Fat-containing lesions of the liver: A pictorial essay

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Abstract The presence of fat within a hepatic lesion is unusual and can help to direct the radiologist’s diagnosis. The aim of this iconographic review is to specify the various hepatic lesions that may contain fat and their appearance particularly on MRI. A histological correlation is also suggested for the most commonly found tumors. The identification of fat within a hepatic tumor, along with other radiological signs and reflection on the clinical and epidemiological context, can lead to a diagnosis being reached or suggested, with confirmation if necessary, by a pathological examination.

The presence of fat in a liver lesion is not a standard finding and it can help to guide the radiologist towards a diagnosis. Fat may be macroscopic or microscopic. MRI is the modality of choice for detecting a fatty component in a hepatic tumor: fat-saturation sequence detects extracellular fat while chemical shift imaging identifies microscopic or intracellular lipids [1].

Once intracellular lipids are demonstrated, this allows a range of diagnoses to be considered, including multifocal hepatic steatosis, focal nodular hyperplasia (FNH), adenomas, hepatocellular carcinoma, and some hepatic metastases.

By contrast, the presence of fat in a tumor that is not within the hepatocytes is suggestive of angiomylipoma, pseudolipoma of the Glisson capsule, fat deposits around the intrahepatic wall of the inferior vena cava or “pericaval fat”, hydatid cyst, teratoma, liposarcoma and some metastases [2,3].

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Liver lesions containing intracellular fat

When steatosis is demonstrated within a focal hepatic lesion through signal drop on the out-of-phase sequence, the following diagnoses should be the first to come to mind: focal steatosis, focal nodular hyperplasia, HNF1α mutated adenoma, inflammatory hepatic adenoma, and hepatocellular carcinoma.

The next stage in the diagnostic process for the radiologist is to determine whether the steatosis within the tumor is homogeneous and diffuse or focal, and whether or not the lesion is hypervascularised, and, if relevant, whether there is contrast washout. These features, taken together with a study of the adjacent parenchyma and the context, will usually allow a diagnosis to be made or strongly suspected.

Focal pseudo-nodular steatosis

The conditions under which hepatic steatosis is most often found are excessive alcohol consumption, insulin resistance, obesity, hyperlipidaemia, hepatitis B and C infection, and the use of certain medications. Hepatic steatosis is the result of a build-up of fat vacuoles in the hepatocytes, and it can be diffuse, focal, or multifocal (Fig. 1). Focal pseudo-nodular hepatic steatosis can be mistaken for a focal lesion on sonography or CT [4]. Areas of focal hepatic steatosis are usually found in the periportal region, in contact with the falciform ligament or the gall bladder. This positioning is due to variations in venous flow within the hepatic parenchyma, resulting from the links to the vascular networks of the pancreas and duodenum, gall bladder, and digestive system [5]. Insulin has also been suggested to play a role due to steatosis being demonstrated in contact with insulinoma metastases [6].

Chemical shift imaging shows fat present in the hepatocytes with a signal drop on the out-of-phase sequence. This finding, when seen together with a characteristic location, a lack of mass effect, geographic borders, and a parallel enhancement gradient to that of the adjacent parenchyma, allows the diagnosis to be made with certainty [6].

Focal nodular hyperplasia

This is the most commonly seen benign tumor of the hepatocytes, with an estimated prevalence of 9/1000 and a female to male ratio of 8:1 [7]. FNH is thought to be an abnormal proliferation of the hepatic parenchyma in response to a congenital vascular malformation. It is usually discovered incidentally or further to non-specific symptoms. It is essential to identify FNH correctly because no monitoring is needed, and contraception does not need to be discontinued. MRI is the most sensitive modality for diagnosis of this condition [8]. Typically, FNH is a well-circumscribed, lobulated lesion with no capsule, with iso- or low signal

Figure 1. Focal steatosis mimicking a tumor (*) in the left lobe and segment I in a patient with chronic liver disease with indented contours and hypertrophy of the caudate lobe (arrow heads). These areas of steatosis appear in iso-signal on in-phase T1 images (a) and T2 images (c), with a marked signal drop on the out-of-phase sequence (b). With contrast enhancement, these areas have iso-signal intensity in the arterial phase (d) and slight low signal intensity in the portal (e) and delayed phases (f). There are vessels coursing through these areas, without displacement.
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There is a characteristic central scar (or area of fibrosis), especially in lesions larger than 2 cm. It presents intense arterial phase enhancement and becomes iso-intense to the adjacent parenchyma in the portal phase. The central area of fibrosis shows low signal intensity on T1-weighted sequences, high signal intensity on T2-weighted sequences, with delayed phase enhancement.

While intracellular lipids are possible in FNH, this is an atypical finding. The frequency of this feature varies enormously between studies, ranging from 22–85% [8–10]. There is probable overestimation due to these being lesions that have undergone biopsy or resection because of their atypical appearance on imaging.

Intratumoral steatosis (Fig. 2) is shown by a signal drop on out-of-phase T1-weighted images. This does not always equate to an atypical appearance on MRI if the other criteria are brought together. It can, however, lead to difficulties in diagnosis, especially in making the distinction from the differential diagnosis of inflammatory hepatic adenoma [9]. The use of hepatocyte-specific contrast agents can give weight to diagnosis in these instances. In this respect, Grazioli et al. [11] showed that over 96% of FNH demonstrated iso- or high signal intensity in a late delayed phase (after 1–3 h) following administration of gadobenate dimeglumine, while 100% of adenomas showed low signal intensity. More recently, the use of gadoxetic acid has been evaluated [12] to study the dynamic contrast enhancement patterns of lesions, focusing particularly on an acquisition taken 20 min after administration (hepatobiliary phase). In this study, 91.2% of FNH showed iso- or slight high signal intensity compared to the adjacent parenchyma 20 min after administration. In cases with atypical enhancement patterns, a large central scar or an abundant fatty component was noted.

**Hepatocellular adenomas (HCA)**

Hepatocellular adenomas are uncommon benign tumors with an estimated prevalence of 0.03% and a female to male ratio of 9:1. Adenomas are usually diagnosed in young women of childbearing age, who are often found to be using oral contraception. Histologically, this tumor corresponds to a benign proliferation of normal hepatocytes without portal tracts [13]. It is crucial to make or suggest the diagnosis of adenoma on imaging due to its potentially serious complications [14]: haemorrhage (20% of cases), and transformation to hepatocellular carcinoma (10%). The latter is a particular risk for men, with 47% affected compared to 4%.

![Figure 2](image_url)  
**Figure 2.** MRI of FNH with fat content. Well-circumscribed lesion at the junction of segments VI and VII (arrow) showing slight high signal intensity on T2 (a), iso-signal intensity on in-phase T1 (b) outside the central scar, which shows low signal intensity (*), and marked low signal intensity on out-of-phase T1 images (c). With gadolinium enhancement, there is contrast uptake in the arterial phase (d) with the central scar showing low signal intensity (*) and enhancement in the delayed phase (e). On histology (f), H and E stain enlarged 100 times shows an area of inflammatory fibrous septa (*) containing bile ducts in the centre of the lesion, around which are vacuolated and steatotic hepatocytes (arrows).
of women [15]. The lesion can be single or multiple. The risk of progression does not correlate to the number of lesions, but to their sub-type.

Recent advances in cytogenetics and molecular biology have led to four sub-types of hepatocellular adenoma being identified: HNF1α mutated adenoma, inflammatory adenoma, β-catenin mutated adenoma, and unclassified adenomas [16–18]. Each type has a specific set of features on MRI [19,20], which means that this modality has increased specificity for the diagnosis of HNF1α mutated and inflammatory adenomas [19,21]. It is essential to identify the sub-type of HCA because each one has specific complications and different management is needed as a result. The two most common sub-types are HNF1α mutated adenoma and inflammatory adenoma, both of which can contain intracellular fat.

**HNF1α (hepatocyte nuclear factor 1 alpha) mutated adenoma**

HNF1α (hepatocyte nuclear factor 1 alpha) mutated adenoma (Fig. 3) accounts for 30–46% of HCA, depending on the study. Histologically, it is characterised by an absence of cytologic atypia and inflammatory infiltrate, while there is diffuse and homogeneous steatosis. These features explain its appearance on imaging. Thus, MRI will show a lesion with high signal intensity on T1-weighted in-phase sequences with a uniform signal drop on out-of-phase imaging. On T2-weighted sequences, the tumor will show iso- or slight high signal intensity. After administration of gadolinium chelates, enhancement is moderate or even absent in the arterial phase, and does not persist into the portal or delayed phase. The main differential diagnosis is hepatocellular carcinoma with fat content.

**Figure 3.** Example of a female with steatotic adenomas (arrows) showing slight high signal intensity on T2 (a), iso-signal on T1 (b) and clear low signal on T1 (*) on the out-of-phase sequence (c). These lesions enhance moderately during the arterial phase (d) with low signal intensity that persists into the portal (e) and delayed phases (f). Histology, H and E stain, enlarged 12.5 times (g), shows an adenoma (*) made up of narrow sheets of hepatocytes with cytoplasm occupied by large vacuoles of steatosis. On the left of the image, a displaced band of healthy liver (arrowheads), and note that none of the hepatocytes here show steatosis.
There is no risk of malignant transformation in HNF1α mutated adenomas, and the risk of haemorrhage is low but it increases with lesion size.

**Inflammatory hepatic adenoma**

Inflammatory hepatic adenoma, previously known as telangiectatic FHN, accounts for 40–55% of HCA. It is clinically associated with obesity, hepatic steatosis, and, in terms of laboratory study signs, raised inflammatory markers. Intracellular fat in the tumor is noted in 11% of cases [18]. In contrast to HNF1α mutated adenoma, steatosis within the tumor is often focal and heterogeneous. However, Ronot et al. [21] report the presence of diffuse steatosis in 21% of cases of inflammatory hepatic adenoma although it was still non-homogeneous (while it was homogeneous in HNF1α mutated adenoma).

In histological terms, inflammatory adenoma is characterised by the presence of inflammatory infiltrates, dystrophic vessels, and dilated sinusoids. A small number (5–10%) can present β-catenin activation and progress to hepatocellular carcinoma [17]. There is greater risk of haemorrhage than in HNF1α mutated adenomas.

MRI most often demonstrates a lesion with iso-signal intensity on T1-weighted sequences, with focal areas of signal drop on out-of-phase images if there is an intracellular fat component. There is marked high signal intensity on T2-weighted images due to the dilated sinusoids. Arterial phase enhancement is intense and persists into the portal and delayed phases. The atoll sign is seen in 43% of cases [20], corresponding to a peripheral band of high signal intensity on T2-weighted sequences with delayed phase enhancement, while the lesion centre is iso-intense.

**B-catenin activated adenomas**

B-catenin activated adenomas are less common; more often found in men [15], and account for 10% of HCA. Cytologic atypia and a pseudoglandular growth pattern may be seen.

Although it has a varying appearance on imaging, a fatty component within the lesion has never been demonstrated. This is a heterogeneous lesion on all sequences, showing iso-signal intensity on T1- and T2-weighted sequences, with arterial phase enhancement and washout following administration of gadolinium chelates. A central scar is possible, being seen in 75% of cases, which will show high signal intensity on T2-weighted sequences, but this is not a specific sign since it can also been seen in other adenoma sub-types.

β-catenin mutated adenoma is associated with an increased risk of malignant transformation [16].

**Unclassified adenomas**

Unclassified adenomas (Fig. 4) are a group of lesions that do not present specific features in terms of morphology or...
immunophenotype. Steatosis within the lesion has not been reported in this adenoma sub-type.

**Hepatocellular carcinoma (HCC)**

HCC is the most common primary hepatic tumor, developing in a cirrhotic liver in 80% of cases [22]. This lesion produces a variable signal on T1- and T2-weighted sequences, with hypervascularisation in the arterial phase and washout in the portal and/or delayed phase. In bulky tumors, the presence of a capsule and mosaic perfusion is possible. The diagnostic criteria for HCC in a cirrhotic liver were amended in 2011 [23]: the diagnosis can be confirmed on CT or MRI for any tumor larger than 1 cm if there is arterialisation and visible contrast washout in the portal and/or delayed phase. Intracellular fat is not an uncommon finding (Fig. 5), being reported in 19.6% of cases [24]. Steatosis within the lesion is mainly seen in small low-grade lesions (particularly those between 1 and 1.5 cm in diameter). This intracellular fat is common and diffuse in well-differentiated HCC (42%). It becomes less common and more focal as the grade and tumor size increase. In one study, Katumi et al. [24] reported that the presence of a capsule was rare in HCC with intracellular fat content (absent in 81% of cases). This feature can be the cause of difficulties in making the distinction with the differential diagnosis of HNF1α mutated adenoma.

**Extracellular fat-containing liver lesions**

**Angiomyolipoma**

More commonly seen in the kidneys, sporadic hepatic angiomyolipoma is rare, with an increased frequency in patients with tuberous sclerosis.

It is a benign lesion made up of smooth muscle cells, vessels, and adipocytes. There is significant variability in the proportions of these three components, resulting in equally variable appearances on imaging, which makes preoperative diagnosis rare. The proportion of fat in particular can range from under 10% to over 90% [25]. Typically, the lesion is non-homogeneous, with variable high signal intensity on T2-weighted sequences, high signal intensity on T1-weighted sequences, and a signal drop on fat-suppressed images. With use of a contrast agent, it demonstrates non-homogeneous enhancement that occurs early and persists, showing that vessels are present in and around the tumor [25].

A small series of cases [26] of atypical AML (Fig. 6) with no fat component brings together the various enhancement characteristics, still showing non-homogeneous

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**Figure 5.** HCC of the dome of the liver (arrow) with a high intracellular fat component. The lesion presents slight high signal intensity on in-phase T1 (a), with a marked signal drop (*) on the out-of-phase T1 sequence (b) and high signal intensity on T2 fat-sat (c). The enhancement pattern is also typical of HCC with marked arterialisation (arrowheads) (d), then washout in the portal (e) and delayed phases (f).
Figure 6. A well-circumscribed angiomyolipoma with heterogeneous high signal intensity on T2 (a), clear low signal intensity on in-phase T1 images (b) outside a central zone (*) that shows slight high signal intensity with signal drop (arrowheads) on out-of-phase T1 sequences (c) and T1 fat-sat (d). After contrast material administration, the tumor shows intense enhancement in the arterial phase (e) with rapid and heterogeneous washout in the portal (f) and delayed phases (g). Note the visualisation of the vessels in and around the lesion (arrows). Immunohistochemistry, enlarged 200 times (h), shows that some of the tumor cells express actin with variable intensity (brown staining). The contrasting stain (pale blue) allows the majority of the smooth muscle cells to be drawn out as epithelioid, as well as showing the adipocytes, which seem to have empty cytoplasm under the microscope. Enlarged 40 times, HE staining (i) shows the lesion to have tree-like vasculature (arrowheads).
arterialisation but with washout in the portal phase and delayed phase, no fibrous capsule, and vessels present in and around the tumor.

**Pericaval fat collection**

This is a rare and benign type of fat formation that develops in contact with the endoluminal side of the inferior vena cava wall (Fig. 7). This "incidentaloma" increases in frequency in patients with chronic liver disease and it must not be mistaken for a neoplasm or a thrombus [27].

**Pseudolipoma of the Glisson capsule**

This is an asymptomatic lesion that is an incidental finding. It is well-circumscribed, sub-capsular, and presents purely fatty density (Fig. 8).

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**Figure 7.** MRI showing pericaval fat developed in a cirrhotic liver. This lesion (white arrow) is indistinguishable from the adjacent fat on T2 imaging (a), in-phase (b) and out-of-phase T1 imaging (c). It is visible because of a marked signal drop (*) on the T2 fat-sat sequence (d). It remains in clear low signal intensity (*) on T1 fat-sat contrast-enhanced sequences in the arterial (e), portal (f), and delayed phases (g) with enhancement of the inferior vena cava at its periphery (black arrowheads). Note the presence of ascites, recanalisation of the round ligament due to cirrhosis, and an unremarkable biliary cyst in segment IV. The pericaval fat (arrow) is more easily seen on CT (h): note this axial view of the same patient.
Hydatid cyst

Echinococcosis is a zoonotic disease caused by *Echinococcus granulosis* and *E. multilocularis* infection, affecting mainly the liver, especially the right lobe. While the parasite *E. multilocularis* causes alveolar echinococcosis, it is *E. granulosis* infection that causes hydatid cyst formation. These can be asymptomatic or they can cause pain, secondary infection, or rupture. The presence of a fat-fluid level within a hydatid cyst is not usual (Fig. 9) and is thought to be an indirect sign of communication with the biliary tree, which may be longstanding [28].
Figure 9. Hydatid cyst in a patient originating from an endemic area. It is a well-delineated lesion, in which two components can be distinguished, the first being dependent fluid (arrow) with high signal intensity on T2 (a) and T2 fat-sat sequences (b), and low signal intensity on T1 (c, d). The second component is fatty (arrowheads), showing high signal intensity on T2 (a), in-phase (c) and out-of-phase T1 sequences (d), with marked signal drop on the T2 fat-sat sequence (b). No uptake after administration of contrast material either in the arterial (f) or portal phase (g).

Conclusion

The presence of fat in a hepatic lesion is not an unusual finding. Identifying the fat is a crucial step in the process of diagnosing aetiology. This finding, especially when demonstrated with the input of MRI, points to different groups of diagnoses depending on whether the fat component is intracellular or extracellular.

Considered together with the other data from imaging and the clinical context, demonstration of a fat component within a lesion can add weight to a theory and guide the radiologist in the diagnostic process.

Disclosure of interest

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

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