British Journal of Hospital Medicine

Br. J. Hosp. Med. (Lond) **2026**; 87(7): 56026
https://doi.org/10.31083/BJHM56026

Case Report

Hepatocellular Carcinoma Presenting With Extensive Portal Vein Tumour Thrombus Without Evidence of Underlying Liver Cirrhosis or Steatosis: A Case Report

Ami Schattner[1,2,3,*], Livnat Uliel[3,4], Itzhak Schechtman[3,5], Ina Dubin[1,3]

[1]Department of Medicine, Laniado Hospital, 4244916 Netanya, Israel
[2]Faculty of Medicine, Hebrew University-Hadassah, 91120 Jerusalem, Israel
[3]Adelson School of Medicine, Ariel University, 40700 Ariel, Israel
[4]Department of Imaging, Laniado Hospital, 4244916 Netanya, Israel
[5]Department of Pathology, Laniado Hospital, 4244916 Netanya, Israel
*Correspondence: amischatt@gmail.com (Ami Schattner)
Academic Editor: Ganesh Radhakrishna
Submitted: 1 January 2026 Revised: 22 April 2026 Accepted: 28 May 2026 Published: 23 July 2026

Abstract

Aims/Background: Most cases of hepatocellular carcinoma (HCC) develop in the setting of chronic liver disease (CLD), usually with chronic inflammation, fibrosis, or cirrhosis. The case aims to highlight a rare presentation without evidence of prior CLD. **Case Presentation:** An older adult patient with no risk factors for CLD other than type 2 diabetes, overweight, and hypertension presented with high-gradient ascites, splenomegaly and hypersplenism due to portal hypertension. **Results:** Imaging identified an extensive tumour thrombus extending from the portal vein and hepatic veins to the inferior vena cava and right atrium—adjacent to a liver mass. Alpha-fetoprotein was extremely elevated. Ultrasound-guided core liver needle biopsy of the mass was diagnostic of HCC. Biosynthetic liver functions were preserved, liver imaging did not show cirrhosis or steatosis, and liver tissue adjacent to the tumour showed no CLD. **Conclusion:** HCC may rarely present with tumour thrombus-associated portal hypertension and ascites, and very rarely arise with no demonstrable background of liver pathology. Absence of demonstrable CLD does not rule out HCC and its complications.

Keywords: portal vein; portal hypertension; tumour thrombus; hypercoagulability; hepatocellular carcinoma; alpha-fetoprotein; case report

1. Introduction

Hepatocellular carcinoma (HCC) accounts for 75–86% of primary liver cancers, remains the sixth most common cancer worldwide, and is an even more common cause of cancer deaths [1]. Most of the cases develop in patients with liver cirrhosis of any aetiology. Chronic liver inflammation is another well-established risk factor of HCC, mostly associated with chronic hepatitis B or metabolic dysfunction-associated steatotic liver disease (MASLD). In these patients, HCC can also develop without cirrhosis. MASLD (previously termed nonalcoholic fatty liver disease) is currently the most common chronic liver disease (CLD) worldwide, affecting approximately 1:4 of the population. Thus, it is projected to increase the incidence of HCC dramatically in the foreseeable future [2]. HCC is diagnosed primarily in at-risk patients such as those with cirrhosis or chronic viral hepatitis. The American Association for the Study of Liver Diseases (AASLD) recommends that the diagnosis should be based on contrast-enhanced computed tomography (CT) or magnetic resonance imaging (MRI), supported by histologic confirmation when imaging results are inconclusive [1]. The treatment is determined by tumour stage using the Barcelona Clinic Liver Cancer (BCLC) staging system [3], as well as liver function and the patient's performance status. Multidisciplinary care is essential, involving hepatologists, oncologists, and surgeons. Options start from surgical resection or percutaneous ablation in early disease, through transarterial chemoembolization for intermediate-stage disease. Advanced-stage HCC is treated with tyrosine kinase inhibitors and immune checkpoint inhibitors, whereas terminal stages are given supportive palliative care [1,3]. We demonstrate here that advanced HCC can very rarely develop with no demonstrable evidence of an underlying CLD of any sort, and present with manifestations related to an extensive tumour thrombus in the portal vein. Thus, clinicians need to be aware that very rarely, absence of demonstrable CLD does not rule out HCC and its complications.

2. Case Report

An independent non-smoking man in his late seventies, with no history of alcohol abuse, was admitted with new-onset ascites and leg oedema, complaining of increasing girth, abdominal pain, and constipation over 3 weeks. He appeared overweight (body mass index [BMI] 28.7 kg/m^2), but the examination was non-contributory other than marked ascites and symmetric 3+ pitting oedema. Specifically, he had no stigmata of chronic liver disease

such as clubbing, spider angiomata, palmar erythema, or gynaecomastia. He had longstanding, relatively well-controlled type 2 diabetes (last outpatient haemoglobin A1c [HbA1c] 7%), hypertension (controlled), coronary artery disease with stent placement, transcatheter aortic valve implantation (TAVI), compensated heart failure (with preserved ejection fraction), and prostate cancer (after resection/irradiation years ago). Thus, the focus of the investigations was elucidating the cause of the ascites, which evolved into symptomatic tense ascites.

Laboratory tests showed pancytopenia (Haemoglobin 11.2 g/dL, white blood cells (WBC) 3.5 × 10^9/L, platelets 130 × 10^9/L); blood urea nitrogen (BUN) 18 mg/dL and creatinine 1.2 mg/dL (estimated glomerular filtration rate 64 mL/min/1.73 m²), with normal electrolytes; glucose 193 mg/dL and HbA1c 6.7% on admission, prothrombin time (PT) 11.5 seconds (prothrombin activity: 99%), albumin 3.8 g/dL, and globulins 2.5 g/dL. Hepatocellular enzymes were normal or only minimally elevated, with alanine aminotransferase (ALT) 29 IU/L (later 37, N <41) and aspartate aminotransferase (AST) 40 IU/L (later 53, N <40). The lactate-dehydrogenase (LDH) was 278 IU/L (N <220). In contrast, cholestatic enzymes were remarkable: alkaline phosphatase (ALP) 394 IU/L (N <105), and gamma-glutamyltransferase (GGT) 705 IU/L (N <36), with normal bilirubin and pancreatic enzymes. C-reactive protein (CRP) was 22.5 mg/L (N <5). Ascites fluid yielded 0.8 g/dL albumin and 63 IU/L LDH, consistent with transudate, since serum-ascites albumin gradient [SAAG] was 3 g/dL and LDH ratio was 0.24. The total protein in the ascites fluid was 1.1 g/dL. This is important, since in transudates due to heart failure it is usually >2.5 g/dL [4]. The fluid contained 256 cells/µL, with 91% monocytes, and normal morphology. Microbiological and cytological workup of the ascites fluid was negative. Serology for hepatitis B (HBV) and C (HCV) viruses was negative, including hepatitis B surface antigen (HBsAg), and neither HBV nor HCV viral load was identified by molecular methods (PCR).

3. Imaging Studies and Histology

Abdominal imaging (which included ultrasound, Doppler ultrasound and contrast-enhanced computed tomography [CT]) revealed a liver mass (Fig. 1A) and an extensive portal vein obstruction with characteristics of a tumour thrombus (Fig. 1A–D). Extension into the distal inferior vena cava (IVC)/right atrium (RA) was demonstrated, and this was confirmed by echocardiography (echo not shown). Thus, tense ascites, with splenomegaly and hypersplenism causing pancytopenia were due to portal hypertension secondary to portal vein obstruction by the thrombus. Chest CT was suggestive of pulmonary metastases (Fig. 1E). However, the background liver appearance on ultrasound and CT imaging was normal: it did not show characteristics of liver cirrhosis (e.g., liver surface nodularity due to regenerative nodules and fibrous septa) and neither did it show fatty infiltration. The liver mass suspicious of cancer was associated with a micronodular lung pattern consistent with carcinomatous lymphangitis (Fig. 1). Alpha-fetoprotein (AFP) levels were high (1576 ng/mL) whereas carcinoembryonic antigen (CEA) and Carbohydrate Antigen 19-9 (CA19-9) markers were not increased. Ultrasound-guided liver core needle biopsy (after abdominal paracentesis) was diagnostic of hepatocellular carcinoma (HCC), moderately differentiated (Figs. 2,3). Immunostaining revealed diffuse cytoplasmic HepPar-1 and arginase-1 positivity. In the liver cells surrounding the tumour, no significant pathology could be seen (Fig. 4). The patient's non-alcoholic fatty liver disease (NAFLD) activity score (NAS) was 0 to the best of our knowledge, and his barcelona clinic liver cancer (BCLC) stage was C, signifying advanced stage due to portal invasion and/or extrahepatic spread, but preserved liver function [3,5].

4. Differential Diagnosis

The differential diagnosis centred on the identification of HCC as well as on the nature of the portal system thrombus and the robust ruling out of a variety of underlying chronic liver diseases. Portal vein thrombosis (PVT) in patients without cirrhosis can be caused by myeloproliferative disorders, inherited or acquired thrombophilia, adjacent inflammation, and abdominal trauma including surgery [6]. In our patient with HCC, tumour thrombus was the major finding, although it may predispose to secondary, non-tumoural PVT [7]. Thus, there was no indication to look further for any thrombophilia. HCC and cholangiocarcinoma can have similar features, especially when the latter presents with mass or vascular invasion. Intrahepatic cholangiocarcinoma also has a predilection for vascular invasion and may cause a tumour thrombus in the portal vein. However, markedly increased AFP is characteristic of HCC (vs. increase CEA, CA19-9) [8] and the histology (e.g., absence of thickened bile duct wall or bile duct invasion) and imaging (Fig. 1) all favour HCC.

The absence of an underlying chronic liver disease was strongly suggested by the negative history of alcohol abuse or of known liver disease, absent stigmata of chronic liver disease on physical examination, normal biosynthetic liver function (serum albumin and PT), normal globulins that were not increased, and negative viral serology/PCR. Moreover, the imaging appearance of the liver was not consistent with cirrhosis or steatosis. This was supported by the bland liver histology adjacent to the tumour (Fig. 4).

Finally, a thrombus composed of tumour cells has to be distinguished from 'bland' thrombus composed of platelets, fibrin, and macrophages. This can be done by biopsy (seldom performed) or autopsy (too late), but tumour thrombi also have distinctive imaging characteristics with high diagnostic specificity [9]. Tumour thrombus appears contiguous with the cancerous mass, has similar imaging features, and demonstrates enhancement, together achiev-

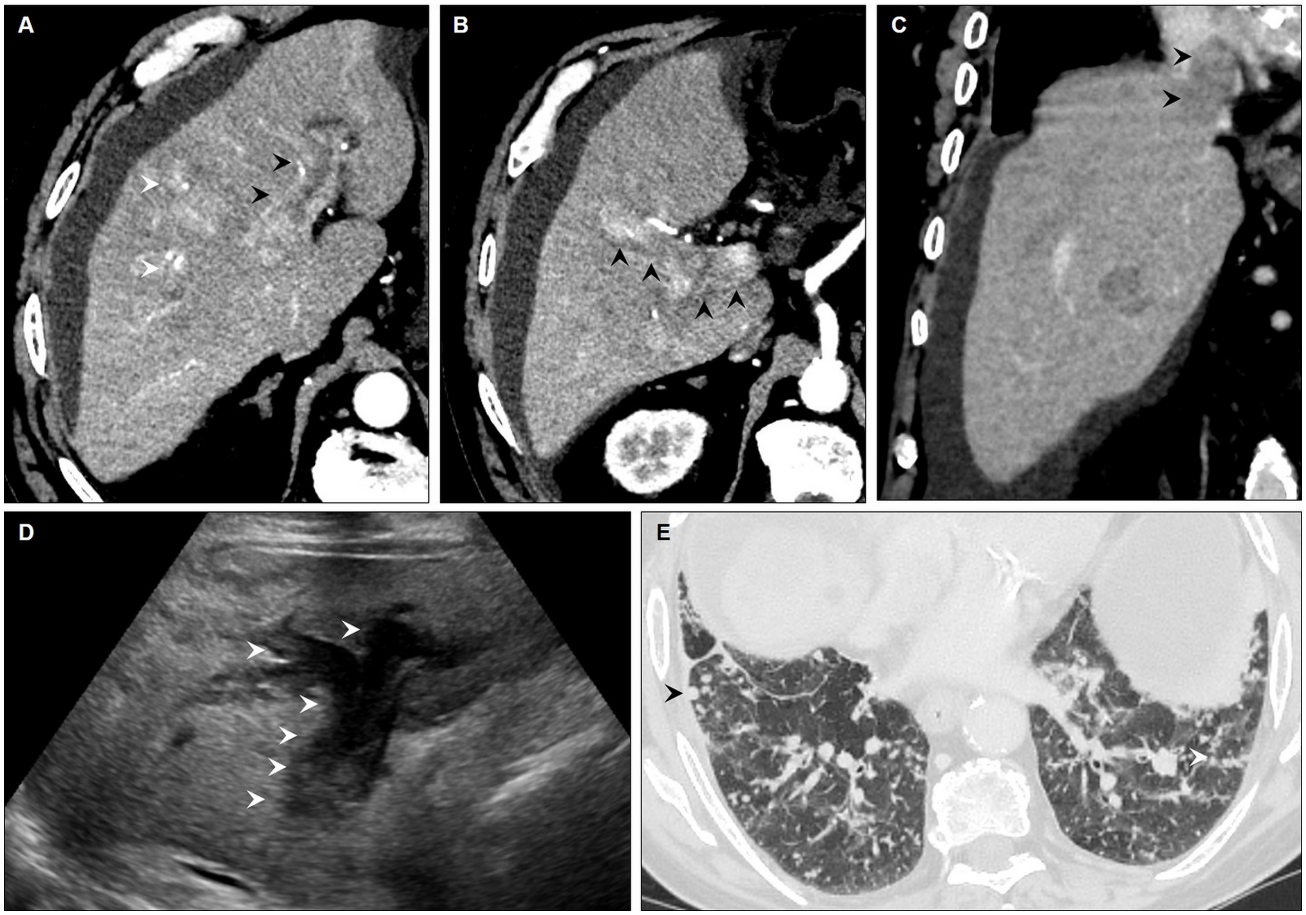

Fig. 1. Infiltrative hepatocellular carcinoma (HCC) with extensive portal vein tumour thrombus. Axial contrast-enhanced computed tomography (CT) images in the arterial phase (A,B) demonstrate tumour thrombus involving the left portal vein (black arrowheads in A), as well as the main and right portal veins (arrowheads in B). An enhancing component of the infiltrative tumour is evident in the right liver (white arrowheads in A). On venous phase imaging (C), tumour extension into the middle hepatic vein with contiguous involvement of the inferior vena cava (IVC) is noted (arrowheads in C). The extensive portal veins tumour thrombus is also visualized on conventional ultrasound (white arrowheads in D) and Doppler ultrasound (not shown). Chest CT reveals multiple pulmonary nodules (black arrowhead in E) and irregular nodular interstitial thickening (white arrowhead in E), suggestive of pulmonary metastases. As can be seen, the liver does not show changes typical of cirrhosis.

ing a specificity of nearly 100% in the portal venous system.

5. Management Approach and Patient Outcome

In the absence of prospective randomized studies, there is no consensus on the optimal management of HCC with tumour thrombus. Classified as Child-Pugh score class B, but advanced disease (BCLC stage C), the median overall survival is 10–16 weeks without treatment [10]. Highly selected patients with preserved liver function may be considered for surgical resection, but this was not feasible here due to the involvement of the IVC and RA, not to mention the suspected pulmonary carcinomatous lymphangitis. First-line systemic options are sorafenib (400 mg bid), lenvatinib (8–12 mg/d), and intravenous atezolizumab plus bevacizumab. Durvalumab-tremelimumab is another Food and Drug Administration (FDA)-approved first-line option for unresectable HCC, recommended by both AASLD and National Comprehensive Cancer Network (NCCN) guidelines [1]. Currently, the most updated evidence-based guidelines come from the European Society for Medical Oncology (ESMO); however, future research may further improve both early detection and therapy [3]. Routine use of low molecular weight heparin (LMWH) is not recommended, unlike ‘bland’ PVT, and our patient received only a prophylactic mentioned; the treatment of portal vein tumour thrombus is not by anticoagulation but should be directed at the underlying malignancy. A retrospective study of 122 HCC patients with PVT (52% of whom had confirmed tumour thrombus in the anticoagulation group) found no survival difference between anticoagulated and non-anticoagulated patients (median survival 6 months in both groups; hazard ratio [HR] 0.91, 95% confi-

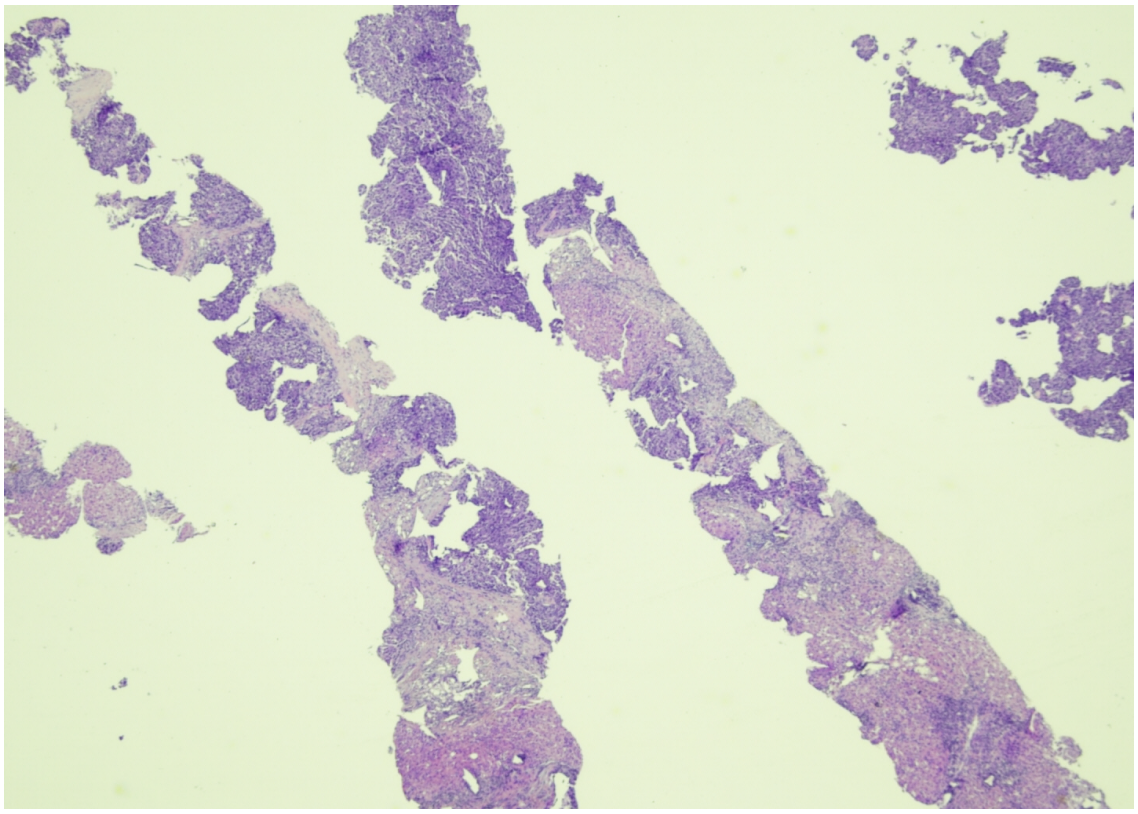

Fig. 2. Cores of liver tissue with hepatocellular carcinoma (H&E, ×40).

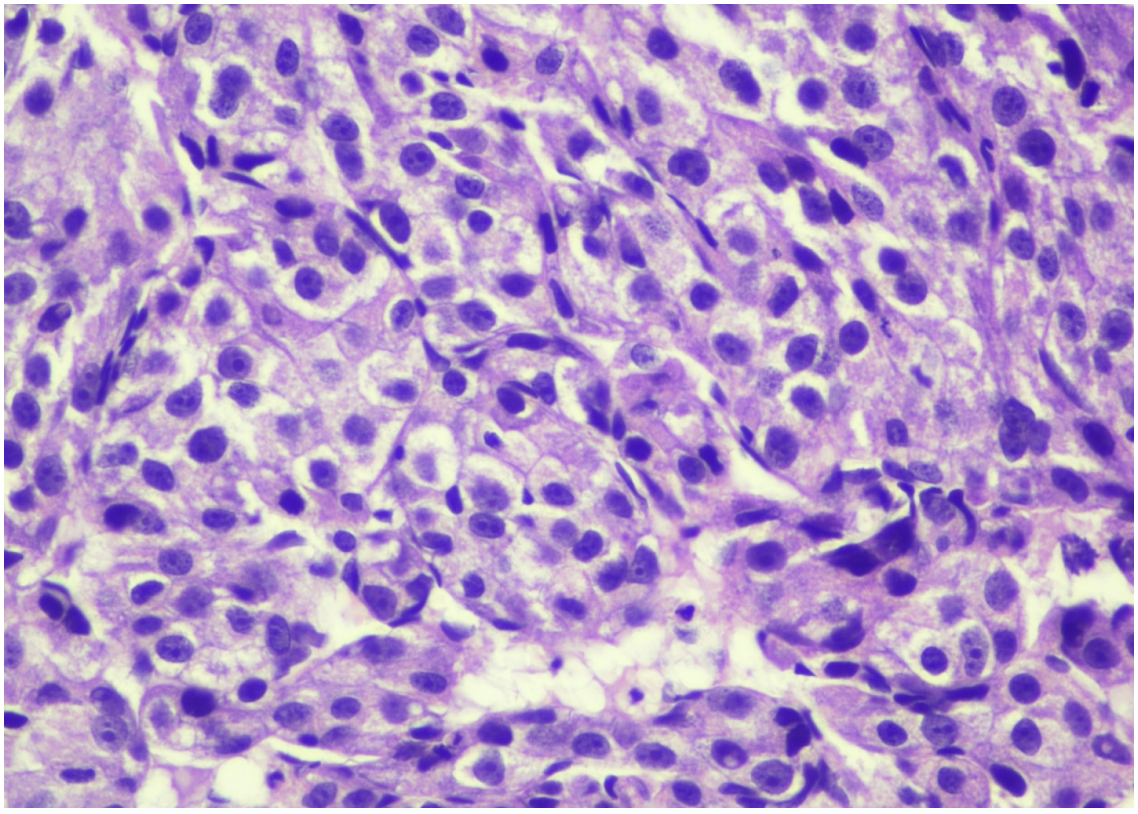

Fig. 3. HCC, moderately differentiated, solid pattern (H&E, ×200).

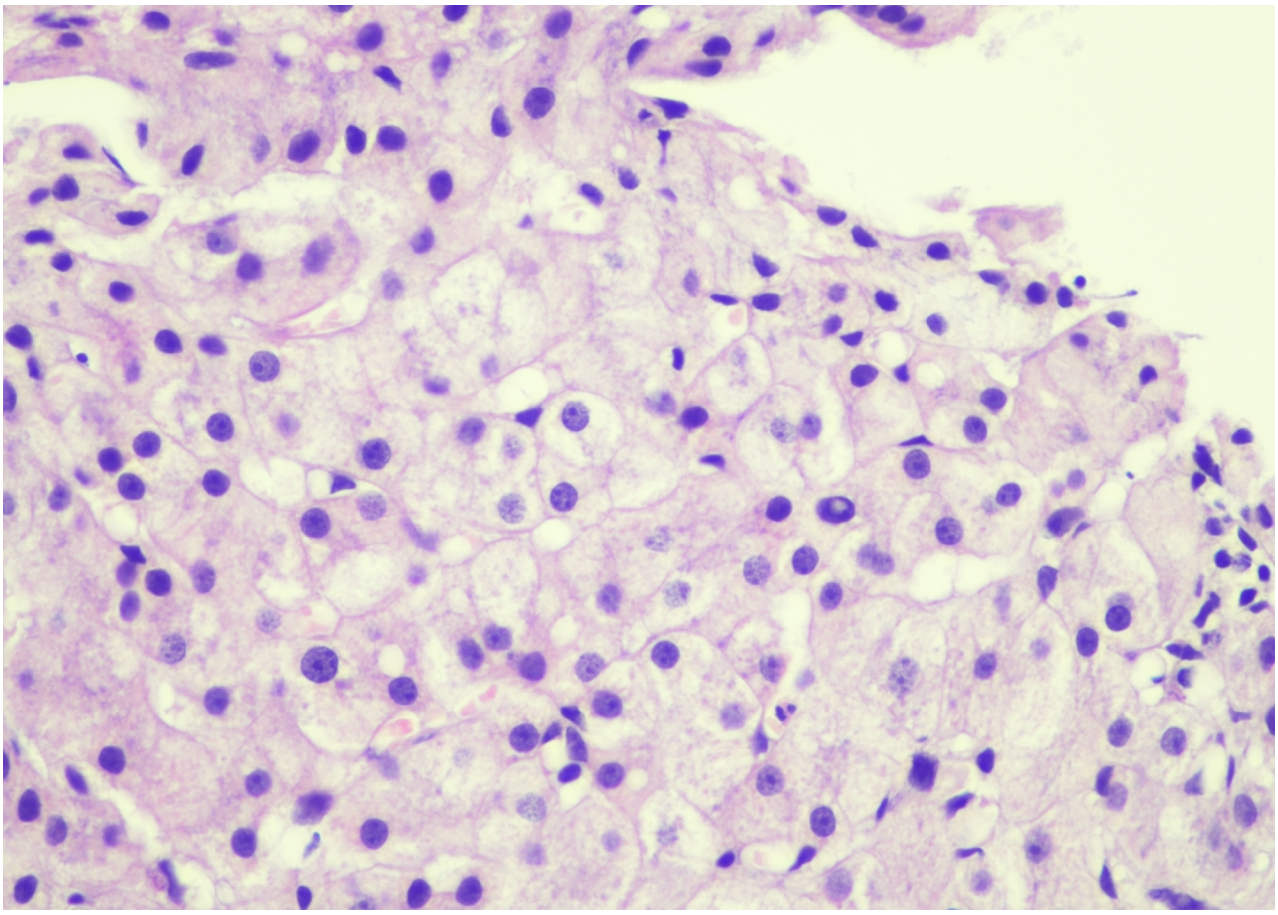

Fig. 4. Normal-appearing liver tissue adjacent to the HCC (H&E, ×200). No steatosis, lobular inflammation, or ballooning were observed in the biopsied tissue.

dence interval [CI] 0.54–1.53, $p = 0.72$), with a 25% bleeding complication rate in the anticoagulation group [11]. The treatment of ascites due to portal hypertension is as usual, based on sodium restriction, a negative sodium balance using spironolactone/furosemide combination, and when needed, large-volume paracentesis supported by albumin infusion [12]. Sadly, the patient deteriorated to BCLC stage D and succumbed to his illness, within 5 weeks, while debating between treatment or no treatment. Survival of patients at this advanced stage is dismal, reported to vary, but remains in the order of weeks, also dependent on the option of treatment.

The Care Checklist has been attached as **Supplementary Material** associated with this article.

6. Discussion

The unique aspect of this case is the finding of an advanced HCC with associated extensive tumour thrombus in the apparent absence of a background of chronic liver disease. The usual patient with HCC has underlying cirrhotic (or at least fibrotic) liver disease, most often due to chronic hepatitis C or B, alcohol use disorder (AUD), or MASLD [13]. The incidence of MASLD is increasing in recent years, becoming the most common CLD worldwide, and involving a small, but distinct, risk of progression to cirrhosis [2,14]. MASLD can predispose to HCC with, or sometimes without cirrhosis [15]. However, our patient had no known risk factors in the history other than the metabolic syndrome, which had been reasonably well-controlled; he was overweight but not obese, his liver biosynthetic function (i.e., normal serum albumin and PT) was preserved, the ALT and AST had been normal, viral serology and PCR were negative, and the liver imaging and histology also did not support a CLD. This is notable and rarely encountered, although prior studies and case series have documented rare instances of HCC developing even in the absence of chronic liver disease [16,17]. Primary liver cancer, most often HCC, is the sixth most frequently diagnosed malignancy worldwide, and strongly associated with underlying inflammation. Over 80% have cirrhosis of any aetiology. Diabetes and metabolic syndrome components, as in our patient, almost double HCC risk even when the BMI is normal [1]. Nevertheless, development of HCC and its complications in apparently normal liver remains rare and noteworthy, reinforcing the AASLD recommendation that suspicious liver nodules in patients without cirrhosis or HBV infection need to be biopsied [1].

Having said that, a sampling error in the liver biopsy cannot be ruled out, and an occult MASLD in our patient with overweight, diabetes, and hypertension cannot be absolutely excluded. Diabetes is an independent risk factor for HCC [18], increasing the risk of HCC through two central mechanisms which are closely interrelated. Chronic hyperglycaemia and insulin resistance promote hepatic inflammation, oxidative stress, and activation of pro-oncogenic pathways (e.g., IGF axis), which enhance cell proliferation and inhibit apoptosis [19]. Diabetes also accelerates the progression of MASLD to fibrosis. His past history of prostate cancer is also of interest. There is currently no strong evidence for a direct genetic link with HCC, but rare hereditary syndromes and gene variants could possibly confer increased risk for both cancers, and rare germline mutations in cancer-predisposing genes do increase the risk of multiple cancers [20].

Our patient's unusually massive thrombosis extending from the portal vein and hepatic veins to the right atrium was identified by its imaging characteristics as a tumour thrombus, in close proximity to the HCC. This is an uncommon but recognised manifestation of HCC [6,13]. Some cancers have the predisposition to extend into an adjacent blood vessel lumen. Imaging studies (and histopathology) identify these tumour thrombi, defined by an intraluminal filling defect extending from an adjacent tumoural mass, and associated with contrast enhancement or vein expansion [7,9,21]. Several recent studies have considerably advanced our understanding of the molecular mechanisms underlying the formation of tumour thrombus in the portal system in patients with HCC [22,23,24], as well as improved our understanding of the challenges in treatment [25]. In a retrospective cohort study of 211 patients with tumour thrombus, HCC was the most common cancer (28%), but renal cell carcinoma, lung cancer, and pancreatic neuroendocrine tumours are other notable associations. The presence of tumour thrombus was associated with a mean survival of 2–3 months, reflecting the 81% of patients with metastatic disease on diagnosis [21]. From the opposite direction, among 194 consecutive HCC patients, roughly one third had 'bland' portal vein thrombosis at diagnosis, and tumour invasion of a major vessel was common, demonstrated in 42% [26].

The history of the association between cancer and thrombosis dates to the mid-1800's with a major long-standing contribution of two outstanding physicians. The intravascular extension of tumour cells, termed tumour thrombus, was first identified by Armand Trousseau in Paris in 1865 [27]. The presence of tumour thrombus increases the risk of 'bland' thrombus [7]. This evokes the ancient renown Virchow's triad, largely identified by the young Rudolph Virchow in Berlin in 1856, which remains highly useful today in considering the pathogenesis of venous thrombosis. Cancer-associated alteration in blood composition (hypercoagulability); tumour mass-adjacent endothelial injury; and disrupted blood flow [28] were likely *all present* in our patient, and may have caused his demise. In a retrospective study of 2762 patients with tumour thrombus (due to renal cell carcinoma), the estimated odds ratio for concurrent 'bland' venous thromboembolism was 8.16 (95% CI 1.48–45) [29].

Limitations are that of a single case report as well as a potential sampling error in the area of the biopsy that demonstrated liver tissue with minimal changes. Nevertheless, our conclusion is supported by ancillary clinical, biochemical, and imaging data, supporting the conclusion that the rare absence of demonstrable CLD does not rule out HCC and its complications.

7. Conclusion

In rare instances, HCC can develop with no evidence of a chronic liver disease and present through its associated portal vein tumour thrombus. Thus, clinicians need to be aware that very rarely, absence of demonstrable CLD does not rule out HCC and its complications.

Learning Points

• Prehepatic (pre-sinusoidal) portal hypertension presenting as high-gradient ascites and hypersplenism can be caused by portal vein thrombus due to tumour invasion.

• Liver cirrhosis and/or hepatobiliary malignancy are the major causes of portal vein thrombus, which can be 'bland', composed to tumour cells, or both.

• Tumour thrombus has specific, highly suggestive imaging characteristics, and carries a dire prognosis.

• The vast majority of hepatocellular carcinomas develop in the context of liver cirrhosis, or MASLD; however, very rarely no significant demonstrable underlying liver pathology can be found.

Availability of Data and Materials

All the data of this study are included in this article.

Author Contributions

AS, LU, IS, and ID designed the work. LU supervised and interpreted the imaging studies, and IS analyzed the pathology specimens. The manuscript was researched and written primarily by AS, with participation from ID. All authors contributed to the critical revision of the manuscript for important intellectual content. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Research was conducted in strict accordance with the ethical principles outlined in the Declaration of Helsinki. Informed consent was obtained from and signed by the participant's next of kin.

Acknowledgment

Not applicable.

Funding

This research received no external funding.

Conflicts of Interest

Given his role as an Editorial Board member, Ami Schattner had no involvement in the peer review of this article and has no access to information regarding its peer review. Full responsibility for the editorial process for this article was delegated to Ganesh Radhakrishna. Other authors declare no conflicts of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.31083/BJHM56026.

References

[1] Singal AG, Llovet JM, Yarchoan M, Mehta N, Heimbach JK, Dawson LA, et al. AASLD Practice Guidance on prevention, diagnosis, and treatment of hepatocellular carcinoma. Hepatology (Baltimore, Md.). 2023; 78: 1922–1965. https://doi.org/10.1097/HEP.0000000000000466

[2] Phoolchund AGS, Khakoo SI. MASLD and the Development of HCC: Pathogenesis and Therapeutic Challenges. Cancers. 2024; 16: 259. https://doi.org/10.3390/cancers16020259

[3] Vogel A, Chan SL, Dawson LA, Kelley RK, Llovet JM, Meyer T, et al. Hepatocellular carcinoma: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. Annals of Oncology. 2025; 36: 491–506. https://doi.org/10.1016/j.annonc.2025.02.006

[4] Biggins SW, Angeli P, Garcia-Tsao G, Ginès P, Ling SC, Nadim MK, et al. Diagnosis, Evaluation, and Management of Ascites, Spontaneous Bacterial Peritonitis and Hepatorenal Syndrome: 2021 Practice Guidance by the American Association for the Study of Liver Diseases. Hepatology (Baltimore, Md.). 2021; 74: 1014–1048. https://doi.org/10.1002/hep.31884

[5] Reig M, Forner A, Rimola J, Ferrer-Fàbrega J, Burrel M, Garcia-Criado Á, et al. BCLC strategy for prognosis prediction and treatment recommendation: The 2022 update. Journal of Hepatology. 2022; 76: 681–693. https://doi.org/10.1016/j.jhep.2021.11.018

[6] Boccatonda A, Gentilini S, Zanata E, Simion C, Serra C, Simioni P, et al. Portal Vein Thrombosis: State-of-the-Art Review. Journal of Clinical Medicine. 2024; 13: 1517. https://doi.org/10.3390/jcm13051517

[7] Tathireddy H, Rice D, Martens K, Shivakumar S, Shatzel J. Breaking down tumor thrombus: Current strategies for medical management. Thrombosis Research. 2023; 230: 144–151. https://doi.org/10.1016/j.thromres.2023.09.004

[8] Marrero JA, Feng Z, Wang Y, Nguyen MH, Befeler AS, Roberts LR, et al. Alpha-fetoprotein, des-gamma carboxyprothrombin, and lectin-bound alpha-fetoprotein in early hepatocellular carcinoma. Gastroenterology. 2009; 137: 110–118. https://doi.org/10.1053/j.gastro.2009.04.005

[9] Rohatgi S, Howard SA, Tirumani SH, Ramaiya NH, Krajewski KM. Multimodality Imaging of Tumour Thrombus. Canadian Association of Radiologists Journal. 2015; 66: 121–129. https://doi.org/10.1016/j.carj.2014.11.001

[10] Lu J, Zhang XP, Zhong BY, Lau WY, Madoff DC, Davidson JC, et al. Management of patients with hepatocellular carcinoma and portal vein tumour thrombosis: comparing east and west. The Lancet. Gastroenterology & Hepatology. 2019; 4: 721–730. https://doi.org/10.1016/S2468-1253(19)30178-5

[11] Antonios K, Antonios B, Al-Banaa K, Chisti MM. Anticoagulation for portal vein thrombosis in patients with hepatocellular carcinoma: A retrospective observational study. Journal of Clinical Oncology. 2023; 41: e16212. https://doi.org/10.1200/JCO.2023.41.16_suppl.e16212

[12] Tapper EB, Parikh ND. Diagnosis and Management of Cirrhosis and Its Complications: A Review. JAMA. 2023; 329: 1589–1602. https://doi.org/10.1001/jama.2023.5997

[13] Kelley RK, Greten TF. Hepatocellular Carcinoma - Origins and Outcomes. The New England Journal of Medicine. 2021; 385: 280–282. https://doi.org/10.1056/NEJMcibr2106594

[14] Targher G, Valenti L, Byrne CD. Metabolic Dysfunction-Associated Steatotic Liver Disease. The New England Journal of Medicine. 2025; 393: 683–698. https://doi.org/10.1056/NEJMra2412865

[15] Phan J, Ng V, Sheinbaum A, French S, Choi G, El Kabany M, et al. Hyperlipidemia and Nonalcoholic Steatohepatitis Predispose to Hepatocellular Carcinoma Development Without Cirrhosis. Journal of Clinical Gastroenterology. 2019; 53: 309–313. https://doi.org/10.1097/MCG.0000000000001062

[16] Jain A, Mazer B, Deng Y, Ciarleglio M, Jain D, Taddei T, et al. Hepatocellular Carcinoma: Does the Background Liver With or Without Cirrhosis Matter? American Journal of Clinical Pathology. 2022; 157: 305–313. https://doi.org/10.1093/ajcp/aqab125

[17] Marcellin P, Thiers V, Degott C, Franco D, Belghitti J, Castaing D, et al. Hepatocellular carcinoma with normal adjacent liver. Hepatitis B virus DNA status. Journal of Hepatology. 1989; 8: 249–253. https://doi.org/10.1016/0168-8278(89)90015-9

[18] Simon TG, King LY, Chong DQ, Nguyen LH, Ma Y, VoPham T, et al. Diabetes, metabolic comorbidities, and risk of hepatocellular carcinoma: Results from two prospective cohort studies. Hepatology (Baltimore, Md.). 2018; 67: 1797–1806. https://doi.org/10.1002/hep.29660

[19] Singh MK, Das BK, Choudhary S, Gupta D, Patil UK. Diabetes and hepatocellular carcinoma: A pathophysiological link and pharmacological management. Biomedicine & Pharmacotherapy. 2018; 106: 991–1002. https://doi.org/10.1016/j.biopha.2018.06.095

[20] Pilié PG, Johnson AM, Hanson KL, Dayno ME, Kapron AL, Stoffel EM, et al. Germline genetic variants in men with prostate cancer and one or more additional cancers. Cancer. 2017; 123: 3925–3932. https://doi.org/10.1002/cncr.30817

[21] Hui S, Zeid K, Kou R, Mallick R, Carrier M, Wang TF. Management and outcomes in patients with tumor thrombus: a retrospective cohort study. Journal of Thrombosis and Haemostasis. 2025; 23: 201–209. https://doi.org/10.1016/j.jtha.2024.10.002

[22] Stella L, De Siati M, Talerico R, Pallozzi M, Cerrito L, Sorrentino S, et al. Thrombotic Risk and Coagulation Imbalance in Cirrhosis and Hepatocellular Carcinoma: Clinical Implications and Management. Cancers. 2025; 17: 3413. https://doi.org/10.3390/cancers17213413

[23] Zhang M, Ding Q, Bian C, Su J, Xin Y, Jiang X. Progress on the molecular mechanism of portal vein tumor thrombosis formation in hepatocellular carcinoma. Experimental Cell Research. 2023; 426: 113563. https://doi.org/10.1016/j.yexcr.2023.113563

[24] Li Z, Zhao M, Qi X, Tang Y, Cheng S. Mechanisms of portal vein tumour thrombus formation and development in patients with hepatocellular carcinoma. Journal of Cellular and Molecular Medicine. 2023; 27: 2103–2111. https://doi.org/10.1111/jcmm.17808

[25] Jiang JF, Lao YC, Yuan BH, Yin J, Liu X, Chen L, et al. Treat-

ment of hepatocellular carcinoma with portal vein tumor thrombus: advances and challenges. Oncotarget. 2017; 8: 33911–33921. https://doi.org/10.18632/oncotarget.15411

[26] Connolly GC, Chen R, Hyrien O, Mantry P, Bozorgzadeh A, Abt P, et al. Incidence, risk factors and consequences of portal vein and systemic thromboses in hepatocellular carcinoma. Thrombosis Research. 2008; 122: 299–306. https://doi.org/10.1016/j.thromres.2007.10.009

[27] Donati MB, Lorenzet R. Thrombosis and cancer: 40 years of research. Thrombosis Research. 2012; 129: 348–352. https://doi.org/10.1016/j.thromres.2011.12.022

[28] Chung I, Lip GYH. Virchow's triad revisited: blood constituents. Pathophysiology of Haemostasis and Thrombosis. 2003; 33: 449–454. https://doi.org/10.1159/000083844

[29] Park H, Jeong CW, Yuk H, Ku JH, Kim HH, Kwak C, et al. Influence of Tumor Thrombus on Occurrence of Distant Venous Thromboembolism and Survival in Patients With Renal Cell Carcinoma After Surgery. Clinical and Applied Thrombosis/Hemostasis. 2019; 25: 1076029618823288. https://doi.org/10.1177/1076029618823288