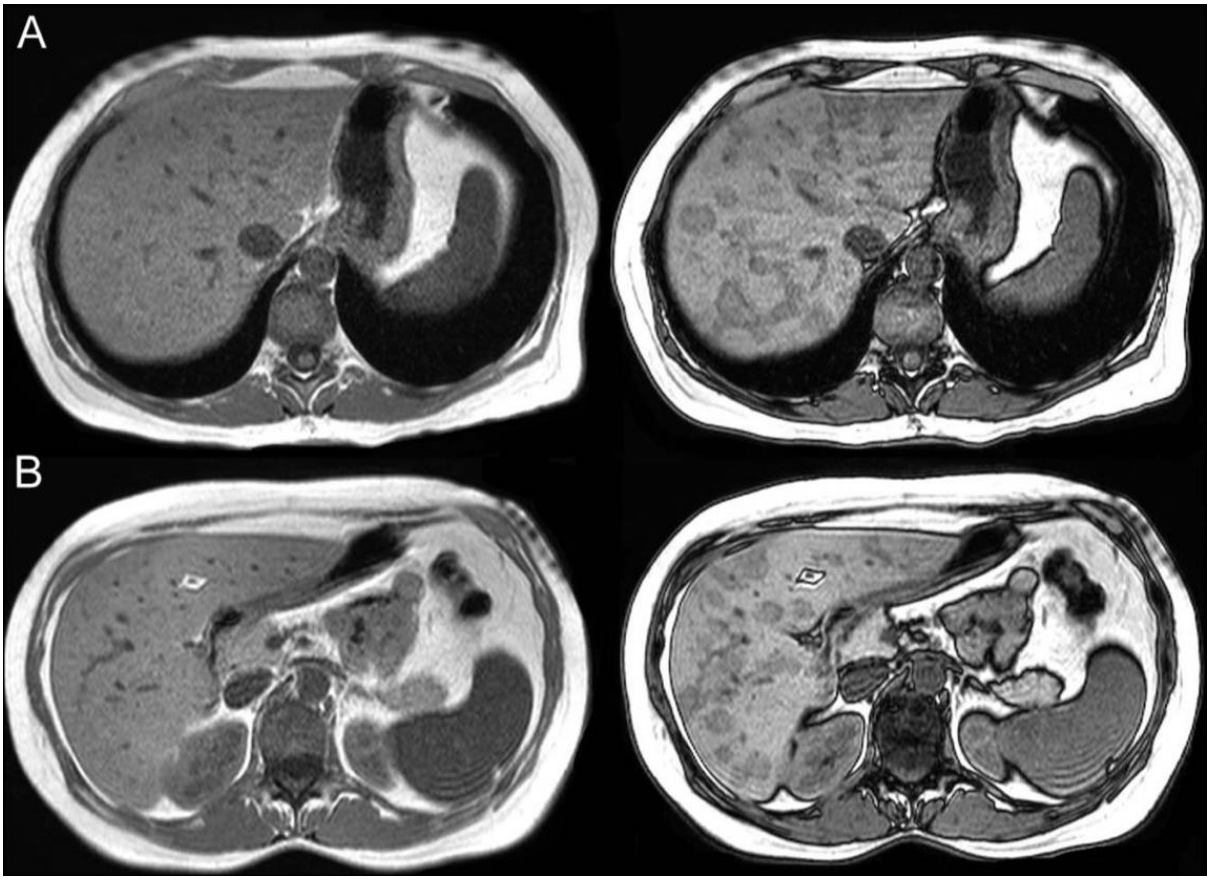

Fig. 3 (A and B) Liver magnetic resonance imaging out-phase (left) and in-phase (right) image showing signal drop on the latter, indicating intracellular lipid content into hepatic lesions.

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