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Hepatic steatosis: A major trap in liver imaging

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Abstract  Hepatic steatosis is a common condition, the prevalence of which is increasing along with non-alcoholic hepatic steatosis. In imaging, it can present in a typical homogeneous or heterogeneous way. Some forms create traps in imaging, whether localised steatosis is concerned or areas which have been spared by steatosis, and the purpose of this paper is to explain and illustrate them. The role of different imaging methods is described while emphasizing the importance of MRI.

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Definition

Steatosis is defined as the accumulation of fatty acids in the form of triglycerides in the cytoplasm of hepatocytes. In histological terms, this usually appears as macrovesicular steatosis, with large intracytoplasmic vacuoles displacing the nucleus to the periphery of the cells. More rarely, microvesicular steatosis is seen, which consists of smaller vacuoles leaving the nucleus in a central position. Microvesicular steatosis can occur with the macrovesicular form. When it is present alone, particular causes should be sought: steatosis in pregnancy, Reye’s syndrome, and certain drug-induced steatoses.

Table 1 summarises the most commonly observed causes of classic macrovesicular steatosis. Alcohol is one of the main causes of hepatic steatosis. Non-alcoholic steatosis (non-alcoholic fatty liver disease [NAFLD]) is mainly observed in patients with metabolic syndrome; what is more, it is considered as the hepatic manifestation of this syndrome. Unlike steatosis of alcoholic origin, different types of steatosis and evolutionary profiles are seen in non-alcoholic steatosis: pure steatosis, steatohepatitis or even cirrhosis.

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In steatohepatitis (non-alcoholic steatohepatitis [NASH]), steatosis is associated with necrotic-inflammatory lesions with hepatocyte ballooning. Mallory bodies may be seen. NASH can present various degrees of fibrosis and evolve towards cirrhosis. Hepatocellular carcinoma complicates this condition and can occur during cirrhosis or even in the stages prior to this [1].

**Epidemiology**

Hepatic steatosis has become a very common cause of liver disease due to the increased prevalence of overweight and obese individuals in the world. In France, more than 46% of the general population are overweight [2]. The prevalence of metabolic steatosis varies worldwide between 43 and 45% [1], and is lower in Asian countries than in Western countries. It is much higher in at-risk populations, such as patients with type II diabetes or obese patients, where it varies between 50 and 90% [1]. A recent French survey has underlined the high frequency of failure to recognise steatohepatitis. A large number of patients being monitored by endocrinologists for a suspected metabolic syndrome are not referred to hepatologists. In addition, the diagnosis of steatohepatitis is difficult in patients with normal transaminases [3].

**What is the role of radiologists in hepatic steatosis?**

They need to know:
- how to recognise hepatic steatosis;
- how to quantify it;
- how to attempt to differentiate pure steatosis from steatohepatitis;
- how to avoid the traps presented by hepatic steatosis in imaging that will be illustrated below.

**Excessive diagnosis of steatosis**

The first difficulty is to avoid false positives for steatosis. The imaging presentation of steatosis is not entirely specific. With ultrasound, steatosis increases liver echogenicity and thus increases the liver/kidney and liver/vascular gradient. There are however other causes of hyperechogenicity, especially overload diseases.

While hypoattenuation, sparing the vessels, suggest steatosis in CT, this appearance can also be encountered during infiltration, particularly by a tumour, and enhancement parallel with the rest of the liver is not totally specific for steatosis (Fig. 1).

**MRI** is of course the most sensitive and most specific imaging method for diagnosing steatosis. In addition, it provides the best quantification of the percentage of fat within the liver. The signal drop on opposed-phase images, which are obtained by putting the water protons and fat protons at 180°, is perfectly characteristic. Iron overload is a classic trap. In this case, a signal drop is seen on in-phase images but not on opposed-phase images in 1.5 Tesla MRI where the first echo time is the one that is opposed-phase, the second being in-phase. This is not a question of hepatic steatosis, but of increased dephasing of the signal becoming greater with increasing TE values (Fig. 2).

**Heterogeneous steatosis**

Heterogeneous steatosis does not always pose a difficult diagnostic problem. Diagnosis is easy when the condition presents as a linear field, with no mass effect, and with vascular integrity. This field appears homogeneous and hyperechoic with ultrasound, hypoattenuating with CT both before and after injection, with a signal drop on MRI opposed-phase T1-weighted images. It is even possible to see a greater fall in the border of the area richer in fat than the rest of the liver (Fig. 3). In other circumstances, steatosis can be misleading as it assumes a pseudotumoral form.

**Localised area of steatosis or localised areas spared by steatosis**

There is usually topographic predominance in the heterogeneous distribution of steatosis. These areas are situated close to the hilum plate: the posterior surface of segment IV, anterior surface of segment I, posterior surface of the left lobe and on either side of the gallbladder (Fig. 4). There is classically also higher incidence of localised steatosis close to the round ligament. Macari et al. [4] found a high percentage of abnormalities close to the round ligament using MRI (in 21 of the 121 patients investigated). The majority of them were instances of hypointensity appearing in the portal phase and most did not show a signal drop on opposed-phase images, which suggests a perfusion disorder much more than localised steatosis.

| Table 1 Principal causes of macrovascular steatosis. |
|-------------------|-----------------|--------------|-----------------|
| Very common        | Common          | Uncommon     | Congenital  |
| Alcohol            | Hepatitis C     | Nutrition    | Genetic       |
| Insulin resistance | Medicinal products | Parenteral nutrition | Metabolic overload |
| Obesity            | Corticosteroids | Under-nutrition |                |
| Hypertriglyceridaemia | Chemotherapy | Weight loss |                |
|                    | Amiodarone      | Bypass       |                |
|                    | Tamoxifen       | Extensive resection of the small intestine |                |
|                    | Methotrexate    | Radiotherapy |                |
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Figure 1.  a–c: tumoral infiltration of the left liver mimicking localised steatosis. Contrast-enhanced CT in the arterial, portal and late phases. Hypoattenuating infiltration of the left liver without vascular involvement or mass effect, corresponding to metastatic infiltration. Presence of a layer of ascites. Note the absence of vascular invasion.

Figure 2.  Hepatic iron overload. In-phase (a) and opposed-phase (b) T1-weighted sequences. Drop in hepatic signal on the in-phase sequence, explained by dephasing of the protons due to disturbance of the magnetic field (high iron concentration in the liver). This signal drop should not be taken for hepatic steatosis. Note that it may be a confusing factor if hepatic steatosis and iron overload occur together.
Figure 3. MRI of heterogeneous steatosis: a: presence of marked hypointensity of the right liver on the T2-weighted sequence with fat suppression; b, c: the right liver is hyperintense with in-phase T1-weighted sequence (b) and there is signal drop on the opposed-phase image (c). Note an even more fatty border zone between the steatotic and less steatotic liver.

In patients with a steatotic liver, Aubin et al. [5] showed fatty sparing of the perivesicular segments IV and V, which was much greater in patients who still had their gallbladder (78%) than in cholecystectomised patients (33%). These authors therefore suggested a venous explanation, as there are almost always small cystic veins that drain directly into the liver and which are interrupted by cholecystectomy.

Similarly, when CT arterial portography was the examination customarily performed in preoperative evaluation of liver metastases, a large number of cases of lack of perihilar or pericholecystic enhancement were observed after selective injection into the superior mesenteric artery, leading to the assumption that venous supply to these territories did not come directly from the portal vein, but perhaps from other branches. This was confirmed by Asian work which demonstrated that patients with lack of enhancement in CTAP had aberrant venous return from the gastric vein or duodenopancreatic venous arcade [6–8].

The physiopathological explanation for these steatoses or fatty sparcings preferentially localised in certain territories...
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Figure 5. Coronal reconstruction of an abdominal CT scan in the portal phase showing the drainage of the gastric and duodenopancreatic veins: a: normal drainage of the gastric veins and the superior branch of the posterior duodenopancreatic arcade (blue). These veins drain into the trunk of the portal vein; b: aberrant drainage of a gastric vein draining directly into the liver (violet). The hepatic territory low in insulin explains an area spared by the fat in a steatotic patient; c: aberrant drainage of the superior branch of the posterior duodenopancreatic arcade draining directly into the liver (green). The hepatic territory receiving this posterior portal branch has a higher insulin level which may explain localised steatosis.

was supported by a theory concerning insulin, which stimulates the conversion of glucose to fatty acids. About 30% of the vascular supply to the liver comes from the hepatic artery and about 70% from the hepatic portal vein. The flow in the portal vein comes from its principle tributaries: the splenic vein, the superior mesenteric vein, the inferior mesenteric vein, and tributaries that empty directly into the hepatic portal vein (the left gastric vein, the right gastric vein and the superior branch of the posterior duodenopancreatic arcade). The insulin content of these tributaries is very variable, as the gastric veins contain little insulin whereas the duodenopancreatic arcades contain more than the rest of the portal system. The drainage of these veins frequently varies. Left, or more frequently right gastric veins can be seen that flow directly into the liver (mainly into segment IV), leading to a lower insulin concentration there and thus resulting in a patient, who moreover has hepatic steatosis, having a focal area of hepatic parenchyma which is less fatty than the rest of the liver (Fig. 5). Similarly, the superior branch of the duodenopancreatic arcade may empty not into the portal vein itself but intrahepatically near the hilum, resulting in a focal area that receives more insulin and thus becomes more fatty. Figs. 6 and 7 illustrate these two situations.

Peripherally distributed steatosis

The appearance of peripheral, subcapsular predominance of hepatic steatosis is particularly misleading. It is usually observed in patients on peritoneal dialysis with intraperitoneal administration of insulin, the insulin being absorbed by diffusion through the portal system. This method is used by some teams to avoid subcutaneous insulin injections [9].

Multiple pseudotumour steatosis

In some patients, heterogeneous steatosis does not appear as a field but as multiple lesions that are more fatty than the rest of the liver and distributed throughout the whole of the liver parenchyma. These lesions strongly suggest liver tumours. They are hyperechoic and homogeneous with ultrasound, hypoattenuating in all CT phases, with enhancement theoretically parallel to that of the liver. However, there is often a reduction in the contrast between these lesions and the rest of the liver in the late phase. MRI with an in-phase and opposed-phase T1-weighted sequence will show the fatty nature of these islets. The differential diagnosis is naturally with other multiple fatty tumours with, in the forefront, the steatotic variety of hepatic adenoma. The
multiplicity of lesions, their small size (less than 2 cm) and their often being the same size, enhancement similar to the liver and the inconsistent but very pathognomonic presence of a still more fatty border of the peripheral part of these fatty islets are features favouring pseudotumour steatosis (Fig. 8). Features in favour of diagnosis of multiple hepatic adenomas are the variable size of the lesions and possible (often moderate) increased vascularisation in the arterial phase [10,11].

Atypical focal fatty sparing

In steatotic patients, a rare but very misleading appearance is an islet of healthy liver, or one containing less fat than the rest of the liver parenchyma, outside the areas particularly exposed to different insulin concentrations. The differential diagnosis is with a hepatic tumour in a steatotic liver. These particularly misleading forms can be diagnosed since they do not show hypervascularisation in a combination of imaging examinations (particularly with contrast-enhanced ultrasound).

Perivascular steatosis

Very exceptionally but very characteristically, steatosis may predominate around vessels (Fig. 9). The largest series reported in the literature consisted of ten patients in whom perivascular steatosis predominated around the hepatic veins in three, around the portal branches in five, and both around the hepatic veins and portal branches in two patients [12]. In three of these ten patients, perivascular steatosis was not recognised on the CT scan and the diagnosis was corrected by MRI. There is no clear explanation for this very particular presentation of steatosis.

Steatosis and hepatic tumours

Diagnostic difficulties

Characterisation of focal liver lesions is based on a different non-contrast enhanced signal and different behaviour of the lesion after injection relative to the rest of the
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Figure 7. Localised steatosis of the posterior part of segment IV: a, b: in-phase and opposed-phase T1-weighted MRI. The posterior part of segment IV is hyperintense in phase (a) and there is a marked homogeneous signal drop on the opposed-phase image (b); c, d: CT scan in the portal phase after injection showing marked hypovascularity of segment IV. A vessel is seen directly entering the liver (c), much clearer on the MIP reconstruction (d). This is aberrant drainage of the superior branch of the posterior duodenopancreatic arcade.

Peritumoral changes

Peritumoral changes can be seen in patients with hepatic steatosis. They generally produce an area that is less fatty than the rest of the liver and is usually seen around hypervascular lesions or tumours, whether they are benign (focal nodular hyperplasia, flash filling hemangioma) or hypervascular malignant tumours (hepatocellular carcinoma, endocrine metastasis). The mechanism of this area spared of fat is not completely understood, although it is probably a matter of remodelling related to modification of the vascularisation. The increased arterialisiation of the tumour is frequently associated with an increased arterial supply to the surrounding territory, which explains the decrease in fat concentration. In imaging, the appearance is misleading as these changes can look like a peritumoral capsule. They are clearly visible with CT and even better with MRI where a hyperintense “collar” between the lesion and the rest of the liver can be seen on opposed-phase T1-weighted images; this collar is invisible in in-phase T1-weighted, T2-weighted and diffusion sequences (Figs. 10 and 11).

More rarely, peritumoral changes may be the result of a change in insulin concentration around the lesion. Thus, very characteristically, there is localised steatosis around liver metastases of insulinomas. Here again, this collar with signal drop on opposed-phase images must not be interpreted as a perilesional capsule. Superimposition of in-phase, opposed-phase, and fat saturation T1-weighted images and other sequences (T2-weighted and diffusion) helps locate the lesion and identify peritumoral changes (Fig. 12).
Figure 8. Multiple pseudotumour steatosis: a, b: in-phase and opposed-phase T1-weighted sequences showing discretely hyperintense in-phase lesions (a), signal drop on the opposed-phase image (b). Note the even more pronounced signal drop around the lesions; c, d: with fat saturation T1-weighted sequence and after injection, the enhancement of these lesions is parallel to that of the rest of the liver; e: with fat suppression T2-weighted sequence, the lesions are very discretely hyperintense.
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Figure 9. Perivascular steatosis: a–c: in-phase (a), opposed-phase (b), and fat saturation (c) T1-weighted sequences MRI. Presence of hyperintensity on both sides of the left branch of the portal vein in phase, with a massive signal drop on the opposed-phase image (b). The signal drop is much more moderate in the fat saturation sequence (c); d: no abnormality is visible in the T2-weighted sequence with fat suppression.
Figure 10. Flash filling hemangioma in a steatotic liver. Presence of peritumoral changes: a; b: with in-phase (a) and opposed-phase (b) T1-weighting, a subcapsular hypointense lesion measuring a centimetre can be seen in the right liver. Presence of perilesional hyperintensity on the opposed-phase image; c, d: in T1-weighting after injection of gadolinium chelates in the arterial and portal phases, clear massive hypervascularisation of the lesion persisting in the late phase; e: with T2-weighting, this centimetre lesion is clearly hyperintense.
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Figure 11. Subcapsular splenosis of the left liver: a; b: in-phase (a) and opposed-phase (b) T1-weighted sequences. Discretely heterogeneous signal drop of the entire liver, indicating marked steatosis. Presence of a subcapsular hypointense lesion of the left lobe, surrounded by a hyperintense border on the opposed-phase image; c, d: T1-weighted sequences after injection of gadolinium chelates in the arterial phase (c) and late phase (d), which shows clear increased arterialisation of the lesion; e: discretely hyperintense subcapsular lesion with fat suppressed T2-weighted sequence; f: coronal view of contrast-enhanced CT showing no spleen in place. Presence of another site of splenosis in the left hypochondrium. This patient had had a splenectomy secondary to trauma. Opposed-phase T1-weighted image showing the hyperintense border around a highly arterialised lesion in a steatotic liver.
Figure 12.  Hepatic metastasis of an insulinoma: a; b: in-phase and opposed-phase T1-weighted MRI: a lesion is visible in the posterior section of the right liver, surrounded by a border which shows opposed-phase signal drop (b); c: with contrast-enhanced T1-weighted sequence after injection of gadolinium chelates, the lesion is highly arterialised; d: in a diffusion-weighted sequence, clear hyperintensity of the lesion surrounded by a hypointense halo indicating steatosis around the lesion. The localised steatosis is induced by the local secretion of insulin.

The opposite mechanism can be seen with liver metastases of glucagonomas in patients with diffuse hepatic steatosis. In this case, the area spared by fat around the lesions is induced by local secretion of hormones [13].

Conclusion

In conclusion, hepatic steatosis is common and increasing. Its atypical forms are easy to recognise in imaging. When it is heterogeneous it is frequently misleading. MRI and the pathophysiology help provide the correct diagnosis in most cases.

**TAKE-HOME MESSAGES**

**General concepts**
- Hepatic steatosis is a common condition.
- Its prevalence is increasing.
- Imaging (ultrasound, CT and MRI) provides the diagnosis easily when it presents in its classic form.
- MRI with in-phase and opposed-phase T1-weighted sequences is essential when the presentation is atypical.
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Principle results

• Localised steatosis and areas spared of fat in a steatotic liver predominate around the hilum.
• These locations are explained by aberrant intrahepatic drainage of veins of the hepatic portal system.
• Aberrant venous drainage modifies the local concentration of insulin.
• Multiple pseudotumour steatosis mimics fatty intrahepatic tumours and, in first place, hepatocellular adenomas.
• In certain cases, steatosis may predominate in the periphery or around the portal vessels or hepatic veins.
• Hepatic steatosis makes characterising liver tumours more difficult.
• In the steatotic liver, peritumoral changes can be seen around hypervascular liver lesions

Clinical case

This 73-year-old man, with no particular medical history, has had a lesion of the posterior surface of the left lobe since 2010. Two MRIs, performed two years apart, show the lesion to be stable. His imaging examinations are visible in Figs. 13 and 14.

Questions

1. Describe the abnormalities.
2. What do you surmise as the diagnosis?
3. How would you confirm the diagnosis?

Answers

1. There is a homogeneous, hyperechoic, non-nodular field on the posterior surface of the left lobe in the ultrasound examination. With MRI, the lesion is not visible on T2-weighted sequence, is hypointense on T1-weighted sequence before injection and little different from the liver after injection.
2. The hardly nodular character, the presence of fat in the lesion and the site suggest heterogeneous steatosis.
3. The diagnosis can be confirmed by finding a vein entering the lesion. This is visible in Fig. 14d but will be easier to identify with Doppler ultrasound (Fig. 15). Contrast-enhanced ultrasound will show lesion enhancement identical to that of the liver (Fig. 16). The diagnosis is that of heterogeneous steatosis of the left lobe with aberrant drainage of a branch of the portal system into the liver lesion.

![Figure 13. a, b: hepatic ultrasound centered on the left lobe (transverse and longitudinal slices).](image-url)
Figure 14. Hepatic MRI: T2-weighted (a), T1-weighted with fat suppression (b), after injection of gadolinium chelates in the arterial and portal phases (c and d). The in-phase and opposed-phase T1-weighted sequences are not presented because of many artefacts but show a signal drop at the posterior surface of the left lobe.

Figure 15. Doppler ultrasound.

Figure 16. Contrast-enhanced ultrasound.
Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

References