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MEDICAL IMAGING

Fatty liver – What does this mean?

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In the gastronomic sense, it would probably induce copious salivation and an urge for a thick slab of foie gras on toast and a glass of tannic red Bordeaux. But Hyperechoic liver texture compatible with fatty infiltration also happen to be frequent introductory statement on many of my abdominal ultrasound reports that are written at a time when I cannot afford such luxury. Fatty liver is a term applied to a wide spectrum of conditions characterized histologically by triglyceride accumulation within the cytoplasm of hepatocytes.

The two most common conditions associated with fatty liver are alcoholic liver disease and nonalcoholic fatty liver disease. Alcoholic liver disease is caused by excess alcohol consumption, whereas the nonalcoholic variant is related to insulin resistance and the metabolic syndrome. Other relatively common conditions associated with fat accumulation in the liver include viral hepatitis and the use or overuse of certain drugs. Rarer associated conditions include dietary and nutritional abnormalities and congenital disorders (Table 1).

Most Common	Common	Rare	Congenital
Alcohol overuse	Viral infection	Nutritional or dietary abnormality	Monogenic disorders
Insulin resistance	Hepatitis C	Total parenteral nutrition	Metabolic disorders
Obesity	Hepatitis B	Rapid weight loss	Fatty oxidation defect
Hyperlipidemia	Drug use	Starvation	Organic aciduria
	Steroids	Surgery (eg, jejuno-ileal bypass)	Aminoacidopathy
	Chemotherapeutic agents	Iatrogenic injury	Storage disorders
	Amiodarone	Radiation therapy	Glycogen storage disorder
	Valproic acid		α_1-Antitrypsin deficiency
			Wilson disease
			Hemochromatosis
			Other
			Cystic fibrosis
			Dysmorphic syndromes associated with obesity
			Bardet-Bridel
			Prader-Willy

Table 1. Conditions associated with fatty liver disease.

These conditions all cause a triglyceride accumulation (steatosis) within hepatocytes by altering the hepatocellular lipid metabolism, in particular, by causing defects in free fatty acid metabolic pathways. Hepatocytes in the centre of the lobule (near the central vein) are particularly vulnerable to metabolic stress and tend to accumulate lipid earlier than those in the periphery. Consequently, in many of these conditions, steatosis tends to be most pronounced histologically in the zone around the central veins and less pronounced in zones around the portal triads. In advanced cases, there is diffuse, relatively homogeneous involvement of the entire lobule.

Figure 1. *Normal liver parenchyma (p) shows echogenicity similar to that of the adjacent right renal cortex (rc).*

In many conditions associated with fatty liver, steatosis may progress to steatohepatitis (with inflammation, cell injury, or fibrosis accompanying steatosis) and then cirrhosis. However, because progression to steatohepatitis is uncommon, a 'two-hit' model has been proposed. The 'first hit' is the cytoplasmic deposition of triglycerides in hepatocytes, which may make the hepatocytes more vulnerable to a 'second hit' but which, in the absence of the second hit, does not lead to progressive disease. The second hit has not yet been identified but is thought to represent a constellation of superimposed cellular events that promote inflammation and cell injury and incite progression to fibrosis and cirrhosis. In support of the two-hit model, there are data that suggest that the coexistence of steatosis with other liver diseases, such as viral hepatitis, increases the risk of disease progression.

The prevalence of fatty liver in the general population is about 15%, but it is higher among those who consume large quantities (>60 g per day) of alcohol (45%), those with hyperlipidemia (50%) or obesity (body mass index, >30 kg/m^2) (75%), and those with both obesity and high alcohol consumption (95%).

Common patterns include diffuse fat accumulation, diffuse fat accumulation with focal sparing, and focal fat accumulation in an otherwise normal liver. Unusual patterns that may cause diagnostic confusion by mimicking neoplastic, inflammatory, or vascular conditions include multinodular and perivascular accumulation. All of these patterns involve the heterogeneous or nonuniform distribution of fat.

On ultrasound, the echogenicity of the normal liver equals or minimally exceeds that of the renal cortex or spleen (Figure 1). Intrahepatic vessels are sharply demarcated, and posterior aspects of the liver are well depicted.

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Fatty liver – Wha

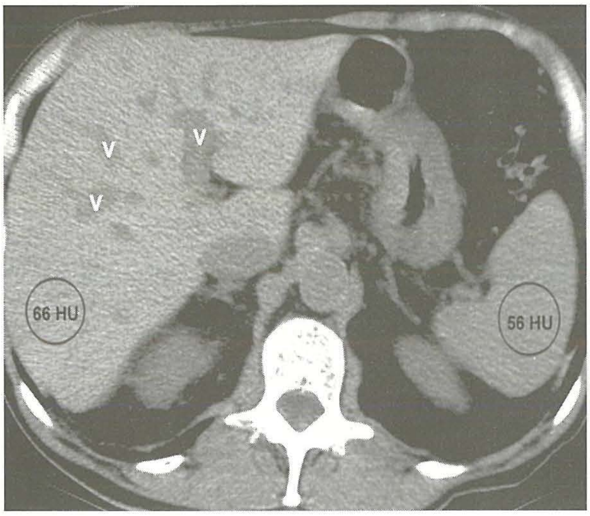

Figure 2. *Normal density of the liver at unenhanced CT (66 HU) is slightly higher than that of the spleen (56 HU), and intrahepatic vessels (v) appear hypodense in comparison with the liver.*

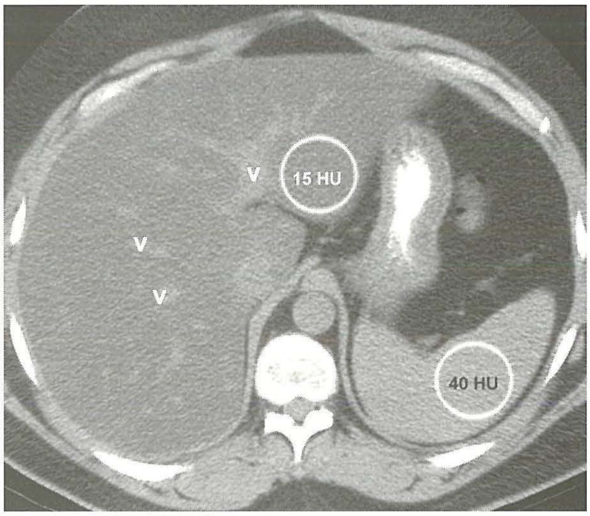

Figure 4. *With diffuse fat accumulation in the liver at un-enhanced CT, the density of the liver (15 HU) is lower than that of the spleen (40 HU) and intrahepatic vessels (v) appear hyperdense in comparison with the liver.*

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Fatty liver may be diagnosed if liver echogenicity exceeds that of renal cortex and spleen and there is loss of definition of more posterior portions of the liver due to beam attenuation (Figure 2).

At unenhanced computed tomography (CT), the normal liver has similar density that the spleen or blood (Figure 3). A liver density less than 40 Hounsfield Units (HU) or more than 10 HU below that of the spleen, is diagnostic of fatty infiltration. In cases of severe fatty liver, the vessels

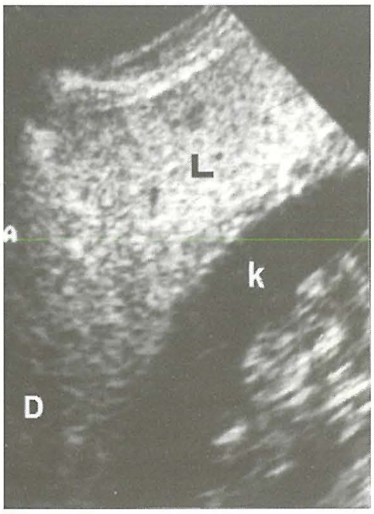


Figure 3. *With diffuse fatty infiltration of the liver, the liver (L) shows increased echogenicity compared to the renal parenchyma (K) and there is loss of definition of the deeper portions of the liver due to beam attenuation (D).*

may appear denser (whiter) than the liver parenchyma (Figure 4). Following IV contrast enhancement, comparison of liver with spleen or vessel density is unreliable due to difference in tissue contrast enhancement in different phases of perfusion.

At MR imaging, chemical shift gradient-echo (GRE) imaging with in-phase and opposed-phase acquisitions is the most widely used technique for the assessment of fatty liver. The signal intensity of the normal liver parenchyma is similar on in-phase and opposed-phase images. Fatty liver shows loss of signal intensity (ie becomes darker) on opposed-phase imaging and loss of signal is proportional to the extent of fat deposition. A simplistic explanation for this phenomenon is that during in-phase imaging, the signals of fat and water protons are in phase and both contribute positively to tissue brightness (Figure 5 a), while on opposed-phase imaging, fat signal is negative compared to water signal and cancels it out resulting in dark parenchyma (Figure 5b).

Less common patterns such as focal fat deposition and diffuse fat deposition with focal sparing characteristically occurs in specific areas; these areas are adjacent to the falciform ligament or ligamentum venosum, in the porta hepatis, and in the gallbladder fossa. This distribution has been attributed to variant venous circulation, such as anomalous gastric venous drainage. Focal fat deposition adjacent to insulinoma metastases also has been reported and is thought to be due to local insulin effects on hepatocyte triglyceride synthesis and accumulation.

The diagnosis of focal fat deposition and focal sparing is more difficult than that of homogeneously diffuse fat deposition because imaging findings may resemble mass lesions. Imaging findings suggestive of fatty pseudolesions rather than true masses include (a) fat content confirmed on opposed-phase MR imaging,

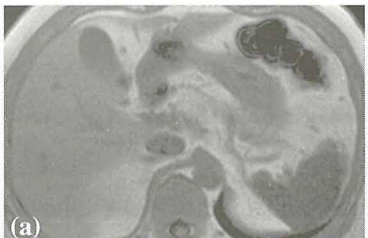
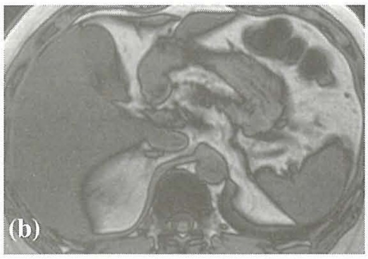


Figure 5. *T1-weighted GRE MR images of a fatty liver show a bright parenchymal signal on the in-phase image (a) and marked decrease in the signal intensity of the liver on the opposed-phase image (b).*



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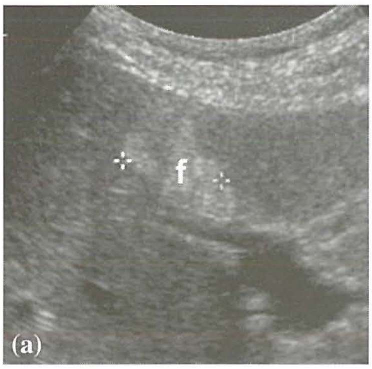
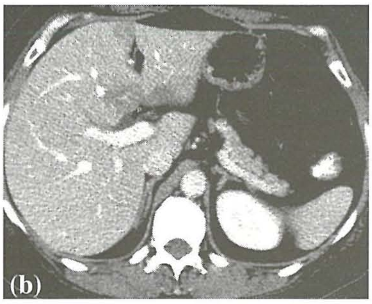


Figure 6. *(a) Transverse US image shows a geographically shaped hyperechoic area (asterisks) anterior to the left portal vein and around the falciform ligament (f). (b) CT scan showing foci of fatty infiltration (darker areas) next to the falciform ligament (f) and anterior to the porta hepatis (p).*



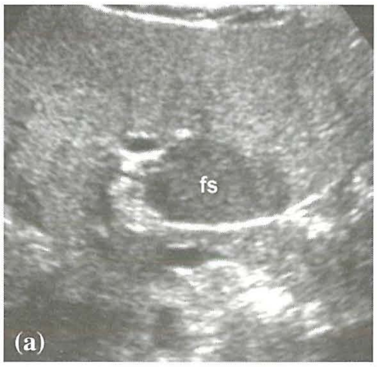


Figure 7. *(a) US image of a diffusely fatty infiltrated liver with focal sparing (fs). (b) Unenhanced CT image shows the area of focal sparing (fs) as hyperdense compared to the remaining diffusely fatty liver. The area of focal sparing exerts no mass effect on the adjacent vessel (v).*

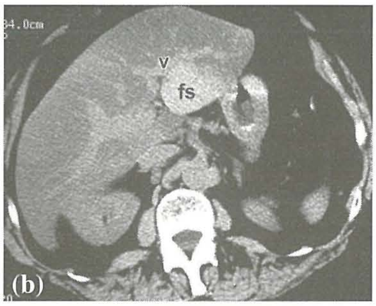
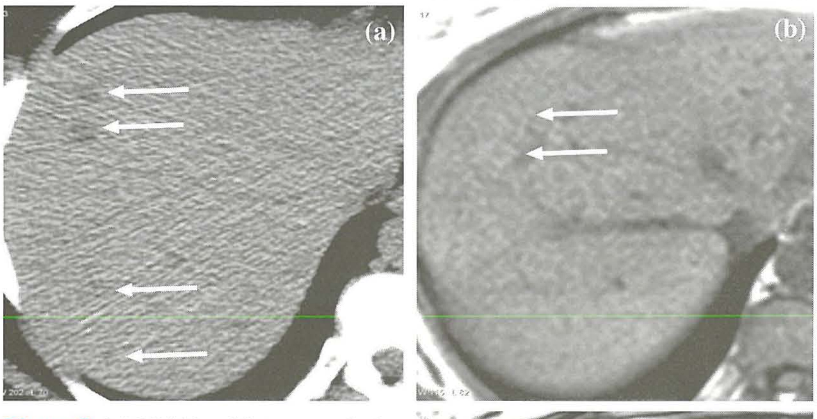


Figure 9. *The hypodense area in the right liver lobe on unenhanced CT (a) may prompt the diagnosis of focal fatty infiltration, however scans obtained during the portal venous phase of IV contrast injection (b) show a nodular liver contour suggestive of cirrhosis, as well as large gastric varices (arrowheads), mass effect with bulging of the anterolateral border of the right liver lobe (arrow), the mosaic enhancement pattern, and the thrombus (t) in the left main portal vein, which are strongly suggestive of an infiltrative hepatocellular carcinoma.*



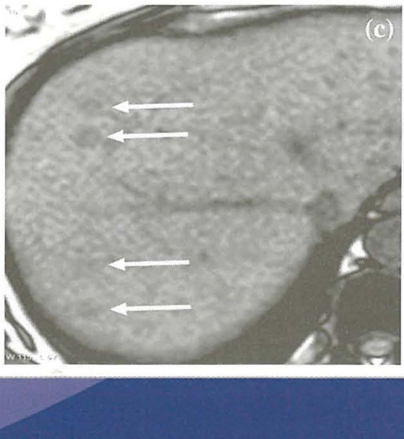


Figure 8. *(a) Multifocal fat accumulation in the liver appears as hypodense foci on unenhanced CT scan in a 48-year-old woman with breast cancer was misdiagnosed as liver metastatic disease on the basis of CT findings. T1 weighted GRE MR images show nodules (arrows) with signal intensity slightly higher than that of the normal liver parenchyma on the in-phase image (b) but with a signal intensity loss on the opposed-phase image (c); this confirms the diagnosis of multifocal fat accumulation.*

(b) typical location in areas characteristic of fat deposition or sparing, (c) absence of a mass effect on vessels and other liver structures, (d) a geographic configuration (wavy outline) rather than a round or oval shape, (e) poorly delineated margins, and (f) contrast enhancement that is similar to or less than that of the normal liver parenchyma. The fatty foci are hyperechoic on US and hypodense on CT compared to surrounding liver parenchyma (Figure 6). As expected, the situation is reversed with focal sparing in a diffusely fatty liver, with the spared focus being hypoechoic on ultrasound and hyperdense on CT (Figure 7).

Multifocal fat Deposition is an uncommon form of fatty liver, where multiple fat foci are scattered in atypical locations. The foci may be round or oval and closely mimic true nodules.

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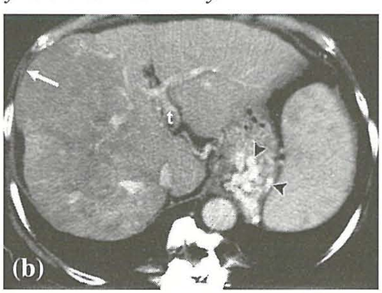
Fatty liver – What does this mean?

Figure 10. *In a woman with a long history of oral contraceptive use in-phase (a) and opposed-phase (b) T1-weighted GRE images show loss of signal in two left lobe liver lesions (arrows) in opposed-phase image suggestive of focal fatty infiltration. However T1-weighted GRE images obtained during the hepatic arterial phase of IV contrast injection (c) show enhancement of the masses. The location of the lesions is atypical for regions of focal fatty infiltration. The two masses remained stable in size for several years and most likely are adenomas.*



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Correct diagnosis is difficult, especially in patients with a known malignancy, and requires the detection of microscopic fat within the lesion with chemical shift GRE imaging, which is more reliable in these cases than CT or US (Figure 8). Other clues indicative of multifocal fat deposition are lack of a mass effect, stability in size over time, and contrast enhancement similar to or less than that in the surrounding liver parenchyma. Multifocal fat deposition may be observed within regenerative nodules in some cirrhotic patients, where foci of fat accumulation correspond to the fat-containing regenerative nodules.

The differential diagnosis of the different types of fatty liver from malignant lesions may not be so easy. Primary liver lesions such as hepatocellular carcinoma (particularly the infiltrative type) (Figure 9) and hepatic adenoma (Figure 10) may closely resemble focal fatty infiltration. While multiple hepatic metastases in a fatty liver, may be mistaken as areas of focal sparing (Figure 11).

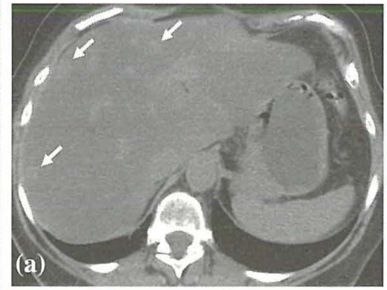

Figure 11. *Pre (a) and post-IV (b) contrast CT scans showing metastases in a fatty liver in a woman undergoing chemotherapy for breast cancer. Multiple round lesions (arrows) enhanced more vividly than the liver parenchyma.*

To help prevent diagnostic errors and guide appropriate work-up and management, one should be aware of the different patterns of fat accumulation in the liver, especially as they are depicted at ultrasonography, computed tomography, and magnetic resonance imaging. In addition, knowledge of the risk factors and the pathophysiologic, histologic, and epidemiologic features of fat accumulation may be useful for avoiding diagnostic pitfalls and planning an appropriate work-up in difficult cases. Finally, should the diagnosis remain unclear, one should not hesitate to perform imaging-guided core biopsy of the suspicious area.

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