Hepatocellular Adenoma: CT and MRI Imaging Findings with Histopathology correlation

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Learning objectives

The correlation between the imaging aspects and the histopathology features is, actually, the best and fastest way to achieve an accurate diagnosis of hepatocellular adenomas (HCA).

With this presentation we propose to achieve these objectives:

- To illustrate and describe the imaging features of hepatocellular adenomas.
- To compare the roles of computed tomography-(CT) and magnetic resonance-(MR) in the evaluation of hepatocellular adenomas.
- To correlate the imaging findings with histopathologic features.

Background

Hepatocellular adenomas are rare, benign tumors of cells closely resembling to normal hepatocytes.

These tumors are seen predominantly in young women, especially when using oral contraceptive pills. They can be located in the right or left hepatic lobe, and are typically solitary (70-80%). (3) Multiple adenomas have been described in patients with prolonged contraceptive use and glycogen storage diseases (GSD), in which case we speak of hepatocellular adenomatosis. (1) Hepatocellular adenoma can also be found in men who are receiving anabolic steroid therapy. (2)

The close relationship between oral contraceptive medication and HCA has been described the first time in 1973 by Baum. This casual relationship appears to be proportional to the hormonal dose and duration of medication and is highest in women over 30 years of age after using oral contraceptives for more than 24 months.(1) In women who have never used oral contraceptives, the annual incidence of hepatic adenoma is about 1 per million. It increases to 30-40 per million in long-term users of oral contraceptives. (3)

Hepatocellular adenoma can reach up to 30 cm in diameter.

The clinical presentation of the HCA usually includes abdominal pain, hepatomegaly and abnormal liver functions.(2)

Pathologically speaking the HCA usually appears as a smooth,
well circumscribed mass that has a fleshy appearance. Having large blood vessels on the surface they sometimes outgrow their arterial blood supply causing necrosis within the lesion.

The most common complication of HCA is intratumoral or intraperitoneal hemorrhage, which occurs in 50-60% of patients. Besides, there is also the risk of malignant transformation that can be as high as 13%. (3) Due to this and to the fact that this lesion may be difficult to distinguish from other benign or malignant hepatic tumors it is extremely important to the physicians to have a good characterization of these tumors through the correlation of imaging features and histopathology.

 Imaging findings OR Procedure details

Computed Tomography:

The main advantage of CT scans is to allow a more accurate detection and a better characterization of focal hepatic lesions. (3)

The comparison of the HCA relative to the liver depends on the composition of the tumor and of the liver as well as on the phase of contrast material enhancement.

Using a 16-slice helical CT, non-enhanced images are the first to be obtained. Then, after the injection of intravenous non ionic contrast (120-150ml at a rate of 3-5mL/s with a 25 to 30s delay) the arterial phase images are obtained. After a 70-80 delay, a scan is made for the portal venous phase.

Imaging findings of HCA in CT:

• Well marginated, nonlobulated mass, that sometimes can be encapsulated and is rarely calcified. (Fig.1)

Homogeneous enhancement in the hepatic arterial phase.(Fig. 2) Typically isoattenuating but sometimes mildly hypoattenuating relative to normal liver on unenhanced, portal venous-phase and delayed-phase images.(6) (Fig.3)

• Can be a hypoattenuating mass if the presence of intratumoral fat is considerable. (Fig.1) If it’s surrounded by a fatty liver it appears hyperattenuating on all contrast phases and unenhanced images.
• Necrosis or old hemorrhage is usually seen as a heterogeneous, hypoattenuating area within the tumor.

• Larger hepatocellular adenomas may be more heterogeneous than smaller lesions, and their CT appearance is less specific.

**Magnetic Resonance Imaging:**

With this technique the detection of fat and hemorrhage is usually more sensitive and accurate, leading to a better understanding of the composition of the focal hepatic lesions. (3)

A 1.5 tesla MRI was used to perform the exams.

Protocol included a sagittal gradient echo, sagittal and axial T1 post gadolinium injection.

**Imaging findings of HCA in MRI:**

• From hyperintense to mildly hypointense relative to the liver tissue on T1-weighted images. This heterogeneous appearance results from areas of high intensity due to fat and acute hemorrhage and low signal-intensity area corresponding to necrosis or old hemorrhage or calcifications. (3) (Fig.4)

• On T2-weighted images hepatocellular adenomas are predominantly hyperintense relative to liver. Although in the presence of necrosis and hemorrhage they can be heterogeneous with hyper and hypo-attenuating signal. (Fig.4 and 5)

• Dynamic postgadolinium show intense arterial phase enhancement with isointensity on portal phase and delayed images.

• A pseudocapsule (rim) can be seen in some patients as a peripheral zone of low signal intensity on both T1 and T2 weighted images. (8). (Fig.6)

• HCA don’t have a central scar so if a central scar enhances after gadolinium is administered, the diagnosis of FNH is strongly favored. A central scar has never been reported in hepatic adenomas.
• With the injection of a hepatocellular-specific contrast agent, gadolinium benzylxypropionictetraacetate (Gd-BOPTA) there is usually no substantial uptake.

These imaging characteristics are still not enough to solely give the final diagnosis of Hepatocellular Adenoma. It is necessary to correlate these characteristics with the findings of a histological evaluation through liver biopsy (Fig.7) and eventually resection of the tumor. (1) Only then can we make the final diagnosis of Hepatocellular Adenoma.

**Differential diagnosis:**

• Focal Nodular Hyperplasia (7)
  o No malignant degeneration or hemorrhage,
  o On T2 weighted images central scar is typically hyperintense.

  • Hepatocellular Carcinoma (7)
  o Similar imaging features as hepatocellular adenoma,
  o Biliary, nodal invasion and metastases establish the malignancy.

  • Fibrolamellar Hepatocellular Carcinoma (7)
  o Large, lobulated mass scar and septa,
  o Heterogeneous on all imaging.

  • Hypervascular Metastases (7)
  o Hypointense on T1 weighted images and markedly hyperintense on T2 weighted images,
  o Typically in large numbers and in the presence of primary tumor (breast, thyroid, kidney and endocrine)

**Histopathology:**
HCA are constituted by large plates of cells closely resembling normal hepatocytes, with the plates being separated by dilated sinusoids. (Fig.8) Adenomas lack a portal venous supply and are fed solely by peripheral arterial feeding vessels. (9) The extensive sinusoids and feeding arteries constitute the hypervascular nature of hepatocellular adenoma. A fibrous capsule is uncommon and can be complete or incomplete. Adenoma cells are larger than normal hepatocytes and contain large amounts of glycogen and lipid. Intra- and intercellular lipid uncommonly manifests as macroscopic fat deposits within the tumor. (9)

Images for this section:

Fig. 1: Multiple HCA in a 28 year old woman. Arterial phase CT scan that shows hypoattenuating lesions due to the high content of intratumoral fat. (A) Histological image of larger adenoma that shows a well-defined and circumscribed tumor. (B)
**Fig. 2:** Single HCA in a 37 year old women. Transverse and sagital CT scans show a lesion with homogeneous enhancement in arterial phase. (A,B)
**Fig. 3:** HCA in a 28 year old woman. Fig. A shows a mildly hypoattenuating lesion on unenhanced CT. On Fig.B we can see a isoattenuating lesion on a delayed-phase CT scan. Notice the absence of pleomorphism in the cells represented on the image from the resection of the HCA.(C)
**Fig. 4:** Large HCA, with 12 cm in diameter, in a 33 year old woman. T1-weighted MR image without fat suppression shows a isointense mass with some areas of low intensity due to old hemorrhage.(A) On T2-weighted image the lesion is predominantly isointense relative to the liver with some areas of hyperintensity.(B)
Fig. 5: Isolated HCA in a 30 year old woman. T2-weighted image with fat suppression shows a heterogeneously hyperintense lesion. (A) On a T1-weighted MR image the mass appears heterogeneously isointense with low intensity areas due to necrosis. (B)
Fig. 6: HCA on left hepatic lobe in a 40 year old men. On the T1-weighted MR image the lesion is heterogeneously isointense. Note the pseudo-capsule as a hypo-attenuating outline. (A) T2-weighted image shows a heterogeneously hyperintense lesion. (B) The result of the biopsy shows a green structure that represents the collagen fibers found in the pseudo-capsule. (C)
Fig. 7: CT guided Liver biopsy
Fig. 8: HCA in a 30 year old woman. Image from the microbiopsy that represents the absence of pleomorphism and cellular atypia. The tumor is composed of cells very similar to normal hepatocytes.
Conclusion

CT and MRI can demonstrate imaging findings suggestive of hepatocellular adenoma. Due to the overlap of some of these characteristics with other hepatic tumors it is very important to better characterize these lesions so that we can achieve a quicker and more accurate diagnosis.

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