Hepatocellular Adenoma

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Abstract

Hepatocellular adenoma is a benign liver tumor that is rare in children and most commonly occurs in association with underlying conditions such as glycogen storage disease. Despite its benign nature, hepatocellular adenoma carries risks of hemorrhage, rupture, and malignant transformation. Patients are often asymptomatic until complications such as hemorrhage or rupture develop. MRI is the preferred imaging modality, providing superior lesion characterization. Management strategies include discontinuation of hormone therapy, serial imaging, and surgical resection. In select cases, liver transplantation may be considered for patients with adenomatosis, and transarterial embolization can be used to control acute hemorrhage.

Keywords: gastrointestinal, liver, neoplasm, benign

Clinical Summary

An adolescent with a history of an ovarian yolk sac tumor underwent surveillance MRI of the abdomen.

Imaging Findings

Abdominal MRI (Figure 1) demonstrated a small lesion within the right posterior section of the liver. The mass was mildly hyperintense on T2-weighted imaging, showed arterial phase hyperenhancement, faint washout on equilibrium phase, and lacked contrast retention on the hepatobiliary phase. On US (Figure 2), the lesion appeared hypoechoic relative to the background liver. Subsequent biopsy confirmed an inflammatory hepatocellular adenoma (HA).

Diagnosis

Hepatic adenoma.

The differential diagnosis for imaging findings suggesting HA in children includes hemangioma, focal nodular hyperplasia, hepatocellular carcinoma (HCC), fibrolamellar carcinoma, and metastatic tumors.

Discussion

HA is a rare, benign epithelial liver neoplasm, accounting for approximately 2% of pediatric liver tumors. They may occur sporadically, but nearly 85% are associated with predisposing factors.[1] Many conditions are associated with the development of HAs. Some of the more common conditions include glycogen storage disease types I and III, maturity-onset diabetes of the young, portosystemic shunts, and therapy with steroids, androgens, or estrogen.[2,3] Notably, HAs are highly associated with oral contraceptive use in adults and adolescents.[2]

HA is significantly rarer in children than in adults, with an estimated incidence of approximately 1 per million children.[4] HAs are most identified incidentally on imaging in patients being screened because of an underlying condition known to increase the risk for HCC or HA. More than a quarter of children with a HA present with abdominal pain.[1] This discomfort may be related to hepatic capsular stretching and can fluctuate in severity without clear positional changes or modifying factors.[4] Acute onset of abdominal pain may result from internal hemorrhage or tumor rupture.

Before puberty, HAs occur equally in boys and girls, but after puberty, they become more common in girls, likely due to increased estrogen levels and the use of oral contraceptives. Consistent with this pattern, a 2024 systematic review of 316 children with HA found that girls accounted for 59.5% of cases.[1] The age distribution in this study further supports the pattern of puberty-related hormone stimulation leading to lesion development, with a mean patient age of 11.5 years[1].

HAs are currently categorized into distinct subtypes: inflammatory, hepatocyte nuclear factor 1-alpha (HNF-1α-mutated), β-catenin-mutated, sonic hedgehog-activated, mixed lesions, and unclassified types that do not share features with the defined categories.[1] Each subtype has a unique pathogenesis, clinical presentation, imaging appearance, and outcome. In children, a 2024 study reported that 43.2% of HAs were HNF-1α-mutated, 25.9% were

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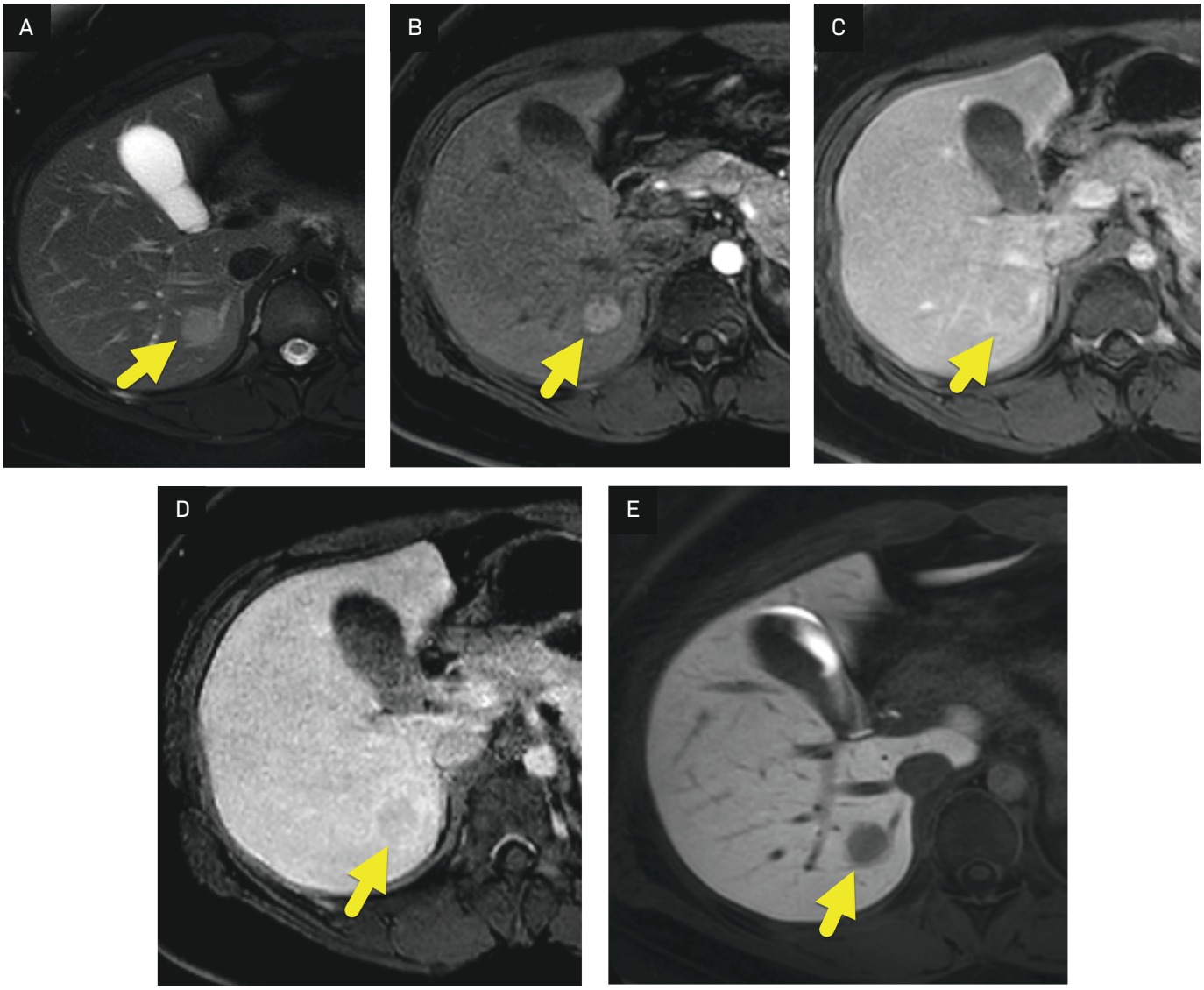
Figure 1. (A) Axial T2-weighted MR image demonstrating a small hyperintense lesion (arrow) in the right posterior section of the liver. (B) Post-contrast axial gradient recall echo images obtained in the arterial phase, (C) portal venous phase, (D) equilibrium phase, and (E) hepatobiliary phase of enhancement show the lesion (arrow) with arterial phase hyperenhancement, isointensity on the portal venous phase, faint washout on the equilibrium phase, and hypointensity on the hepatobiliary phase.

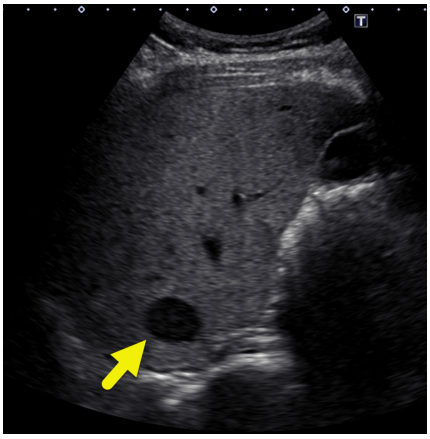


β-catenin mutated, 21% were inflammatory, and 9.9% demonstrated combined inflammatory and β-catenin mutations.[1] Mixed subtypes were identified in 7.6% of children, most commonly involving combinations of HNF-1α-mutated and β-catenin mutated adenomas, or inflammatory and β-catenin mutated lesions. Notably, the sonic hedgehog pathway mutated adenoma, which has been described in adults, has not yet been reported in children.[1]

Adult guidelines continue to be relied upon to classify and manage HAs in pediatric patients. However, this is less than optimal because the presentation, pathophysiology, and predisposing factors for HAs in children differ from those in adults.[1] In addition, the frequency of complications and management strategies for children is also distinct from the adult population.[1] Given the challenges in applying adult data to children, imaging and subsequent biopsy play a particularly important role in pediatric cases to guide diagnosis and management.

Imaging plays a central role in the diagnosis and monitoring of HAs in children. These tumors are typically large at diagnosis, with a mean lesion size of 7.4 cm.[1] US is the most common initial imaging modality used to assess the liver. HAs usually appear as heterogeneous, well-defined solid masses with internal vascularity. The lesions are typically hypoechoic to isoechoic relative

Figure 2. Transverse US of the liver showing a hypoechoic lesion (arrow) in the right posterior section.



to the surrounding liver parenchyma.[3] Contrast-enhanced US can improve diagnostic specificity by demonstrating centripetal enhancement.[5]

MRI is considered the gold standard for imaging HAs, especially when performed with the hepatocyte-specific contrast agent gadoxetate disodium. The MRI appearance of HAs varies depending on the degree of fat content, vascularity, hemorrhage, and necrosis within the lesion. Acute intratumoral hemorrhage presents as high signal intensity on T1-weighted imaging, while chronic hemorrhage demonstrates low signal intensity on both T1- and T2-weighted sequences.

The MRI appearance of HAs varies by subtype in adults, although these imaging patterns have not yet been fully validated in children. In adults, HNF-1α-mutated HAs most commonly demonstrate diffuse signal loss on out-of-phase imaging due to intratumoral fat deposition.[4,6,7] These lesions can have variable signal intensity, with slight hyperintensity on T2-weighted imaging and moderate arterial phase enhancement without retention of hepatocyte-specific contrast on the hepatobiliary phase. The background liver is often diffusely steatotic.[6] Inflammatory adenomas appear heterogeneous on T2-weighted imaging. The lesions may have peripheral T2 hyperintense signal in a pattern known as the "atoll sign."[6,7] Inflammatory adenomas exhibit avid arterial phase enhancement that persists into the portal venous and equilibrium phases.[6] Hemorrhage occurs in approximately 30% of inflammatory adenomas. β-Catenin-mutated adenomas do not have specific imaging features but can show intense arterial phase enhancement with subsequent washout, resembling HCC.[7] These lesions may retain contrast on the hepatobiliary phase, which can aid in differentiation.

The prognosis of HAs in children remains incompletely defined but primarily depends on 2 major risks: hemorrhage and malignant transformation.[1,8,9] Malignant transformation to HCC is rare in children. When it does occur, it is typically associated with predisposing conditions such as glycogen storage disease and congenital portosystemic shunts.[2] Among the subtypes, β-catenin-mutated adenomas carry the highest risk of malignant transformation. Hemorrhage is believed to be a more frequent complication, although the incidence and risk factors have not been well defined in children. In adults, hemorrhage has been associated with adenomas larger than 5 cm in diameter and with the inflammatory subtype.[4]

Management of HAs is based on several factors, including the presence of symptoms, lesion size, number of lesions, subtype classification, and overall surgical risk. Strategies may include discontinuation of hormone therapy, serial imaging surveillance, screening for malignant transformation with serum AFP, and, in select cases, surgical resection. For small lesions that are not subcapsular or atypical in appearance, monitoring with serial imaging and AFP levels is typically recommended. Lesions measuring less than 5 cm can often be managed conservatively with surveillance imaging. Patients with underlying cirrhosis require routine US surveillance due to their elevated risk of HCC.[8,9]

Elective surgical resection is generally advised for males with HAs regardless of lesion size, and for females with lesions larger than 5 cm. Lesions greater than 7 cm warrant close monitoring or surgical intervention due to their increased risk of hemorrhage. In patients with acute hemorrhage, transarterial embolization of the hepatic artery may be performed to control bleeding. Liver transplantation may be considered in patients with adenomatosis (defined as more than 10 lesions), given the higher potential for malignant transformation.[8,9]

Summary

HA is a benign liver tumor that is rare in children and most commonly occurs in association with underlying conditions such as glycogen storage disease. Despite its benign nature, HA carries risks of hemorrhage, rupture, and malignant transformation. Patients are often asymptomatic until complications such as hemorrhage or rupture develop. MRI is the preferred imaging modality, providing superior lesion characterization. Management strategies include discontinuation of hormone therapy, serial imaging, and surgical resection. In select cases, liver transplantation may be considered for patients with adenomatosis, and transarterial embolization can be used to control acute hemorrhage.

References

1) Scheers I, Tambucci R, De Magnee C, et al. Paediatric hepatocellular adenomas: lessons from a systematic review of relevant literature. *JHEP Rep*. 2024;6(6):101078. doi:10.1016/j.jhepr.2024.101078

2) Shreenath AP, Grant LM, Adenoma KAH. Hepatocellular adenoma. In: *StatPearls* [Internet]. StatPearls Publishing. 2024.

https://doi.org/10.37549/JPCR-25-0058

3) Franchi-Abella S, Branchereau S. Benign hepatocellular tumors in children: focal nodular hyperplasia and hepatocellular adenoma. *Int J Hepatol*. 2013;2013:215064. doi:10.1155/2013/215064

4) Espinoza AF, Vasudevan SA, Masand PM, Lòpez-Terrada DH, Patel KR. Pediatric hepatocellular adenomas: what is known and what is new? *Cancers*. 2023;15(19):4790. doi:10.3390/cancers15194790

5) Fang C, Bernardo S, Sellars ME, Deganello A, Sidhu PS. Contrast-enhanced ultrasound in the diagnosis of pediatric focal nodular hyperplasia and hepatic adenoma: interobserver reliability. *Pediatr Radiol*. 2019;49(1):82-90. doi:10.1007/s00247-018-4250-5

6) Dharmana H, Saravana-Bawan S, Girgis S, Low G. Hepatocellular adenoma: imaging review of the various molecular subtypes. *Clin Radiol*. 2017;72(4):276-285. doi:10.1016/j.crad.2016.12.020

7) van Aalten SM, Thomeer MGJ, Terkivatan T, et al. Hepatocellular adenomas: correlation of MR imaging findings with pathologic subtype classification. *Radiology*. 2011;261(1):172-181. doi:10.1148/radiol.11110023

8) Grazioli L, Olivetti L, Mazza G, Bondioni MP. MR imaging of hepatocellular adenomas and differential diagnosis dilemma. *Int J Hepatol*. 2013;2013:374170. doi:10.1155/2013/374170

9) Aziz H, Underwood PW, Gosse MD, et al. Hepatic adenoma: evolution of a more individualized treatment approach. *J Gastrointest Surg*. 2024;28(6):975-982. doi:10.1016/j.gassur.2024.03.010