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CASE REPORT

Long-Term Survival in an Elderly HCV Patient with Double Primary Malignant Tumors Managed with Local Therapy Only

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Abstract: Hepatitis C virus (HCV) infection is associated with both hepatic and extrahepatic malignancies. We report a 95-year-old male with chronic HCV infection who developed recurrent hepatocellular carcinoma (HCC) and subsequent splenic diffuse large B-cell lymphoma (DLBCL), achieving a 13-year survival. This patient was managed exclusively with local therapies, receiving multiple rounds of radiofrequency ablation (RFA) for five episodes of HCC recurrence and undergoing splenectomy for the primary splenic DLBCL, entirely avoiding systemic chemotherapy. Despite his advanced age and dual primary malignancies, he has maintained normal liver function and shows no evidence of lymphoma progression at the latest follow-up. This case underscores the potential of a patient-centric treatment approach, highlighting that in select very elderly or high-risk patients, aggressive systemic therapy may not be necessary to achieve long-term survival and high quality of life. The successful outcome challenges conventional management paradigms and contributes to the growing evidence supporting minimally invasive, localized interventions for complex oncological scenarios in geriatric populations. It emphasizes the importance of individualized risk-benefit assessment and tumor biology in guiding treatment decisions, offering a new perspective on optimizing outcomes for patients where standard aggressive therapies are contraindicated.

Keywords: dual primary malignancy, hepatitis C virus, hepatocellular carcinoma, diffuse large B-cell lymphoma

Introduction

Hepatitis C virus (HCV) infection is closely linked to the development of both liver diseases and extrahepatic manifestations, including B-cell lymphoma.[1] Epidemiological studies demonstrate a significantly higher risk of lymphoma in HCV-infected individuals.[2] Hepatocellular carcinoma (HCC) and diffuse large B-cell lymphoma (DLBCL) represent two distinct malignancies with complex etiologies and management challenges, particularly in elderly patients with comorbidities.[3] HCV infection serves as a common risk factor for both conditions, by driving oncogenesis through persistent inflammation and immune dysregulation.[4] While HCC typically arises in cirrhotic livers, HCV-associated DLBCL often manifests in extrahepatic sites with variable aggressiveness. Current guidelines for HCC emphasize surgical resection, transplantation, or ablation for early-stage disease, whereas DLBCL management relies heavily on immunochemotherapy.[5] However, elderly patients are often excluded from aggressive treatment protocols due to frailty and competing health risks.[6]

This case study examines a 95-year-old male with HCV-related HCC and splenic DLBCL who was managed exclusively with localized treatments over 13 years. His clinical course challenges conventional paradigms by demonstrating sustained disease control in the absence of systemic chemotherapy. These findings contribute to a growing body of evidence supporting individualized, minimally invasive approaches for complex oncological scenarios, and advocate for tailored strategies in very elderly and multimorbid populations.

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Case Presentation

The patient is a 95-year-old male with a complex medical history providing rare insights into the long-term management of HCV-related dual malignancies. Prior to his HCV diagnosis, he underwent successful surgical resection for nasal basal cell carcinoma at age 78, demonstrating his resilience to medical procedures despite advanced age. In 2012 (age 82 years), he was diagnosed with chronic HCV infection with a baseline HCV-RNA level of 5.04×10^6 IU/mL. Liver function was preserved at diagnosis, and antiviral therapy was not initiated at that time. Family history included HCC in a first-degree relative.

At age 83, ultrasound revealed liver cirrhosis. Laboratory evaluations demonstrated elevated alanine aminotransferase (ALT, 130 U/L), aspartate aminotransferase (AST, 114 U/L), and alpha-fetoprotein (AFP, 10–24 ng/mL). Contrast-enhanced computed tomography (CT) identified two arterial-enhancing lesions with venous washout (<3 cm) in segments IV/V/VIII, without vascular invasion or extrahepatic metastasis. After comprehensive risk-benefit evaluation, the multi-disciplinary team (MDT) concluded that radiofrequency ablation (RFA) was the most appropriate first-line treatment strategy, offering comparable local control to surgical resection while minimizing procedural morbidity. The decision prioritized preservation of liver function and quality of life, with the option of repeat local therapy in the event of recurrence. Following the first RFA, AFP levels normalized.

At age 86, a small intrahepatic recurrence in segment VII measuring approximately 11×8 mm with typical enhancement pattern was detected and successfully treated with a second RFA. Concurrently, direct-acting antiviral (DAA) therapy (sofosbuvir plus daclatasvir for 6 months) was initiated. HCV-RNA became undetectable and remained negative at 12 weeks, 24 weeks, and throughout subsequent annual follow-up, consistent with sustained virologic response (SVR).

At age 87, the patient presented with left upper quadrant discomfort and early satiety. Imaging identified a splenic mass without additional nodal or extranodal involvement. Laparoscopic splenectomy was performed for diagnostic and therapeutic purposes. Histopathology confirmed diffuse large B-cell lymphoma of non-germinal center subtype (Figure 1A). Immunohistochemistry demonstrated the following profile: LCA(+), CD79a(+), CD20(+), CD43(-), CD21(+), CD23(+),Bcl-2(+90%), Bcl-6(+), CD10(partially +), Mum-1(-), CD35(-), C-myc(-), CD5(-), Cyclin-D1(-), ALK(-), CD30(-), S100(-), Ki-67(+70%), and CD3(-).

The disease was clinically classified as Ann Arbor stage IS, group A, indicating localized splenic involvement without systemic B symptoms. A simplified comprehensive geriatric assessment (CGA)[7] demonstrated preserved independence in activities of daily living and instrumental activities of daily living, with controlled hypertension as the only comorbidity. ECOG performance status was 0–1. A second MDT concluded that the risks of anthracycline-induced cardiotoxicity and myelosuppression outweighed the benefits of systemic immunochemotherapy; thus, active surveillance was elected. Bone marrow involvement was clinically excluded based on imaging and hematologic assessments. Post-splenectomy surveillance demonstrated sustained normal lactate dehydrogenase (LDH) levels, stable hematologic parameters, and no extranodal disease on periodic CT assessments. Collectively, these findings confirmed sustained complete remission of splenic DLBCL following splenectomy without systemic chemotherapy.

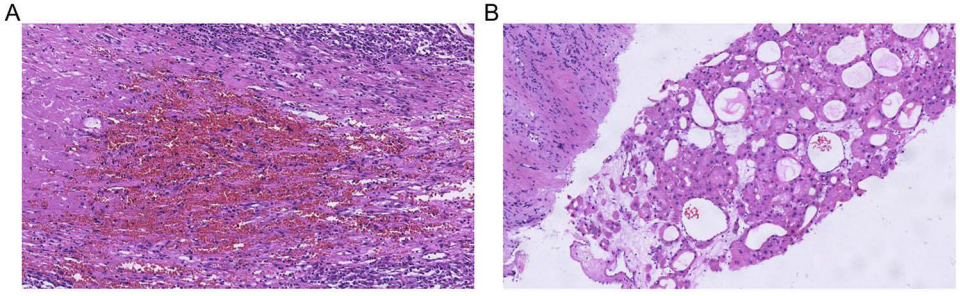

Figure 1 Hematoxylin and eosin (H&E) staining of splenic DLBCL (**A**) and HCC (**B**). (10×).

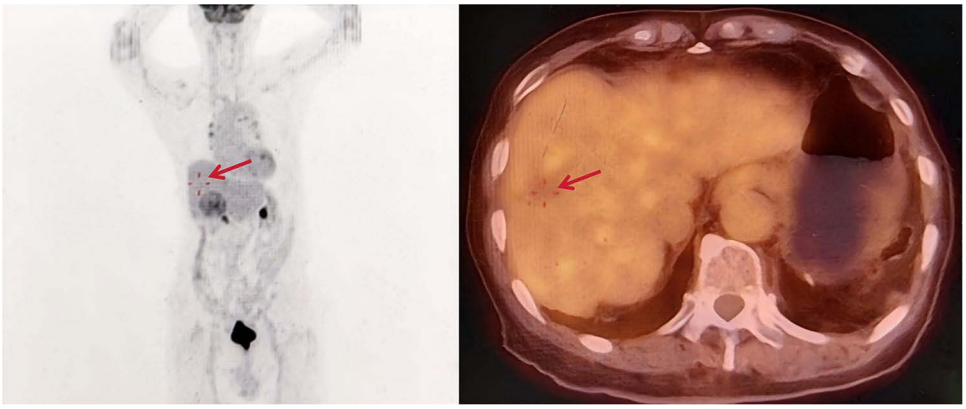

Figure 2 Focal intensely increased FDG uptake was observed in the PET/CT image with SUVmax of 3.9–6.1 (indicated by the red arrow).

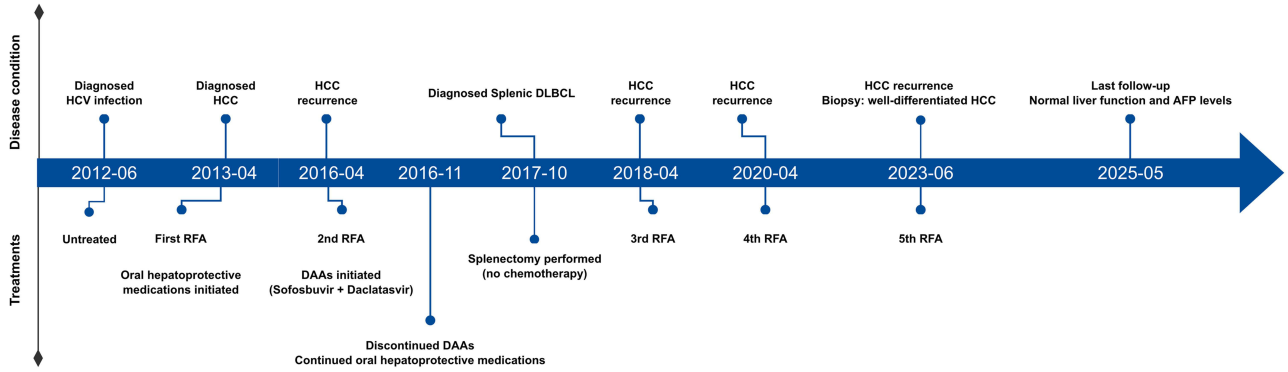

Figure 3 Clinical timeline of the patient. The timeline shows the major clinical events during the course of the patient's treatment.

At ages 89 and 90, the patient experienced third and fourth localized HCC recurrences (segment VII, followed by segments V/VII; all nodules <3 cm), both successfully eradicated using targeted RFA without macrovascular or extrahepatic spread. Subsequent imaging demonstrated loss of arterial enhancement in treated regions.

At age 93, despite durable HCV clearance, AFP levels began to rise. Imaging identified a 5.5–6.8cm necrotic lesion in the left hepatic lobe with internal necrosis but no portal vein tumor thrombus or distant metastasis. Biopsy confirmed recurrent hyperdifferentiated HCC (Figure 1B) accompanied by significantly elevated Prothrombin induced by vitamin K absence-II (PIVKA-II, 1212 mAU/mL). Immunohistochemistry showed GPC-3(+), GS(+), HSP70(+), focal CK7(+), CEA(-), CK19(-), CD34 endothelialization, and Ki-67 (+10%). RFA was performed, and follow-up imaging showed absence of residual arterial enhancement. Considering the patient's advanced age, maintenance therapy was provided solely with oral hepatoprotective agents. Subsequent 18F-FDG PET/CT (Figure 2) demonstrated hypermetabolic hepatic lesions without abnormal uptake in lymph nodes, bone marrow, or extranodal sites. Serial hematologic parameters and LDH levels remained normal, confirming sustained complete remission of splenic DLBCL.

Throughout follow-up, liver function remained Child-Pugh class A. No macrovascular invasion or extrahepatic spread occurred during the entire disease course. Currently, at age 95, he remains alive with preserved functional status, demonstrating the profound efficacy of this localized approach. Clinical course is summarized in Figure 3. The case details and accompanying images published were approved by The First Affiliated Hospital of Xi'an Jiaotong University. Written, informed consent was obtained from the patient for publication of this case report and accompanying images.

Discussion

This case describes an exceptionally rare clinical scenario involving long-term survival in a very elderly patient with chronic HCV infection who developed two distinct primary malignancies: recurrent HCC and primary splenic DLBCL.

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Over a 13-year period, durable disease control was achieved exclusively through localized therapeutic strategies. This case suggests that durable survival and organ preservation may be achievable without systemic therapy in carefully selected elderly patients.

Chronic HCV infection is an established oncogenic driver for both hepatic and extrahepatic malignancies.[8] Persistent inflammation, cirrhosis, and genomic instability contribute to hepatocarcinogenesis, whereas chronic antigenic stimulation and immune dysregulation promote B-cell transformation.[9] Although coexistence of HCC and B-cell lymphoma in HCV-infected individuals has been reported, most cases emphasized the shared viral oncogenic background and were managed with systemic therapy and lacked long-term follow-up data.[10–13] Durable long-term survival achieved through exclusively localized treatment strategies has rarely been emphasized, especially in very elderly patients. This patient achieved sustained remission of primary splenic DLBCL following splenectomy alone, and experienced repeated intrahepatic HCC recurrences that were successfully controlled with RFA while maintaining preserved liver function, thereby expanding the clinical spectrum of HCV-associated dual malignancies.

The efficacy of RFA for the longitudinal management of HCC in this patient was definitive. Despite five distinct intrahepatic recurrences spanning a decade, precise local ablation achieved consistent tumor control while preserving liver function. This supports prior cohort data[14] validating repeat ablation as a definitive modality for elderly patients when surgical resection is not feasible. Recent genomic and transcriptomic research further demonstrates that HCC is driven by complex regulatory networks involving hub genes, microRNAs, circular RNAs, and diverse signaling pathways, reflecting marked molecular heterogeneity.[15–17] Emerging therapeutic investigations also underscore the multiplicity of biologically targetable pathways in HCC.[18] The relatively indolent recurrence pattern observed in this patient suggests a less aggressive intrinsic tumor biology, which may have been mediated by complex molecular heterogeneity rather than isolated viral activity.

The patient achieved sustained virological response (SVR) following DAA treatment, with persistently undetectable HCV-RNA during long-term follow-up. Despite confirmed viral eradication, HCC recurrences continued to occur. This observation aligns with emerging evidence that accumulated epigenetic aberrations in fibrotic liver tissue perpetuate hepatocarcinogenesis independent of active viral replication.[19,20] This underscores the necessity of continued oncologic surveillance even after viral clearance.

HCV-related DLBCL classically exhibits aggressive clinical behavior necessitating systemic immunochemotherapy.[21,22] However, the unique immunological microenvironment of the spleen, combined with potential viral-induced epigenetic modifications, likely tempered malignant proliferation.[23,24] In this case, splenic DLBCL was confined to a single lymphoid organ (stage IS, group A) and achieved sustained remission following splenectomy alone. This case suggests that, in highly selected elderly patients with localized disease and favorable clinical features, surgery followed by surveillance may be an acceptable strategy. The absence of recurrence over long-term follow-up supports the importance of stage, disease distribution, and host factors in therapeutic decision-making.

Importantly, this case underscores the necessity of structured multidisciplinary evaluation incorporating tumor stage, organ preservation, geriatric assessment, procedural safety, and patient preference. Structured MDT discussions played a central role in tailoring therapy, ensuring that treatment intensity was guided by functional status and disease biology rather than chronological age alone. While this report is limited by its single-case design and potential selection bias, this patient provides compelling evidence that individualized de-escalated and organ-preserving strategies may achieve outcomes comparable to more aggressive approaches for complex dual malignancies in the very elderly.

Conclusion

In summary, this case provides compelling evidence that in selected very elderly patients with localized HCV-associated malignancies, individualized organ-preserving strategies guided by multidisciplinary evaluation may achieve prolonged survival. Therapeutic decisions should be guided by tumor stage, biological behavior, functional reserve, and patient-centered goals rather than chronological age alone. For elderly patients with multiple malignancies, an individualized treatment strategy based on multidisciplinary evaluation is of significant clinical value.

Ethical Approval and Consent to Participate

This study was reviewed and approved by the Ethics Committee of The First Affiliated Hospital of Xi'an Jiaotong University. Institutional approval was required for publication of the case details and was granted accordingly. Written informed consent for publication of clinical data and images was obtained from the patient. All procedures performed complied with the ethical standards of the institutional research committee and the Declaration of Helsinki.

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Disclosure

The authors report no conflicts of interest in this work.

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