X-ray Corner

Current Concept of Hepatic Adenomas: MRI and Genetic Correlation

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Hepatic adenoma is an uncommon benign liver tumor, found in young women with history of prolonged use of oral contraceptive pills, mature onset of diabetes, and obesity. Hepatic adenomas are currently categorized into three distinct genetic and pathologic subtypes: (a) inflammatory hepatic adenomas, (b) hepatocyte nuclear factor 1 (HNF-1) alpha-mutated hepatic adenomas, and (c) Beta-catenin-mutated hepatic adenomas[1]. These 3 subtypes of hepatic adenomas have different prognosis and management strategies. Although histopathologic and immunohistochemical analysis is necessary for complete characterization of hepatic adenomas, imaging, particularly MRI, plays an important role in diagnosis, subtype characterization, identification of complications, and surveillance.

This article will emphasize on MRI findings based on genetic subtypes, and role of MRI for guiding management and surveillance.

Inflammatory Hepatic Adenoma (IHA)

IHA is the most common subtype and accounts for about 40-50% of all hepatic adenomas[2]. Patients may present with chronic anemia or systemic inflammatory syndrome. Previously known "telangiectatic focal nodular hyperplasia" is now believed to be IHA[1]. IHAs are the result of mutation of interleukin-6 signal transducer gene (IL-6ST), and over-expression of wild-type glycoprotein 130. These abnormalities lead to recruitment of inflammatory cells, marked peliosis, and proliferation of hepatocytes, which are hallmarks of IHAs[3,4].

MRI findings of IHAs include iso-intense or mildly hyperintense on T1-weighted images, minimal or no signal loss on in-phase/opposed-phase T1 gradient echo sequences, and diffusely hyperintense on T2-weighted images. After administration of gadolinium, IHAs usually show intense enhancement during the arterial phase, which persists in the portal venous and delayed phases[2] (Figure 1).

Approximately 30% of IHAs show bleeding[5], which is secondary to high vascularity and marked peliosis. About 10% of IHAs show an increased risk of malignancy[5].

Hepatocyte Nuclear Factor 1 (HNF-1) alpha-mutated Hepatic Adenoma (HA)

HNF-1alpha-mutated HA is the second most common subtype, and constitutes about 30-35% of all HAs[2]. This type is usually detected incidentally, and could be multiple. HNF-1alpha-mutated HAs are the result of mutation of both somatic and germ-line HNF-1alpha genes[5]. These abnormalities lead to accumulation of intracellular fat, and proliferation of hepatocytes, which are hallmarks of HNF-1alpha-mutated HAs.

MRI findings of HNF-1alpha-mutated HAs include predominantly hyper- or iso-intense on T1-weighted images, and diffuse signal loss on in-phase/opposed-phase T1 gradient echo sequences because of intracellular steatosis. Tumors show iso-intense to slightly hyperintense on T2- weighted images, moderate enhancement in the arterial phase after administration of gadolinium, with no persistent enhancement in the portal venous and delayed phases[2] (Figure 2).

HNF-1alpha-mutated HA is the least aggressive type. Tumors less than 5 cm have minimal risk of bleed-

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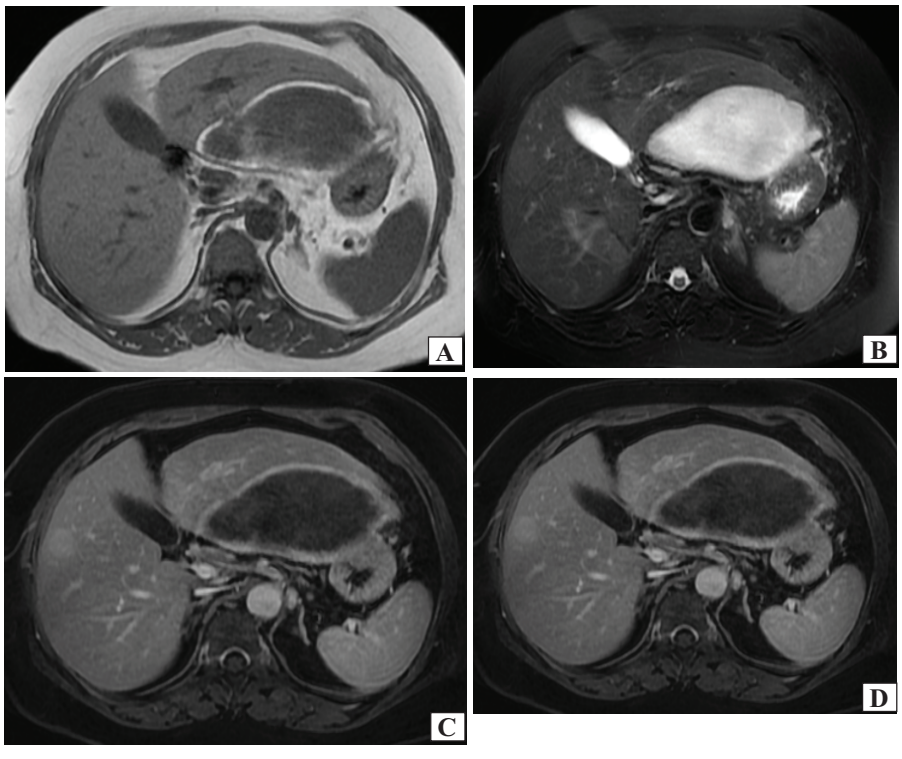

Figure 1. MRI of inflammatory hepatic adenoma.
A-B: T1 (A) and T2-weighted images (B) show a large bleeding tumor of left hepatic lobe (arrow). Tumor bleeding is characteristic for inflammatory adenoma.
C-D: Another small adenoma is noted at segment 5 of right hepatic lobe (arrow). This nodule shows arterial enhancement (C), which persists to venous phase (D).

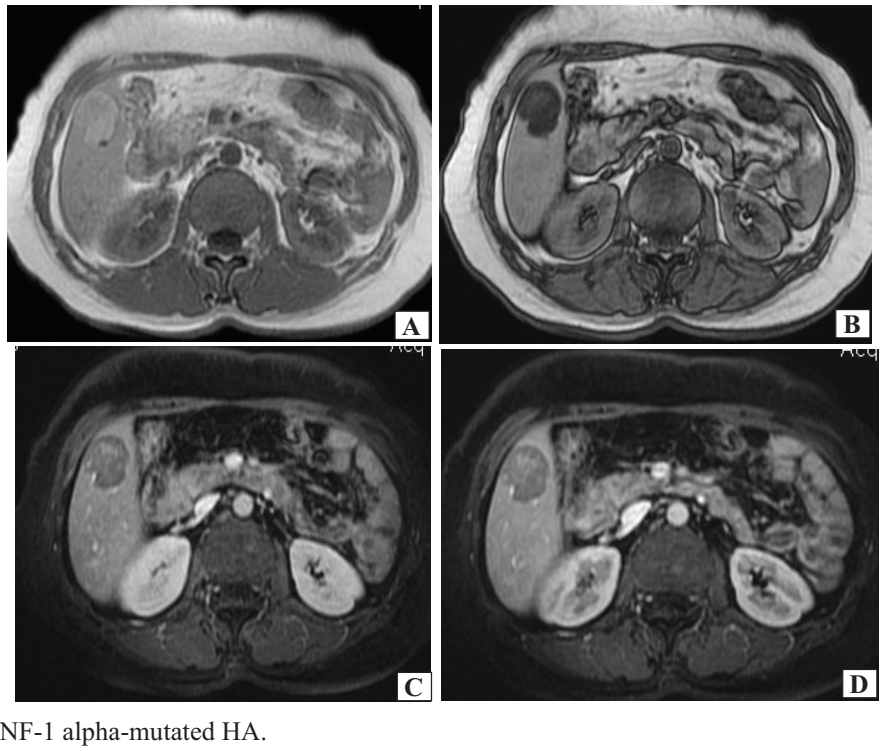

Figure 2. MRI of HNF-1 alpha-mutated HA.
A-B: T1 in-phase (A) and opposed-phase (B) gradient echo reveal a mass at segment 5 of right hepatic lobe. This mass shows signal loss on opposed phase (B) comparing to in-phase (A), indicative of steatosis. Tumor containing fat is characteristic for HNF-1 alpha-mutated HA.
C-D: This mass shows minimal enhancement on both arterial (C) and venous phases (D).

ing and almost no risk of malignancy[2].

Beta-catenin-mutated Hepatic Adenoma (HA)

Beta-catenin-mutated HA is the least common subtype, and constitutes about 10-15% of all HAs[2]. This subtype of HAs occurs frequently in men, is associated with glycogen storage disease, and familial adenomatous polyposis[(6)]. Beta-catenin-mutated HAs are the result of mutation of beta-catenin gene, leading to uncontrolled hepatocyte proliferation with high nuclear-cytoplasmic ratio, and nuclear atypia[(5)].

MRI findings are non-specific. These tumors may show homogeneous or heterogeneous hyperintense signal intensity on both T1 and T2-weighted images, depending on the presence of hemorrhage and/ or necrosis. Tumors commonly demonstrate strong arterial enhancement that may or may not persist on the portal venous and delayed phases, which may mimic hepatocellular carcinomas[(2)] (Figure 3).

Beta-catenin-mutated HA is the most aggressive type, and the risk of malignant change to become hepatocellular carcinoma is quite high even in a small tumor, particularly in men[(7)]. Although Beta-catenin-mutated HA has a risk of bleeding, the exact incidence of this complication is not known.

Management and surveillance application

If HAs are diagnosed on imaging, the management and surveillance guidelines are recommended based on symptoms[2]. Details are as following:

1. Asymptomatic patients:
   - If the mass is more than 5 cm, resection is suggested.
   - If the mass is less than 5 cm and contains fat, follow-up is recommended.
   - If the mass is less than 5 cm, without fat, and occurs in male, resection is recommended.
   - If the mass is less than 5 cm, without fat but in females, biopsy is recommended, followed by surgical resection if it is beta-catenin-mutated HA; and follow-up for other types.
2. Symptomatic patients from tumor rupture or bleeding
   - If hemodynamically stable, surgical resection is recommended.
   - If hemodynamically, unstable, hepatic artery

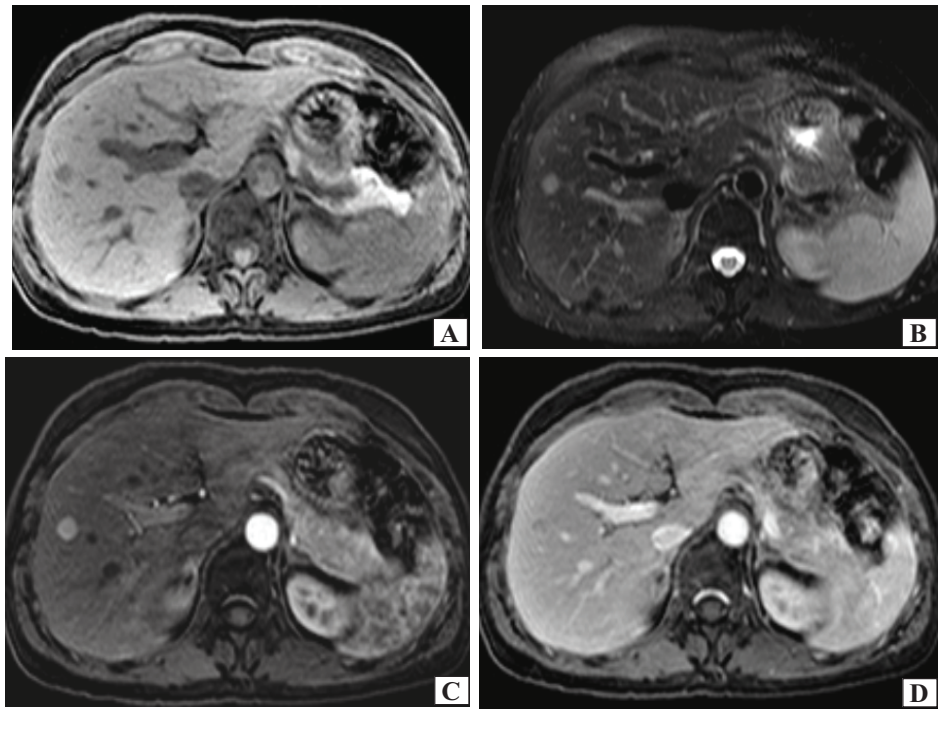

Figure 3. MRI of beta-catenin-mutated HA in a 35-year-old male. Male sex is characteristic for this subtype of HA.
A-B: T1 (A), and T2-weighted images (B) reveal a small nodule at segment 5 of right hepatic lobe. This nodule shows low signal intensity on T1 (A), and high signal intensity on T2 (B).
C-D: The nodule shows rapid arterial enhancement (C), and washout on venous phase (D). This finding mimics enhancement pattern of hepatocellular carcinoma.

embolization and/or surgery are recommended.

Conclusions

1. Hepatic adenomas are currently subdivided into 3 genetic and pathologic subtypes, which are inflammatory HAs, HNF-1 alpha-mutated HAs, and beta-catenin-mutated HAs.

2. These 3 subtypes have distinct MRI pattern and different prognosis.

3. MRI may help guiding management and planning strategy for surveillance of HAs.

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