Hepatic lesions - the scar as the discriminatory feature

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Learning objectives

1. Review pathophysiology and clinical manifestations of scar-bearing hepatic lesions.
2. Discuss the importance of differentiating scar-bearing hepatic lesions for timely diagnosis and appropriate management.
3. Describe and demonstrate the spectrum of imaging findings on ultrasound, CT and MRI.
4. Review imaging examples and highlight the pitfalls and mimics, such as central necrosis in large hepatic lesions.
5. Discuss new imaging techniques available to differentiate the various lesions with hepatic scars.
6. Review treatment options and management.

Background

Hepatic lesions with scars are a relatively uncommon radiological finding, although the scar can be a useful diagnostic feature. Scars may be found in a variety of hepatic pathologies and the histological nature of the scar differs in each disorder.

Important characteristic components for scar differentiation include: size, enhancement pattern and associated findings.

The importance of establishing an appropriate diagnosis through identifying key distinguishing features is essential, and these will be illustrated.

Findings and procedure details

Hepatic lesions with scars are a relatively uncommon radiological finding, although the scar can be a useful diagnostic feature. Scars may be found in a variety of hepatic pathologies and the histological nature of the scar differs in each disorder. Other important characteristic components for scar differentiation include: size, enhancement pattern and associated findings.

Hepatic scars are commonly found in **benign** lesions such as giant hemangiomas and **focal nodular hyperplasia** (FNH) and **malignant** lesions such as **fibrolamellar hepatocellular carcinoma** (fHCC).
They are found more rarely in cholangiocarcinoma and hepatocellular carcinoma (HCC). Mimics include central necrosis in large hepatic lesions, hepatic adenomas, and epithelioid hemangioendotheliomas.

The importance of establishing an appropriate diagnosis through identifying key distinguishing features is essential, and these will be illustrated.

**HEMANGIOMA**

Hemangiomas are the most common benign liver lesions. **Scars are typically found in giant hemangiomas**, which are those greater than 5 centimeters.

The scar itself is composed of thrombosed tissue where hyalinization leads to cystic lakes and fibrosis [1]. Their growth is thought to be due to ectasia of vessels, rather than hypertrophy or hyperplasia.

The **clinical presentation** of hemangiomas is in middle-aged women and is typically associated with increased estrogen use, such as with oral contraceptives, in pregnancy and puberty.

The **treatment** of hemangiomas is by surgery, embolization or radiation frequency ablation, which is suggested to be undertaken should the patient present with severe symptoms or disease-associated complications [2].

**IMAGING FEATURES OF HEMANGIOMA**

On **ultrasound (U/S)**, hemangiomas appear hyperechoic to the normal liver, but hypoechoic if the background liver is hyperechocic, such as in cases of steatosis.

On unenhanced images, it will appear hypodense on **computed tomography (CT)** due to its mainly cystic nature [1], hypointense on T1-weighted **magnetic resonance (MR)** images, and hyperintense on T2-weighted MR images.

On **post-contrast** images, there will be early peripheral enhancement with progressive centripetal enhancement (Fig. 1 on page 8). Hepatic hemangiomas do not typically demonstrate calcification [3, 4].
In large hemangiomas, regions of **scarring** may represent areas of fibrosis, sclerosis, cystic degeneration or thrombosis. Morphologically, scars are usually central and eccentric. Thus, the scar appears hypodense and without enhancement on CT (Fig. 2 on page 9) and has low signal on both T1 and T2 weighted images (Fig. 3 on page 9) [3].

**FOCAL NODULAR HYPERPLASIA (FNH)**

Focal nodular hyperplasia is a benign tumor of the liver, which is the second most prevalent benign hepatic tumor, after hemangioma [4].

It is composed of foci of normal hepatocytes, Kupffer cells, blood vessels, primitive bile ducts, encased in a fibrous stroma, originating from the central scar. Its **pathophysiology** is unclear, but it is thought to be hyperplastic as a result of a vascular malformation and injury.

Patients are usually young healthy females (male:female ratio of 1:8) and it is typically found as an incidental finding [4].

It does not require **treatment** as it has no malignant potential and is asymptomatic, however it appears hypervascular on imaging, hence the importance of proper diagnosis and differentiation from a malignancy.

**IMAGING FEATURES OF FOCAL NODULAR HYPERPLASIA (FNH)**

Focal nodular hyperplasia is usually **subcapsular** in location, with a lobulated contour and does not have a capsule. It does not typically contain fat, calcification, necrosis or hemorrhage. FNH is composed of nodules surrounded by radiating fibrous septa originating from a central scar where calcifications are rare. A scar is seen in 85% of FNH cases and is composed of a collection of malformed vessels and bile ducts [3].

On **ultrasound**, its appearance is variable although typically, lesions are isoechoic to surrounding parenchyma and contain a hypoechoic scar (Fig. 4 on page 10). The scar demonstrates hypervasularity with colour Doppler US. **Contrast-enhanced ultrasound (CEUS)** is useful in showing the centrifugal enhancement and spoke-wheel vessel structure, especially in lesions less than 3 cm (Fig. 5 on page 10). In these lesions (<3 cm), this modality has been shown to be diagnostically comparable to contrast-enhanced CT and MRI [5].
On **CT**, the lesion is hypo- or iso-attenuating on unenhanced images, hyperattenuating in the arterial phase due to hypervascularity of lesion, and isoattenuating on portal venous and delayed scans (Fig. 6 on page 11) [3].

On **MRI**, FNH is iso- to hypointense on T1-weighted images and iso- to hyperintense on T2-weighted images. A key imaging feature of the FNH scar is its T2 signal hyperintensity and delayed enhancement with extracellular contrast agents (Fig. 7 on page 12).

With **liver-specific hepatobiliary agents**, such as gadoxetic acid (Eovist®, Bayer HealthCare Pharmaceuticals, Canada/USA; Primovist™, Bayer Schering Pharma AG, EU), hepatocyte uptake results in an increase in T1 signal within the lesion and hypointensity within the scar [4].

**FIBROLAMELLAR HEPATOCELLULAR CARCINOMA (fHCC)**

fHCC is a rare variant of hepatocellular carcinoma with laminated fibrous tissues interspersed between tumor cells.

It is usually found in young adults without prior liver disease or underlying cirrhosis. **fHCC is often detected in advanced stages where the lesion will be >10 cm in size with a well-defined lobulated margin**, as there is an overall lack of symptoms (no specific association with serum markers). However, it is critical to distinguish it from FNH, as they are both hypervascular lesions, since fHCC requires surgical resection and/or chemotherapy [4].

**IMAGING OF FIBROLAMELLAR HEPATOCELLULAR CARCINOMA (fHCC)**

The lesion itself is predominantly hypodense on **CT** with heterogeneous enhancement in the arterial phase.

On **MRI**, it is a large and well circumscribed focal lesion, hypointense on T1, and hyperintense on T2. There is early heterogeneous contrast enhancement with washout.

In fHCC, **calcification** is common (in ~70% of cases), whether punctate, nodular or stellate and is usually found near the center of the tumor.

A **scar** is seen in 70% of fHCC cases and it is composed of fibrous tissue, developing in the center of the lesion, stellar or amorphous in shape. It is usually hypodense and nonenhancing on CT and MRI, and usually does not enhance on delayed phases (Fig. 8 on page 12).
This lack of delayed enhancement can be used as a distinguishing feature from cholangiocarcinoma or FNH [3].

**INTRA-HEPATIC CHOLANGIOCARCINOMA**

Intra-hepatic cholangiocarcinoma is a primary tumor arising from bile ducts within the liver and is the most common primary hepatic malignancy after hepatocellular carcinoma (HCC). The only treatment option that has been shown to prolong survival is surgical resection [6].

**IMAGING OF INTRA-HEPATIC CHOLANGIOCARCINOMA** (Fig. 9 on page 13)

On imaging, intra-hepatic cholangiocarcinoma is a nonencapsulated hypodense mass with irregular margins. An internal scar is found in 30-52% of cases which is characterized by fibrous stroma and appears hypodense on CT [1]. Intra-hepatic cholangiocarcinoma can be associated with biliary dilatation, retraction of the liver capsule and vascular encasement.

Intra-hepatic cholangiocarcinoma demonstrates peripheral enhancement in the arterial phase with progressive central enhancement on delayed images. Its peripheral enhancement and retraction of overlying liver capsule are characteristic features (Fig. 10 on page 14).

On MRI, it is T1 hypointense and T2 hyperintense. After gadolinium injection, the lesion shows early moderate peripheral enhancement, progressive concentric enhancement, and delayed enhancement on delayed imaging (Fig. 11 on page 15).

**Hepatocyte specific MR contrast agents**, such as gadoxetic acid have been shown to be beneficial in further assessing hepatic lesions [6, 7]. For intra-hepatic cholangiocarcinoma, Kang et al. reported that a thin peripheral rim with internal heterogeneous enhancement during the early arterial phase can be appreciated with gadoxetic acid. In the hepatobiliary phase, there was a better delineation of daughter nodules and intrahepatic metastases [6].

**HEPATOCELLULAR CARCINOMA (HCC)**

Hepatocellular carcinoma (HCC) is the 3rd leading cause of cancer worldwide and the most common primary malignancy of the liver [4, 8]. It is usually found in a background of chronic liver disease such as cirrhosis due to viral hepatitis B and C. On imaging, hepatic scars are found in about one quarter of HCC cases.
On **CT**, HCC is typically hypervascular with a scalloped margin and heterogeneous enhancement, demonstrating washout in the portal venous and/or delayed phases (Fig. 12 on page 16).

On **MR**, it is hypointense on T1 and hyperintense on T2.

On **SPIO-enhanced MRIs** (SPIO: superparamagnetic iron oxide, a liver targeting agent taken up by Kupffer cells), some HCCs, unlike metastases, have been shown to take up SPIO and show hypo- or isointensity relative to the surrounding liver parenchyma [9].

On **diffusion-weighted images (DWI)**, malignancies in general have been shown to be hyperintense, likely due to increased cellularity [10]. However, due to the overlapping appearance of benign and malignant hepatocellular lesions, DWI MR might not be ideal for characterization [7]; it has instead been suggested as a tool for hepatic lesion detection due to its high sensitivity where Nasu et al. showed that the probability was higher for hyperintensity to be noted on DWI than on T2-weighted images for HCCs [10]. When DWI was used in combination with SPIO-enhanced MRI however, the sensitivity of depicting HCCs was higher than that of SPIO-enhanced MRI alone [9].

Studies have shown that gadoxetic acid-enhanced MR images allowed for better cancer management in patients with HCC and even colorectal metastases to the liver [11, 12], as this contrast media is found minimally in tumors, as it's taken up by hepatocytes [7, 13]. Recent studies have also shown that the diagnostic role of **dynamic contrast-enhanced ultrasound** might provide additional information to CT and MR images, such as the transient signal intensity enhancement of HCC's hypervascular lesions. It has since 2005 been included in the diagnostic algorithm for suspected HCC of the American Association for the Study of Liver Diseases (AASLD) [7].

**MIMICS AND OTHER HEPATIC TUMORS**

There are other hepatic lesions which may display features resembling a scar. **Hepatocellular adenomas** have low density foci of fat, necrosis and old hemorrhage that may mimic a scar. It can present as a hypervascular lesion, resembling FNH, however the mass is usually more heterogeneously enhancing. **Epithelioid hemangioendothelioma (EHE)** has a central "target" appearance that can be confused for a scar, however EHE has a peripheral location and is usually multifocal. **Hepatic metastases** can also show the appearance of a target sign or necrosis, often accompanied by fibrotic involution [1, 4] (Fig. 13 on page 16).

**SUMMARY AND KEY DIFFERENCES**
In summary, hepatic scars are common in giant hemangiomas, focal nodular hyperplasia (FNH) and fibrolamellar hepatocellular carcinoma (fHCC). Scars are more rarely found in lesions such as cholangiocarcinoma and hepatocellular carcinoma (HCC). Other tumors can be mimics, such hepatic adenomas, epithelioid hemangioendothelioma and metastases with central necrosis.

**Highlights of key differences** can be found in Table 1 on page 17. A hyperintense scar on T2 is quite a unique feature of FNH. fHCC’s scar is fibrotic, therefore shows no enhancement. It can be distinguished from a vascular scar in FNH, with the spoke-wheel sign. fHCC also typically shows calcification in its lesions, while FNH and hemangioma rarely do. Hepatobiliary specific MR contrasts can be taken up by hepatocytes in benign lesions, such as FNH, while there is an absence of uptake in malignancies, such as fHCC and progressed HCC.

**Images for this section:**

![Enhanced CT of hemangioma: peripheral nodular enhancement on arterial phase (left) and centripetal filling in on delayed CT (right).](image-url)
**Fig. 2:** Enhanced CT of hemangioma: eccentrically located scar appears hypodense.

**Fig. 3:** Giant hemangioma is demonstrated replacing much of segment II/III of the liver in a 53 year old patient on MR sequence T1 weighted with fat saturation in delayed
phase following gadolinium enhancement (left), and T2-weighted fat saturated sequence showing hypertense mass (right).

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**Fig. 4:** Ultrasound of focal nodular hyperplasia (FNH) showing spokewheel sign.

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Fig. 5: Doppler ultrasound of focal nodular hyperplasia (FNH) showing spokewheel sign.

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**Fig. 6:** Enhanced CT of FNH lesion hyperattenuating in arterial phase due to hypervascularity of lesion (left), and isoattenuating on delayed scans (right).

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**Fig. 7:** Axial (left) and coronal (right) MRI hepatobiliary phase images demonstrate a central scar with retention of hepatocyte-specific contrast agent consistent with FNH and hypointensity within the scar.

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Fig. 8: fHCC: Lobulated hyperenhancing mass with significant washout and with no apparent cirrhosis in a 23 year old female.

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**Fig. 9:** Intrahepatic peripheral cholangiocarcinoma on ultrasound demonstrates a fairly well-defined hypoechoic mass in the right lobe, with no associated biliary duct dilatation.

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Fig. 10: Contrast-enhanced CT of peripheral cholangiocarcinoma demonstrating heterogeneous on homogeneous with pooling contrast on delayed images with peripheral enhancement.

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**Fig. 11:** Intrahepatic peripheral cholangiocarcinoma on T1 post-gadolinium MR sequence (left) where the low signal mass demonstrates peripheral rim enhancement, and on T2 weighted image (right), the mass demonstrates high T2 signal, suggesting necrosis.

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**Fig. 12:** CT images of hepatocellular carcinoma showing a hypervascular, scalloped tumor margin with heterogeneous enhancement. There is early arterial enhancement (left), wash out by portal venous (isodense) (middle), then hypodense on delayed (right).

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**Fig. 13:*** Contrast enhanced CT of a mimic (metastasis from colon adenocarcinoma) demonstrates a large heterogeneous, but predominantly hypodense segment in 4A mass with peripheral enhancement and capsular retraction.

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**Table 1: Key features of hepatic scars**

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Conclusion

In conclusion, the central scar is an important feature used to distinguish between hepatic lesions. However due to overlapping features, knowledge of specific enhancement patterns and associated clinical findings is critical. Multiphasic CT and MR with liver specific MR media contrast such as gadoxetic acid are becoming more commonplace in helping to improve differentiation between similar lesions.

Personal information

References


