

Hepatocellular Adenoma Mimicking Hepatocellular Carcinoma in a 15-Year-Old Girl: A Diagnostic and Imaging Challenge

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"Cite this Article" Received: 12 December 2025; Accepted: 07 February 2026; Published: 28 February 2026

Author Contributions: Concept: RTYK, NHL; Design: RTYK, NH, NR, GA; Data Collection: KHK, KUK, AR, DK, MUK; Analysis: RTYK, DK, NH, NR, GA, NHL; Drafting: KHK, KUK, RTYK, AR, DK, NH, MUK, NR, GA, NHL **Ethical Approval:** Sindh Institute of Urology and Transplantation. **Informed Consent:** Written informed consent was obtained from all participants; **Conflict of Interest:** The authors declare no conflict of interest. **Funding:** No external funding; **Data Availability:** Available from the corresponding author on reasonable request; **Acknowledgments:** NA

ABSTRACT

Background: Hepatocellular adenoma (HCA) is an uncommon benign hepatocellular neoplasm that predominantly affects young women and is frequently associated with hormonal, metabolic, or genetic risk factors. HCA is rare in children and adolescents, and its radiological appearance may overlap with other hepatocellular tumors, creating substantial diagnostic uncertainty. **Case Presentation:** A 15-year-old girl presented with a two-year history of intermittent right hypochondrial pain without jaundice, constitutional symptoms, oral contraceptive exposure, alcohol or drug use, or known chronic liver disease. Hepatitis B and C serology was negative. Contrast-enhanced computed tomography demonstrated multiple bilobar hepatic lesions with arterial-phase enhancement and subsequent portal venous/delayed-phase washout, raising concern for a hepatocellular malignancy. The largest lesion measured $3.6 \times 4.6 \times 3.8$ cm and mildly compressed the inferior vena cava without invasion. Serum alpha-fetoprotein was normal at 0.75 ng/mL, whereas protein induced by vitamin K absence or antagonist-II was markedly elevated at 333.9 mAU/mL. Core-needle biopsy demonstrated mildly thickened hepatocellular trabeculae, focal alteration of the reticulin framework, fatty change, and unpaired arteries without significant cytological atypia, necrosis, or mitotic activity; the findings were interpreted by an expert pathologist as hepatocellular adenoma. **Outcomes:** Following multidisciplinary review, no immediate oncological or surgical intervention was initiated, and interval imaging at three months was planned. **Conclusion:** Multifocal HCA in an adolescent may exhibit enhancement characteristics that overlap with HCC. Discordance between imaging, tumor markers, and limited biopsy findings requires cautious multidisciplinary interpretation rather than reliance on a single diagnostic modality. **Keywords:** Hepatocellular Adenoma, Hepatocellular Carcinoma, Liver Neoplasms, Adolescent, Liver Biopsy, Diagnostic Imaging

INTRODUCTION

Hepatocellular adenoma (HCA) is a benign hepatocellular neoplasm characterized by substantial biological, pathological, and radiological heterogeneity. Although classically associated with women of reproductive age and exposure to estrogen-containing oral contraceptives, HCA may also occur in association with obesity, metabolic abnormalities, androgen exposure, glycogen-storage disorders, and specific molecular alterations. Contemporary molecular classification has further established that HCA comprises several biologically distinct subtypes with differing imaging characteristics and risks of hemorrhage and malignant transformation (1,2,7,10).

HCA is distinctly uncommon in the pediatric population, in whom the spectrum of predisposing factors and differential diagnoses differs from that encountered in adults. Pediatric HCA may occur as a solitary lesion or as multifocal disease, and recent pediatric imaging data demonstrate that arterial-phase hyperenhancement and even apparent washout are not exclusive to malignant hepatocellular tumors. In a recent series of histologically proven pediatric HCAs, arterial-phase hyperenhancement was observed in most evaluable lesions and washout was present in a substantial proportion, highlighting

the potential for radiological overlap with malignant hepatocellular neoplasms (3,11). Magnetic resonance imaging (MRI), particularly with hepatobiliary contrast agents, therefore plays an important role in lesion characterization in children and adolescents (2–4,11).

The distinction between HCA and hepatocellular carcinoma (HCC) becomes particularly challenging when a lesion demonstrates arterial hyperenhancement followed by relative hypoenhancement or washout on later phases. Importantly, non-invasive imaging criteria used for diagnosing HCC have primarily been validated in populations at sufficiently high risk for HCC, particularly adults with cirrhosis or selected patients with chronic hepatitis B, and should not automatically be extrapolated to an otherwise healthy adolescent without established chronic liver disease (5,12). Histopathological assessment may therefore be necessary when clinical probability and radiological findings are discordant.

We report an unusual case of multiple bilobar hepatocellular lesions in a 15-year-old girl without known chronic liver disease or conventional hormonal risk factors. The lesions demonstrated an HCC-like enhancement pattern on multiphasic CT, while serum alpha-fetoprotein (AFP) was normal and protein induced by vitamin K absence or antagonist-II (PIVKA-II) was substantially elevated. Core-biopsy findings were interpreted as HCA. The case illustrates the diagnostic difficulty created by discordant clinical, imaging, biochemical, and histopathological findings and emphasizes the need for multidisciplinary assessment before committing a young patient to oncological treatment.

CASE REPORT

A 15-year-old girl from Punjab, Pakistan, presented to the outpatient department with intermittent right hypochondrial pain of approximately two years' duration. The pain had initially been mild but had gradually become more noticeable. She reported no associated weight loss, jaundice, vomiting, fever, or other constitutional symptoms. There was no reported history of oral contraceptive use, smoking, alcohol consumption, or recreational drug use. No family history of chronic liver disease or hepatic malignancy was reported. Serological testing for hepatitis B and hepatitis C was negative.

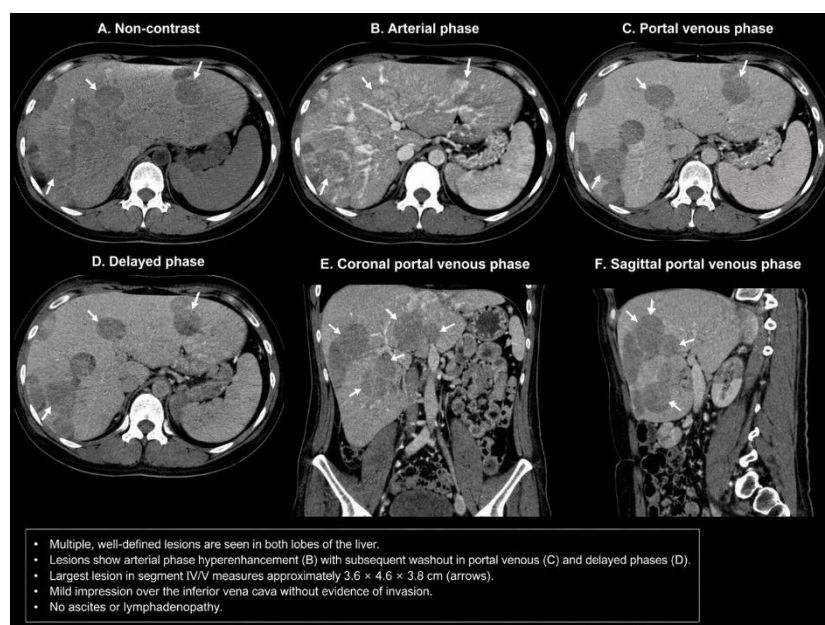


Figure 1. Contrast-enhanced CT showing multiple bilobar hepatic lesions with arterial-phase hyperenhancement and subsequent portal venous/delayed-phase washout.

On initial clinical assessment, the patient appeared pale but was otherwise clinically stable. The abdomen was soft, non-tender, and non-distended, without clinically evident features of chronic liver disease. Cardiovascular, respiratory, and neurological examinations were unremarkable. Her pulse rate was 78 beats/min and respiratory rate was 20 breaths/min. A blood pressure of 100/90 mmHg was recorded in

the source clinical documentation; because of the unusually narrow pulse pressure, confirmation of this measurement from the original clinical record is advisable before final publication.

Laboratory investigations demonstrated hemoglobin of 10.3 g/dL, total leukocyte count of $9.6 \times 10^9/L$, and platelet count of $306 \times 10^9/L$. Total bilirubin was 0.45 mg/dL, alanine aminotransferase was 31 U/L, aspartate aminotransferase was 29 U/L, alkaline phosphatase was 103 U/L, and gamma-glutamyl transferase was 13 U/L. Serum AFP was within the reported laboratory reference range at 0.75 ng/mL (reference <8.5 ng/mL). In contrast, serum PIVKA-II was markedly elevated at 333.9 mAU/mL.

Abdominal ultrasonography demonstrated multiple hepatic lesions. Contrast-enhanced multiphasic CT of the abdomen subsequently demonstrated multiple lesions involving both hepatic lobes. These lesions showed arterial-phase enhancement followed by relative hypoenhancement/washout on portal venous and delayed-phase imaging. Given this enhancement pattern, a hepatocellular malignancy, including HCC, was considered radiologically. However, interpretation was complicated by the patient's very young age, absence of known cirrhosis or chronic viral hepatitis, and normal AFP.

The largest lesion measured approximately $3.6 \times 4.6 \times 3.8$ cm and produced mild compression of the inferior vena cava without radiological evidence of vascular invasion. No biliary dilatation, ascites, or lymphadenopathy was identified. The bilobar distribution raised the possibility of multifocal HCA or an adenomatosis-type presentation, although the precise number of lesions available in the original radiology report was not specified. Because the imaging appearance and clinical context were discordant, tissue diagnosis was pursued. Percutaneous liver biopsy yielded two core samples. Histological examination demonstrated mildly thickened hepatocellular trabeculae, focal alteration/loss of the reticulin framework, fatty change, and unpaired arteries. No significant cytological atypia, tumor necrosis, or increased mitotic activity was identified. Following expert pathological review, the findings were interpreted as consistent with hepatocellular adenoma.

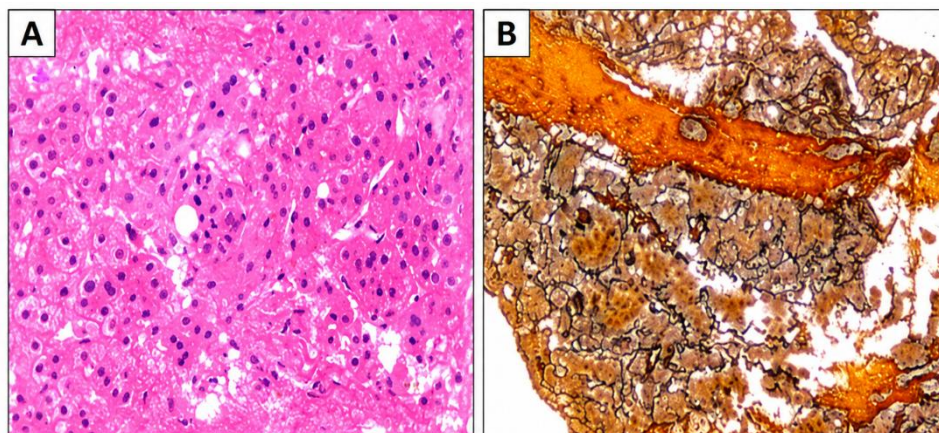


Figure 2. Histopathological images showing mildly thickened hepatocellular trabeculae, fatty change, unpaired arteries, and focal reticulin alteration, consistent with hepatocellular adenoma.

The pathological assessment materially altered the initial diagnostic impression; however, the findings were interpreted in the context of the limited core-biopsy sample rather than being considered independently definitive for every hepatic lesion. In a patient with multifocal disease, two biopsy cores may not establish that all radiologically identified lesions share identical histological characteristics. Furthermore, because molecular or immunohistochemical HCA subtyping was not reported in the available clinical record, a specific HCA molecular subtype could not be assigned.

The differential diagnosis included HCA, HCC, focal nodular hyperplasia, and other less common hepatocellular neoplasms occurring in adolescents. HCC was initially considered because of arterial enhancement, subsequent washout, bilobar involvement, and elevation of PIVKA-II. Against a straightforward diagnosis of conventional HCC were the patient's age, absence of established chronic

liver disease, normal AFP, lack of vascular invasion or metastatic disease, and absence of overt malignant cytological features in the biopsy material. HCA was favored following expert histopathological review. Focal nodular hyperplasia remained a radiological differential consideration but was considered less consistent with the reported histopathological architecture.

The markedly elevated PIVKA-II remained an important discordant finding. PIVKA-II, also known as des-gamma-carboxy prothrombin, has established value as a biomarker associated with HCC and can complement AFP in selected clinical populations (6,8,13). Nevertheless, an abnormal PIVKA-II result cannot independently establish HCC, particularly in a low-pretest-probability population. Interpretation should take into account assay-specific reference ranges and potential disturbances in vitamin K metabolism or coagulation. Repeat PIVKA-II measurement together with assessment of vitamin K status and coagulation parameters would therefore be clinically valuable if not already performed.

Table 1. Clinical and Diagnostic Timeline

Time Point	Clinical Event	Findings/Actions	Clinical Significance
~2 years before presentation	Symptom onset	Intermittent right hypochondrial pain	Prompted evaluation
Initial presentation	Clinical assessment	No jaundice, systemic symptoms, or known liver disease	Low pre-test probability for HCC
Initial labs	Hematology/biochemistry	Mild anemia; otherwise normal liver profile	Preserved liver function
Tumor markers	AFP, PIVKA-II	AFP normal; PIVKA-II elevated	Diagnostic discordance
Imaging	Ultrasound/CT	Multiple arterially enhancing lesions with washout	HCC-like pattern
Biopsy	Core liver biopsy	No malignancy; features of HCA	Shifted diagnosis
MDT review	Management decision	Surveillance planned	Conservative approach
Follow-up	Planned imaging	3-month reassessment	Monitor stability

MRI with hepatobiliary contrast would also provide important additional characterization if not previously obtained. Contemporary evidence supports MRI as the preferred modality for characterization and longitudinal assessment of HCA, and hepatobiliary-agent MRI has particular utility in pediatric liver tumors because it may improve characterization while avoiding repeated ionizing-radiation exposure (2–4,11).

Following multidisciplinary tumor-board review, no immediate surgical or oncological treatment was initiated. The largest lesion remained below 5 cm, there was no evidence of hemorrhage, rupture, vascular invasion, ascites, or metastatic disease, and the biopsy favored a benign hepatocellular neoplasm. Interval imaging after three months was planned to assess lesion stability. Development of substantial interval growth, new radiologically suspicious characteristics, progressive biochemical abnormalities, hemorrhage, or other evidence challenging the working diagnosis would prompt repeat multidisciplinary reassessment, additional diagnostic evaluation, and consideration of definitive treatment.

DISCUSSION

This case illustrates a clinically important diagnostic conflict between radiological, biochemical, and histopathological findings in an adolescent with multifocal hepatocellular lesions. A 15-year-old girl without recognized chronic liver disease or conventional hormonal risk factors demonstrated multiple bilobar lesions with arterial-phase enhancement and subsequent washout, an imaging pattern that raised significant concern for HCC. Conversely, AFP was normal, biopsy showed no overt cytological malignancy and was interpreted as HCA, while PIVKA-II was markedly elevated. Rather than providing a simple example of a benign lesion being mistaken for HCC, the case demonstrates the limitations of interpreting any single diagnostic modality in isolation.

HCA represents a heterogeneous group of benign hepatocellular tumors rather than a single pathological entity. Molecular classification has identified biologically distinct subtypes associated with differing risk factors, imaging appearances, and malignant potential, including HNF1A-inactivated, inflammatory, β -catenin-activated, sonic hedgehog-associated, and unclassified forms (1,2,7,10). β -catenin-activated lesions are particularly relevant due to their higher risk of malignant transformation

(7,10). Consequently, molecular and immunohistochemical characterization can be clinically relevant when morphology is equivocal or imaging raises concern for malignancy.

The patient's age makes the case particularly unusual. HCA is rare in children, and pediatric cases are more frequently associated with underlying metabolic disorders such as glycogen-storage disease (3,11,14). Nevertheless, pediatric HCA can also occur without an obvious predisposing condition. Recent imaging evidence is especially relevant: pediatric HCAs may demonstrate arterial hyperenhancement and washout in a substantial proportion of cases, limiting specificity for malignancy (3,11). Thus, arterial enhancement followed by washout is not pathognomonic for HCC in adolescents.

This distinction is essential because HCC diagnostic pathways are strongly context-dependent. AASLD guidance supports non-invasive imaging diagnosis primarily in at-risk populations such as cirrhosis or chronic hepatitis B (5,12). In patients without such risk factors, imaging findings should be interpreted as suggestive of a hepatocellular neoplasm rather than diagnostic of HCC. The absence of cirrhosis, viral hepatitis, vascular invasion, metastasis, and AFP elevation significantly lowers the pre-test probability of HCC in this case.

MRI is particularly important in this setting. Hepatobiliary contrast-enhanced MRI is considered the preferred modality for HCA characterization and may help distinguish subtypes and improve diagnostic confidence (2,4,11,15). Pediatric guidelines also emphasize MRI to reduce radiation exposure during follow-up (4,11). The absence of MRI in this case is therefore a limitation.

PIVKA-II elevation adds further complexity. PIVKA-II is a recognized biomarker for HCC and may complement AFP, including in AFP-negative disease (6,8,13). However, its diagnostic performance is primarily validated in adult high-risk populations. Non-malignant causes and vitamin K-related disturbances may also influence levels. Therefore, isolated elevation cannot establish malignancy in a low-risk adolescent. Histopathology remains central but is not infallible. Limited core biopsy may not fully represent multifocal disease, and distinguishing well-differentiated HCC from HCA can be challenging. Immunohistochemical markers such as glutamine synthetase, serum amyloid A, CRP, liver fatty acid-binding protein, and β -catenin staining may assist in subtyping and malignancy exclusion (1,7,10,15). These were not available in this case. Multifocal disease raises additional considerations, including hepatic adenomatosis and underlying metabolic predisposition (3,14). In pediatric patients, evaluation for metabolic disorders is recommended when multifocal lesions are present. Management of HCA is increasingly individualized based on size, symptoms, sex, molecular subtype, and risk features (7,9,15). Lesions <5 cm without high-risk features are often managed conservatively with surveillance, as in this case.

CONCLUSION

Multifocal hepatocellular adenoma in an adolescent may closely mimic hepatocellular carcinoma on imaging, particularly when arterial hyperenhancement and washout are present. In the absence of cirrhosis or chronic viral hepatitis, such imaging findings should not be considered diagnostic of HCC. Discordance between imaging, tumor markers, and histopathology requires careful multidisciplinary evaluation. Limited biopsy sampling and absence of molecular subtyping introduce additional uncertainty. Hepatobiliary MRI and structured follow-up are essential to refine diagnosis and guide safe management in pediatric patients.

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