RJ INTERNAL MEDICINE

DOI: 10.63495/9902459 • e00011 • Published: 2026-07-01

# Giant Hepatocellular Carcinoma in a Young Adult Without Cirrhosis: A Case Report

Shamas Rafique; Iqra Rafiq; Saad A. Janjuah

## ABSTRACT

Background: Hepatocellular carcinoma (HCC) is the most common primary malignancy of the liver and typically arises in patients with chronic liver disease and cirrhosis. The occurrence of HCC in young adults without underlying liver disease is uncommon and presents distinct diagnostic and therapeutic challenges.

Case Presentation: A 23-year-old male with no significant past medical history presented with persistent right upper quadrant abdominal pain and anorexia. Laboratory investigations revealed mildly elevated liver enzymes and a significantly elevated alpha-fetoprotein (AFP) level of 817.9 ng/mL. Viral serology for hepatitis B and C was negative. Additional etiologic evaluation revealed no clinical evidence of metabolic syndrome, obesity, significant alcohol use, or family history of liver disease. Iron studies, ceruloplasmin testing, and alpha-1 antitrypsin deficiency evaluation were not available at the treating facility. Ultrasound and triphasic contrast-enhanced computed tomography demonstrated a large heterogeneous hepatic mass measuring approximately 20 cm involving segments IV, V, and VIII, with compression of adjacent hepatic vasculature but without definite vascular invasion or tumor thrombus. Imaging characteristics were categorized as LI-RADS 5. An ultrasound-guided liver biopsy confirmed well-differentiated hepatocellular carcinoma with positive CD34 and HepPar-1 immunostaining. Histopathology did not demonstrate lamellar fibrosis or morphologic features suggestive of fibrolamellar carcinoma. The tumor was deemed unresectable due to its size, bilobar involvement, and vascular compression. Following multidisciplinary tumor board evaluation, a combined treatment plan with transarterial chemoembolization (TACE) and systemic therapy with sorafenib was recommended. Immunotherapy-based combinations were not selected because treatment planning occurred in a setting where these regimens were not routinely available. Short-term follow-up is planned to assess the response.

Conclusion: Although rare, hepatocellular carcinoma can occur in young individuals without cirrhosis or viral hepatitis. This case highlights the importance of maintaining clinical suspicion for HCC when evaluating large hepatic masses in young patients and emphasizes the importance of differentiating conventional HCC from fibrolamellar carcinoma in atypical presentations. Multidisciplinary evaluation remains critical in determining appropriate management strategies for advanced unresectable disease.

## INTRODUCTION

Hepatocellular carcinoma (HCC) is the most common primary liver malignancy and represents a major global health burden,

accounting for a substantial proportion of cancer-related mortality worldwide [1]. The majority of cases develop in patients with underlying cirrhosis, most frequently associated with chronic hepatitis B virus (HBV) infection, hepatitis C virus (HCV) infection, alcohol-related liver disease, and metabolic dysfunction-associated steatotic liver disease (MASLD) [2].

HCC arising in a non-cirrhotic liver represents a distinct clinical entity, accounting for approximately 10-20% of cases in Western populations [3]. In these patients, tumors are often diagnosed at an advanced stage due to the absence of routine surveillance programs that are typically recommended for individuals with cirrhosis or chronic viral hepatitis.

HCC occurring in adolescents and young adults is particularly rare. Population-based analyses have demonstrated that younger patients frequently present with larger tumors and more advanced disease at diagnosis compared with older adults, despite having a lower incidence of underlying cirrhosis [4]. The absence of cirrhosis often results in preserved hepatic function, which may influence therapeutic decision-making.

Several etiologies have been implicated in non-cirrhotic HCC, including MASLD, chronic HBV infection, inherited metabolic disorders such as hemochromatosis and Wilson disease, alpha-1 antitrypsin deficiency, environmental toxin exposure, including aflatoxin, anabolic steroid exposure, and rare molecular subtypes such as fibrolamellar carcinoma [5-7].

Hepatocellular carcinoma occurring in young adults without cirrhosis is relatively uncommon and represents a distinct clinical entity. Tumors exceeding 20 cm in this population are rarely reported, making this case notable due to both the patient's young age and the unusually large tumor size at presentation.

## CASE DESCRIPTION

A 23-year-old male with no known chronic medical conditions presented with several weeks of persistent right upper quadrant abdominal pain associated with decreased appetite. There was no history of jaundice, fever, abdominal distension, gastrointestinal bleeding, or significant weight loss. The patient denied alcohol consumption, smoking, illicit drug use, anabolic steroid exposure, or use of herbal supplements. There was no known family history of chronic liver disease or hepatic malignancy. No clinical features of obesity or metabolic syndrome were identified. His functional status corresponded to an Eastern Cooperative Oncology Group (ECOG) performance status of 0, indicating full activity without restriction.

On physical examination, the patient was hemodynamically stable. Mild tenderness was noted in the right upper quadrant without signs of ascites or splenomegaly. No peripheral stigmata of chronic liver disease were observed.

Although viral hepatitis testing was completed, broader etiologic evaluation was limited by resource availability at the treating facility. Iron studies, autoimmune liver disease serologies, alpha-1 antitrypsin deficiency testing, elastography, and Wilson disease evaluation were not available.

### Laboratory Findings

Initial laboratory investigations (summarized in Table 1) provided important diagnostic clues. The complete blood count revealed mild anemia (hemoglobin 10.4 g/dL; reference: 13.5-17.5 g/dL), which may be attributable to chronic disease. The normal platelet count (311 × $10^3$/microL; reference: 140-440 × $10^3$/microL) argued against the presence of significant portal

hypertension or hypersplenism.

Liver function tests demonstrated a predominantly cholestatic pattern. Total bilirubin was within normal limits (1.0 mg/dL; reference: <1.1 mg/dL), while alkaline phosphatase (ALP) was elevated at 210 U/L (reference: 40-150 U/L), suggesting biliary compression or mass effect. Gamma-glutamyl transferase (GGT) was elevated at 185 U/L (reference: <60 U/L), further supporting cholestasis. Alanine aminotransferase (ALT) was mildly elevated at 44 U/L (reference: 10-41 U/L), and aspartate aminotransferase (AST) was 52 U/L (reference: 10-40 U/L), indicating minimal hepatocellular injury. Lactate dehydrogenase (LDH) was elevated at 312 U/L (reference: 140-280 U/L), which may reflect tumor burden and cellular turnover. Serum albumin was within normal limits at 37 g/L (reference: 35-50 g/L), reflecting preserved hepatic synthetic function. The coagulation profile (PT 14 seconds; aPTT 32 seconds) was within normal limits. Viral serology was negative for both hepatitis B (HBsAg) and hepatitis C (anti-HCV). The serum alpha-fetoprotein (AFP) level was markedly elevated at 817.9 ng/mL (reference: 0.89-8.78 ng/mL), strongly suggesting hepatocellular carcinoma.

**Liver Disease Severity and Tumor Staging**

Based on preserved hepatic synthetic function, normal bilirubin, and absence of clinical evidence of portal hypertension, the patient was classified as Child-Pugh Class A. Radiologically, the lesion demonstrated arterial phase hyperenhancement and portal venous washout, corresponding to LI-RADS 5 classification, highly suggestive of hepatocellular carcinoma.

The tumor was categorized as Barcelona Clinic Liver Cancer (BCLC) Stage C. Although no definite vascular invasion, tumor thrombus, or distant metastasis was identified, the massive tumor burden, bilobar involvement, and significant compression of major hepatic vasculature rendered the patient unsuitable for potentially curative therapies such as surgical resection or transplantation. Importantly, imaging demonstrated vascular compression rather than definite vascular invasion.

**Imaging Studies**

Ultrasound revealed a large heterogeneous hepatic mass measuring approximately 16 × 12 cm involving both lobes with internal vascularity on Doppler imaging. Triphasic contrast-enhanced CT demonstrated hepatomegaly with a craniocaudal span of approximately 25 cm. A lobulated heterogeneous mass measuring approximately 20 cm was identified involving hepatic segments IV, V, and VIII (Figure 1). The lesion demonstrated arterial phase hyperenhancement with washout during the portal venous phase, imaging characteristics highly suggestive of hepatocellular carcinoma (Figure 2). Significant compression of the middle and left hepatic veins as well as the portal vein was observed, although no definite tumor thrombus or direct vascular invasion was identified. No evidence of extrahepatic metastasis was detected.

**Biopsy and Histopathology**

Although imaging findings strongly suggested hepatocellular carcinoma, histopathological confirmation was obtained because of the patient's young age, absence of cirrhosis, and the need to exclude fibrolamellar hepatocellular carcinoma. An ultrasound-guided percutaneous liver biopsy was performed using an 18-gauge core biopsy needle.

Microscopic examination demonstrated nests and clusters of neoplastic hepatocytes with mildly pleomorphic nuclei and abundant eosinophilic cytoplasm. Lamellar fibrosis, large polygonal cells with prominent nucleoli, and pale bodies

characteristic of fibrolamellar carcinoma were not identified in the sampled tissue.

Immunohistochemical staining demonstrated strong CD34 positivity, consistent with sinusoidal capillarization typically observed in hepatocellular carcinoma. HepPar-1 staining was positive, confirming hepatocellular differentiation.

The markedly elevated AFP level, absence of characteristic lamellar fibrosis, and conventional hepatocellular morphology favored conventional well-differentiated HCC rather than fibrolamellar carcinoma, which more commonly presents with normal or minimally elevated AFP levels.

The pathology report concluded well-differentiated hepatocellular carcinoma, although interpretation was limited by the small biopsy specimen size.

**Differential Diagnosis**

Given the patient's age and non-cirrhotic background, the differential diagnosis included fibrolamellar hepatocellular carcinoma, conventional hepatocellular carcinoma in a non-cirrhotic liver, intrahepatic cholangiocarcinoma, and metastatic liver tumors.

Fibrolamellar carcinoma was considered a particularly important differential diagnosis because it commonly occurs in adolescents and young adults without cirrhosis. However, several findings favored conventional HCC over fibrolamellar carcinoma in this case. The markedly elevated AFP level was more typical of conventional HCC, whereas fibrolamellar carcinoma often demonstrates normal or minimally elevated AFP levels. Imaging did not reveal a characteristic central scar or calcification commonly associated with fibrolamellar carcinoma. Histopathology lacked lamellar fibrosis and large eosinophilic tumor cells with prominent nucleoli characteristic of fibrolamellar carcinoma. Collectively, the morphologic and immunohistochemical findings supported conventional well-differentiated hepatocellular carcinoma.

**Multidisciplinary Management**

The case was reviewed by a multidisciplinary tumor board consisting of gastroenterology, hepatobiliary surgery, oncology, interventional radiology, and anesthesia specialists.

The tumor was considered unresectable due to massive size, bilobar involvement, and vascular compression, which precluded safe surgical resection with an adequate future liver remnant.

The consensus management plan included transarterial chemoembolization (TACE) as the primary locoregional therapy and systemic therapy with sorafenib starting at 200 mg daily with planned gradual escalation toward the standard target dose of 400 mg twice daily as tolerated.

Although contemporary first-line management for advanced unresectable HCC increasingly favors immunotherapy-based combinations such as atezolizumab-bevacizumab or durvalumab-based regimens, these therapies were not routinely available at the treating center during treatment planning. Therefore, sorafenib-based therapy was selected as the most feasible systemic option within the available treatment setting.

The sequence of clinical evaluation, diagnostic investigations, and management decisions is summarized in Table 2.

**Follow-up and Outcomes**

At the time of manuscript preparation, the patient had begun TACE and sorafenib therapy. A follow-up evaluation, including repeat AFP

measurement and contrast-enhanced imaging, was scheduled to assess treatment response according to mRECIST criteria. Detailed long-term outcome data, including tumor response, progression, or survival, are not yet available. This absence of outcome data is a limitation of the present report, and the authors plan to provide follow-up information in future correspondence if possible.

## DISCUSSION

This case highlights the unusual presentation of hepatocellular carcinoma in a young adult without known cirrhosis or viral hepatitis. HCC most commonly develops in the setting of chronic liver disease; however, a minority of cases arise in non-cirrhotic livers. Young patients with HCC frequently present with advanced disease and very large tumors because they are not included in routine surveillance programs [3,4].

Although HCC in young adults has been described previously, tumors approaching or exceeding 20 cm remain distinctly uncommon in non-cirrhotic patients. Reported cases in the literature often present with abdominal pain, palpable abdominal masses, or constitutional symptoms after substantial tumor enlargement has already occurred.

Several mechanisms have been proposed for hepatocarcinogenesis in non-cirrhotic livers, including activation of Wnt/beta-catenin signaling pathways, telomerase activation, metabolic dysfunction associated with MASLD, inherited metabolic disorders, and environmental carcinogenic exposures [5]. Chronic hepatitis B infection may also induce hepatocarcinogenesis independent of cirrhosis [6].

The etiologic evaluation in this patient was limited by resource availability. Although HBV and HCV testing were negative and there was no clinical evidence of cirrhosis, obesity, alcohol misuse, or metabolic syndrome, additional investigations, including iron studies, autoimmune serologies, ceruloplasmin testing, elastography, and alpha-1 antitrypsin deficiency evaluation, were not available. Therefore, the absence of underlying liver disease should be interpreted cautiously.

Diagnostic confirmation relied on characteristic imaging findings, markedly elevated AFP levels, and histopathological evaluation. Imaging demonstrated arterial phase hyperenhancement with portal venous washout corresponding to LI-RADS 5 classification. Biopsy was particularly important because fibrolamellar carcinoma is a key differential diagnosis in young adults without cirrhosis [7]. In contrast to conventional HCC, fibrolamellar carcinoma typically presents with normal AFP levels, central scar formation on imaging, and lamellar fibrosis histologically. The absence of these features, combined with positive HepPar-1 and CD34 staining and markedly elevated AFP, supported the diagnosis of conventional well-differentiated HCC.

Management of advanced unresectable HCC continues to evolve rapidly. Surgical resection and liver transplantation remain potentially curative options for selected patients with localized disease [8]. However, this patient's tumor was considered unresectable because of extreme tumor burden, bilobar involvement, and major vascular compression.

The multidisciplinary tumor board recommended combined TACE and sorafenib therapy. TACE induces ischemic necrosis through selective arterial embolization, while sorafenib inhibits angiogenesis and tumor proliferation pathways [9]. Although immunotherapy-based combinations have become contemporary

first-line standards for advanced HCC, treatment access and resource limitations significantly influence real-world therapeutic decisions in many healthcare settings.

Recent studies evaluating TACE combined with sorafenib have demonstrated potential benefits in advanced HCC, particularly in patients with vascular involvement [10]. Emerging data exploring combinations of TACE, targeted therapy, and immunotherapy, including PD-1 inhibitors, have shown promising outcomes in intermediate and advanced HCC [11,12]. This evolving therapeutic landscape suggests that combination immunotherapy-based approaches may further improve outcomes in future patients with similar presentations.

The prognosis for patients with non-cirrhotic HCC depends primarily on tumor stage and resectability. Preserved hepatic function may permit greater tolerance of systemic therapy; however, the massive tumor burden and vascular compression observed in this patient remain poor prognostic indicators requiring close longitudinal follow-up.

### Conclusions

Hepatocellular carcinoma may rarely occur in young adults without cirrhosis or viral hepatitis and may present with extremely large tumors due to the absence of routine surveillance. This case emphasizes that the absence of traditional risk factors does not exclude the diagnosis of HCC when evaluating large hepatic masses in young patients. The case also highlights the importance of distinguishing conventional HCC from fibrolamellar carcinoma in atypical presentations through integrated radiologic and histopathologic evaluation. Multidisciplinary assessment remains essential for determining optimal treatment strategies in advanced unresectable disease.

## ARTICLE INFORMATION

Published: 2026-07-01

Corresponding Author: Shamas Rafique
drjanjuah@gmail.com

Author Contributions: All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.
Concept and design: Shamas Rafique, Iqra Rafiq
Acquisition, analysis, or interpretation of data: Shamas Rafique, Iqra Rafiq, Saad Janjuah
Drafting of the manuscript: Shamas Rafique, Iqra Rafiq
Critical review of the manuscript for important intellectual content: Shamas Rafique, Iqra Rafiq
Supervision: Shamas Rafique

Author Affiliations

Shamas Rafique, MBBS, MD, MMed: Internal Medicine, BayCare Medical P.C., New York, USA; Internal Medicine, First Affiliated Hospital of Xinjiang Medical University, Urumqi, CHN; Medicine and Surgery, Bee Well Int. Hospital, Islamabad, PAK; General Medicine, Shabbir Clinic, Lahore, PAK

Iqra Rafiq, MBBS, MD: General Medicine, Services Hospital Lahore, Lahore, PAK; General Medicine, Shabbir Clinic, Lahore, PAK; Medicine and Surgery, Xinjiang Medical University, Urumqi, CHN

Saad Janjuah, BPS, PharmD, Rph: PharmD, Long Island University, Brooklyn, New York, USA

Acknowledgements: None.

The full article and any supplementary material are available at rjmedicine.org/publications/e00011

## REFERENCES

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer Statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2021;71(3):209-249. 10.3322/caac.21660

2. Marrero JA, Kulik LM, Sirlin CB, Zhu AX, Finn RS, Abecassis MM, et al. Diagnosis, staging, and management of hepatocellular carcinoma: 2018 practice guidance by the American Association for the Study of Liver Diseases. Hepatology. 2018;68(2):723-750. 10.1002/hep.29913

3. Gaddikeri S, McNeeley MF, Wang CL, Bhargava P, Dighe MK, Yeh MM, et al. Hepatocellular carcinoma in the noncirrhotic liver. AJR Am J Roentgenol. 2014;203(1):W34-W47. 10.2214/AJR.13.11511

4. Guan Y, Gan Y, An J. Clinical characteristics and prognosis of early-onset hepatocellular carcinoma: a retrospective cohort study based on population data. Dig Dis Sci. 2024;69(9):3563-3573. 10.1007/s10620-024-08549-9

5. Baffy G, Brunt EM, Caldwell SH. Hepatocellular carcinoma in non-alcoholic fatty liver disease: an emerging menace. J Hepatol. 2012;56(6):1384-1391. 10.1016/j.jhep.2011.10.027

6. Botto I, Serrazina J, Freitas CR, Carvalhana S,

Nogueira-Costa G, Cortez-Pinto H. Hepatocellular carcinoma with vascular and cardiac involvement in a young patient with non-cirrhotic hepatitis B: a case report. GE Port J Gastroenterol. 2025;32(2):134-138. 10.1159/000539093

7. Lafaro KJ, Pawlik TM. Fibrolamellar hepatocellular carcinoma: current clinical perspectives. J Hepatocell Carcinoma. 2015;2:151-157. 10.2147/JHC.S75153

8. Mazzaferro V, Regalia E, Doci R, Andreola S, Pulvirenti A, Bozzetti F, et al. Liver transplantation for the treatment of small hepatocellular carcinomas in patients with cirrhosis. N Engl J Med. 1996;334(11):693-699. 10.1056/NEJM199603143341104

9. Llovet JM, Ricci S, Mazzaferro V, Hilgard P, Gane E, Blanc JF, et al. Sorafenib in advanced hepatocellular carcinoma. N Engl J Med. 2008;359(4):378-390. 10.1056/NEJMoa0708857

10. Yang D, Du J, Nie W, Wang C, Ma Z. Combination treatment of transcatheter arterial chemoembolization, intensity-modulated radiotherapy, and sorafenib for hepatocellular carcinoma with macrovascular invasion. Medicine (Baltimore). 2023;102(45):e35713. 10.1097/MD.0000000000035713

11. Sun B, Chen L, Lei Y, Zhang L, Sun T, Liu Y, et al. Sorafenib plus transcatheter arterial chemoembolization with or without camrelizumab for the treatment of intermediate and advanced hepatocellular carcinoma. Br J Radiol. 2024;97(1159):1320-1327. 10.1093/bjr/tqae087

12. Liang L, Zhou J, Huang J, Guo Y, Zhou Z, Chen Y, et al. Sorafenib combined with tislelizumab and transarterial chemoembolization for advanced-stage hepatocellular carcinoma: a phase II study. Immunotargets Ther. 2025;14:1187-1200. 10.2147/ITT.S543741

| Parameter | Result | Reference Range | Interpretation |
|---|---|---|---|
| Hemoglobin | 10.4 g/dL | 13.5–17.5 g/dL | Mild anemia |
| White blood cells | 8.3 × $10^3$/µL | 4–11 × $10^3$/µL | Normal |
| Platelets | 311 × $10^3$/µL | 140–440 × $10^3$/µL | Normal |
| Total bilirubin | 1.0 mg/dL | ≤1.1 mg/dL | Normal |
| ALT | 44 U/L | 10–41 U/L | Mild elevation |
| AST | 52 U/L | 10–40 U/L | Mild elevation |
| Alkaline phosphatase (ALP) | 210 U/L | 40–150 U/L | Elevated |
| Gamma-glutamyl transferase (GGT) | 185 U/L | <60 U/L | Elevated |
| Lactate dehydrogenase (LDH) | 312 U/L | 140–280 U/L | Elevated |
| Albumin | 37 g/L | 35–50 g/L | Normal |
| HBsAg | Non-reactive | Non-reactive | Negative |
| Anti-HCV | Non-reactive | Non-reactive | Negative |
| AFP | 817.9 ng/mL | 0.89–8.78 ng/mL | Markedly elevated |
| PT | 14 sec | 11–14 sec | Normal |
| aPTT | 32 sec | 25–35 sec | Normal |

Table 1: Laboratory findings on admission.

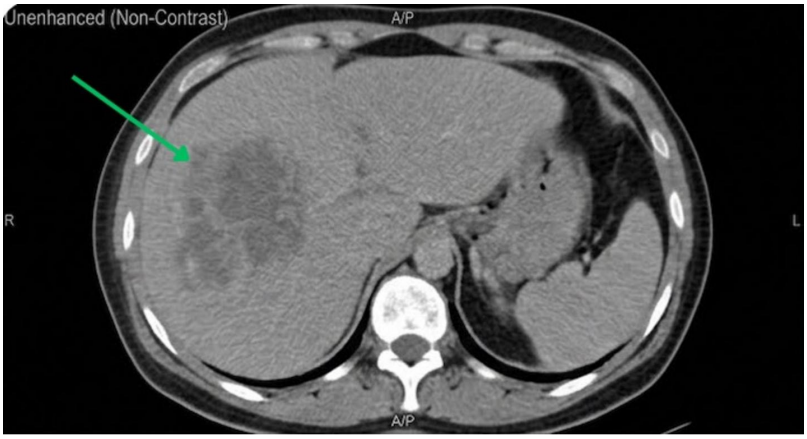


Figure 1: Unenhanced (non-contrast) axial CT image of the upper abdomen
A large heterogeneous hypodense lesion is visible in the right hepatic lobe (green arrow), demonstrating the mass before contrast administration.

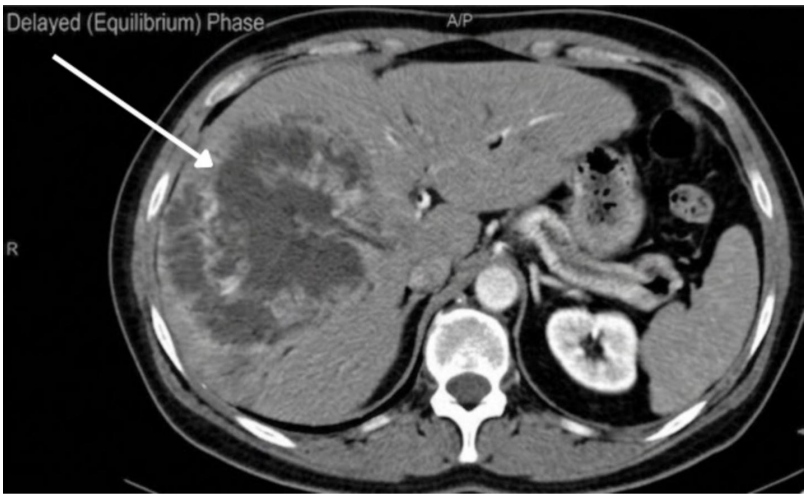


Figure 2: Delayed (equilibrium) phase contrast-enhanced axial CT image
The same lesion demonstrates heterogeneous enhancement (white arrow), with internal heterogeneity characteristic of a hepatic malignancy. The imaging findings illustrate a large hepatic mass requiring further multiphasic imaging and clinical correlation for definitive characterization.

| Time | Event |
|---|---|
| Week 0 | Symptom onset |
| Week 2 | Clinical evaluation and initial laboratory testing |
| Week 3 | Ultrasound detected hepatic mass |
| Week 4 | Triphasic CT demonstrated LI-RADS 5 lesion highly suggestive of HCC |
| Week 5 | AFP level reported markedly elevated |
| Week 6 | Ultrasound-guided biopsy performed |
| Week 7 | Histopathology confirmed HCC |
| Week 8 | Multidisciplinary tumor board discussion |
| Week 9 | Treatment initiated |

Table 2: Clinical Timeline of Events.