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– CASE REPORT –

Whispers from the Liver: A Hidden Case of CD10+ High-Grade B-cell Lymphoma

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Abstract

Background: *High-grade B-cell lymphomas involving the liver are rare and often present with vague, nonspecific symptoms. Clinically, these lymphomas can easily be mistaken for more common hepatic or infectious diseases, which, unfortunately, tends to delay both diagnosis and treatment.*

Case Presentation: *In this instance, a 66-year-old male with a prior history of Lyme disease and numerous tick bites presented with right upper quadrant discomfort and deranged liver enzymes. Imaging demonstrated hepatomegaly and multiple hepatic lesions, along with a progressive pattern of cholestatic liver injury. Extensive serologic, infectious, and autoimmune workups yielded no significant findings. Ultimately, a liver biopsy identified a CD10-positive high-grade B-cell lymphoma, most likely representing either diffuse large B-cell lymphoma (DLBCL, germinal center B-cell type) or a Burkitt variant. The patient received dexamethasone and was subsequently scheduled to begin R-EPOCH chemotherapy following PET staging.*

Conclusion*: This case underscores the importance of a multidisciplinary approach in evaluating unexplained liver disease. Clinicians should maintain a high index of suspicion for high-grade hepatic lymphomas in patients with rapid hepatic deterioration and B symptoms, especially if serologic testing is unrevealing. Prompt recognition and diagnosis are critical to improving patient outcomes in these rare but aggressive malignancies.*

Keywords: *B-cell lymphoma, high-grade lymphoma, liver masses, hepatomegaly, CD10+, DLBCL, RUQ pain, liver biopsy, oncology, case report*

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Introduction

Liver involvement in non-Hodgkin lymphomas (NHL), particularly among high-grade B-cell subtypes, remains relatively uncommon yet clinically significant, posing significant diagnostic challenges. Hepatic infiltration frequently arises as a component of widespread systemic disease, but, on rare occasions, a primary hepatic lymphoma (PHL) may develop. PHL is exceptionally rare, representing less than 1% of all extranodal lymphomas, and is associated with a poor prognosis, largely due to its infrequency and the consequent propensity for delayed diagnosis [1].

Secondary liver involvement is more often seen in advanced systemic lymphomas and similarly signals a poor clinical outcome [2,3]. Clinical presentations are typically nonspecific, including abdominal pain, hepatomegaly, abnormal liver function tests, and systemic "B symptoms" such as fever, night sweats, or unintended weight loss. These manifestations are easily mistaken for

more common hepatic or infectious diseases, further complicating timely diagnosis.

High-grade lymphomas, such as the germinal center B-cell (GCB) subtype of diffuse large B cell lymphoma (DLBCL) and Burkitt lymphoma (BL), are notable for their rapid progression and aggressive clinical course, as they express CD10. While these malignancies may involve extra-nodal sites, a predominant hepatic presentation with minimal lymphadenopathy is atypical and often leads to diagnostic uncertainty, especially during initial imaging evaluations [4,5]. Early histological confirmation, including liver biopsy and immunophenotyping, is critical, as prompt initiation of intensive chemotherapy regimens can markedly improve patient outcomes.

This report describes a diagnostically complex case of a 66-year-old male who presented with vague right upper quadrant abdominal pain and elevated liver enzymes, ultimately diagnosed with CD10-positive high-grade B-cell lymphoma involving the liver. This case highlights the importance of considering a broad differential diagnosis in patients with unexplained hepatic dysfunction and underscores the essential role of early tissue diagnosis and immunophenotyping in guiding effective management.

Case Presentation

Clinical Presentation

A 66-year-old male with an unremarkable medical history presented to the Emergency Department, reporting a one-week duration of sharp, intermittent pain localized to the right upper quadrant of the abdomen, radiating to the back. He denied associated symptoms such as nausea, vomiting, fever, chills, chest pain, or any prior similar episodes. He did note the onset of dark-colored urine, but no changes in his bowel habits were observed.

His medical history includes multiple prior tick bites and a diagnosis of Lyme disease. Family history is notable for a granddaughter with pyruvate kinase deficiency, a father with unspecified hepatitis, and a mother with an undiagnosed malignancy. He also has a history of gout.

One week earlier, he sought evaluation from his primary care physician for vague abdominal discomfort and decreased appetite, though he reported no weight loss. He also denied recent illnesses, chest pain, shortness of breath, or other new findings. He described intermittent, mild night sweats over several years, which had increased in frequency over the past two weeks. He reported no alcohol consumption, recent travel, blood transfusions, medication or supplement use, or exposure to sick contacts.

Physical examination was unremarkable: no palpable masses, lymphadenopathy, hepatosplenomegaly, or ascites were identified.

Histopathological examination of the ultrasound-guided liver biopsy revealed dense aggregates of medium- to large-sized atypical lymphoid cells, characterized by marked mitotic activity and apoptotic bodies. The Ki-67 proliferation index was markedly elevated at approximately 80%. Immunohistochemical analysis revealed strong positivity for CD20, CD10, BCL6, and PAX5, with BCL2 showing focal or weak expression. Staining was negative for CD3, CD5, CD23, and Cyclin D1 (BCL1). These morphological and immunophenotypic features most strongly supported a diagnosis of high-grade, CD10-positive B-cell lymphoma, consistent with the germinal center B-cell (GCB) subtype of diffuse large B-cell lymphoma (DLBCL). Nevertheless, Burkitt lymphoma remained a consideration in the differential diagnosis. Fluorescence in situ hybridization (FISH) analysis was performed to assess for MYC, BCL2, and BCL6 rearrangements, as well as the t (8;14) translocation, to further distinguish between DLBCL and Burkitt lymphoma. **Figure 1** shows examples of the histopathological features seen in the liver biopsy.

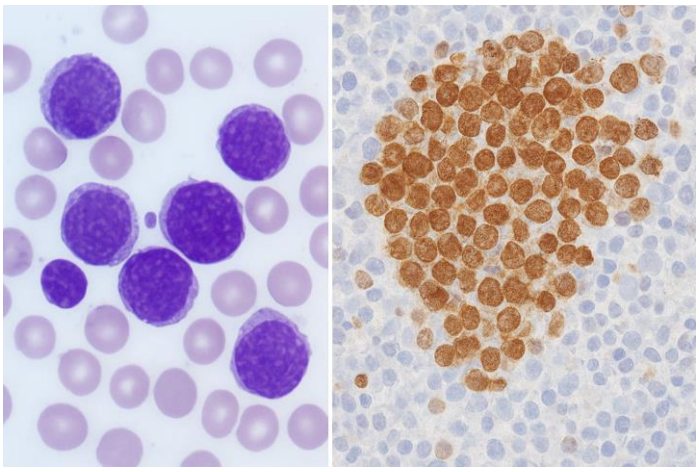

Figure 1. *Liver biopsy sample showing diffuse large B-cell lymphoma. Hematoxylin & Eosin stain, high magnification: The image shows large atypical lymphoid cells with open (vesicular) chromatin, distinct nucleoli, and scant cytoplasm infiltrating the liver parenchyma. There is no bone marrow or peripheral blood smear shown in this panel.*

Imaging studies Abdominal pelvic CT scan (Figure 2) demonstrated marked hepatomegaly, measuring approximately 21 cm, with numerous hypoechoic lesions distributed throughout the liver on abdominal ultrasound, initially raising suspicion for either cystic processes or metastatic disease. The gallbladder was unremarkable, with no evidence of cholelithiasis, sludge, or wall thickening, and the common bile duct was of normal caliber (3 mm), without ductal dilation or venous thrombosis.

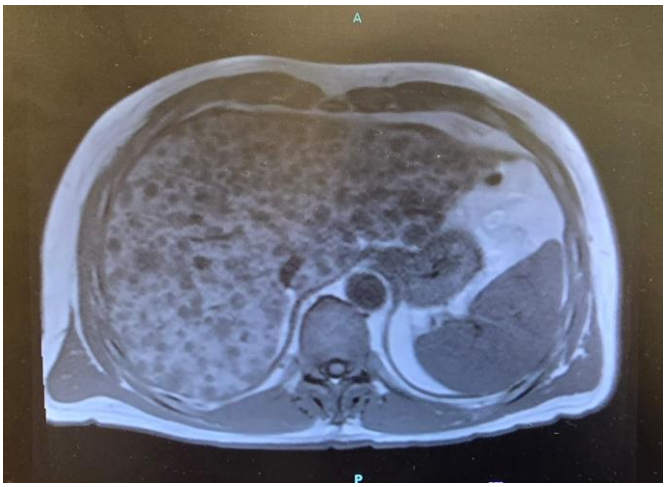

Figure 2. *Imaging and histopathologic correlation of diffuse large B-cell lymphoma affecting the liver. Left: Contrast-enhanced CT scan showing multiple hypodense lesions disseminated throughout the liver, consistent with lymphomatous infiltration. Right: Hematoxylin and eosin-stained section illustrating diffuse proliferation of atypical large lymphoid cells with vesicular nuclei and prominent nucleoli, consistent with diffuse large B-cell lymphoma.*

MRI of the abdomen with MRCP confirmed the presence of innumerable hepatic lesions, though their characterization was limited in the absence of contrast. Additionally, there was mild fatty infiltration of the pancreas and mild splenomegaly (estimated at approximately 400 cc). No biliary obstruction, ductal dilation, ascites, or lymphadenopathy was observed. A minimal amount of pericholecystic fluid was noted.

Nuclear medicine hepatobiliary imaging revealed no evidence of acute cholecystitis and demonstrated patent cystic and common bile ducts. The hepatic tracer uptake was heterogeneous, consistent with underlying parenchymal liver disease.

Chest CT imaging revealed no pulmonary or mediastinal masses. There was mild basilar atelectasis or infiltrate, without dominant lesions, trace right pleural effusion, no

thoracic lymphadenopathy, and no suspicious osseous lesions.

Collectively, these findings indicate significant hepatomegaly with numerous indeterminate hepatic lesions and evidence of parenchymal liver disease, while imaging of the biliary tract, spleen, pancreas, and thorax revealed only mild or incidental abnormalities. Further diagnostic evaluation is warranted.

During hospitalization, bridging therapy with dexamethasone and doxycycline was initiated pending final staging. Liver transaminases (AST and ALT) improved mildly, though hyperbilirubinemia persisted. The oncology team was consulted, and R-EPOCH chemotherapy was recommended following completion of PET-CT staging. The patient received comprehensive counseling regarding the diagnosis and proposed management and consented to proceed with systemic therapy upon completion of staging. **Table 1** highlights the diagnostic ambiguity at presentation and underscores the need for histological confirmation.

Test	Result	Reference Range
Total Bilirubin	4.9 mg/dL	0.1–1.2 mg/dL
Direct Bilirubin	2.7 mg/dL	<0.3 mg/dL
AST	310 U/L	5–40 U/L
ALT	564 U/L	7–56 U/L
Alkaline Phosphatase	212 U/L	44–147 U/L
Albumin	3.0 g/dL	3.5–5.0 g/dL
Total Protein	6.0 g/dL	6.4–8.3 g/dL
A/G Ratio	1.0	1.2–2.2
CA 19-9	164 U/mL	<37 U/mL
CEA	4.7 ng/mL	<5.0 ng/mL
AFP	<1.8 ng/mL	<10 ng/mL
ANA, ASMA, AMA, CMV, EBV, HSV Panels	Negative	
EBV VCA IgG, EBNA	>600 (positive past exposure)	
Lyme IgG	Positive	
Hepatitis B & C Panels	Negative	
ANCA/p-ANCA	Negative	
Anti-MPO / PR3	<0.2	
Complement C3/C4	Normal	
Rheumatoid Factor / SSA / SSB	Negative	

Table 1: *Key Laboratory Findings*

Discussion

High-grade B-cell lymphomas (HGBCLs) represent an exceptionally aggressive subset of non-Hodgkin lymphomas, encompassing diffuse large B-cell lymphoma (DLBCL), Burkitt lymphoma, and the so-called "double-hit" or "triple-hit" lymphomas characterized by rearrangements involving MYC, BCL2, and/or BCL6 [6]. Clinically, these malignancies are notable for their rapid proliferation, elevated mitotic activity, and frequent involvement of extra-nodal sites; hepatic presentation, however, remains an uncommon manifestation.

Atypical Hepatic Presentation

This case underscores a rare scenario in which HGBCL presented with isolated hepatic involvement. The patient experienced right upper quadrant pain and elevated transaminase levels, yet lacked systemic symptoms or a prior history of malignancy. Imaging modalities, including ultrasound and MRI, revealed hepatomegaly and multiple hypoechoic hepatic lesions, but did not indicate biliary obstruction or vascular thrombosis. Initial considerations included metastatic disease or hepatic cysts, although the absence of a primary neoplastic source and unremarkable gallbladder and bile duct findings argued against these possibilities. Additional negative viral serologies and the lack of typical risk factors further narrowed the differential to infiltrative or hematologic malignancies [7].

The Role of Imaging and Liver Biopsy

While imaging is indispensable for detecting hepatic abnormalities, it often cannot reliably distinguish between infectious, inflammatory, and neoplastic etiologies. In this

instance, a definitive diagnosis was achieved only through ultrasound-guided liver biopsy. Histopathological examination revealed extensive infiltration by atypical lymphoid cells, exhibiting a high proliferation index (Ki-67, ~80%). Immunohistochemical staining was positive for CD20, CD10, BCL6, and PAX5, with weak BCL2 expression, supporting a diagnosis of high-grade B-cell lymphoma—most likely DLBCL of the germinal center B-cell subtype or Burkitt lymphoma [4,8]. **Table 2** outlines key clinical, imaging, and pathological characteristics associated with such presentations. Recognizing this pattern is essential for guiding clinicians toward prompt liver biopsy and expedited hematopathologic workup.

Feature	Typical Findings
Presentation	RUQ pain, hepatomegaly, fatigue
Labs	Elevated bilirubin, ALP, transaminases
Imaging	Hypoechoic or hypodense hepatic lesions
Histopathology	Large atypical B-cells, high mitotic index
Immunophenotype	CD20+, CD10+, BCL6+, Ki-67 >70%
Common Subtypes	DLBCL (GCB), Burkitt, High-grade BCL
Preferred Treatment	R-EPOCH ± CNS prophylaxis

Table 2: *Key Features of Hepatic Involvement in B-cell Lymphomas*

Differential Diagnosis and Immunophenotyping

The immunophenotypic profile of CD10+, CD20+, BCL6+, and a high Ki-67 index is characteristic of GCB-DLBCL, but overlaps significantly with Burkitt lymphoma. Thus, the diagnosis cannot be made solely on the basis of histology and immunophenotyping. Molecular studies, such as fluorescence in situ hybridization (FISH) for MYC, BCL2, and BCL6 rearrangements, are essential for distinguishing among DLBCL, Burkitt lymphoma, and double- or triple-hit lymphomas—entities with divergent prognostic implications and treatment strategies (Figure 3) [6,9].

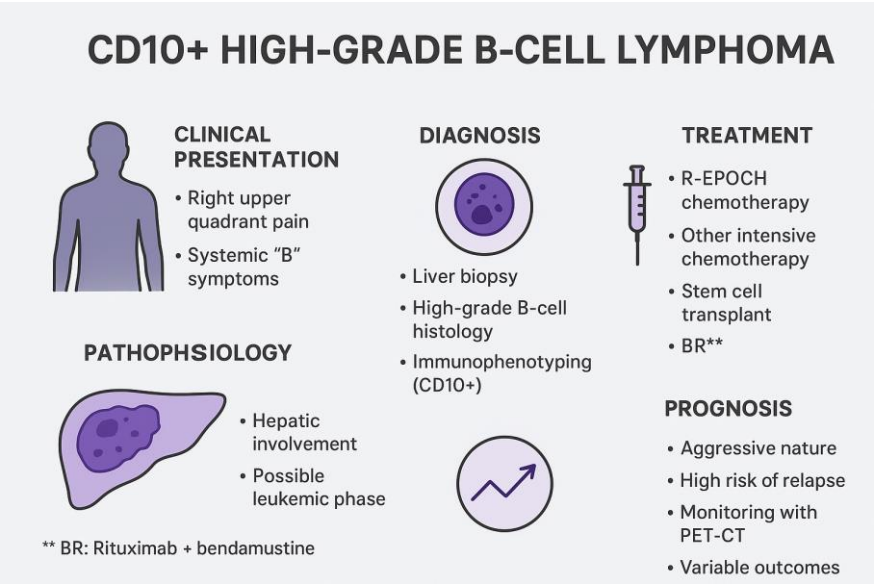

Figure 3*. Schematic overview of CD10+ high-grade B-cell lymphoma with liver involvement. The schematic outlines the integrated framework of disease pathophysiology, diagnostic methods, and treatment options. It shows a germinal-center B-cell origin, the salient immunophenotypic markers (CD10, BCL6, MYC, BCL2), and the order of diagnostic work-up (biopsy/immunohistochemistry/molecular studies), as well as current and emerging therapies (immunochemotherapy/targeted therapy/autologous stem cell transplantation).*

A comprehensive systemic evaluation remains essential when assessing suspected lymphoma, particularly when the presentation is atypical. In this instance, imaging with both CT and PET scans was performed to determine disease burden. Notably, the chest CT did not reveal thoracic lymphadenopathy or mass lesions, which points toward either primary hepatic involvement or an isolated extra-nodal process. Although primary hepatic lymphoma is exceptionally rare, especially in immunocompetent individuals with no history of chronic hepatitis B, hepatitis C, or HIV infection, it should still be considered in the differential diagnosis when hepatic masses are present without nodal disease or an identifiable primary tumor [10].

From a therapeutic perspective, management of high-grade B-cell lymphomas is influenced by both molecular subtype and clinical context. R-EPOCH, a regimen that includes rituximab, etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin, is often preferred for patients with high-risk features or double/triple-hit genetic abnormalities, given its superior central nervous system penetration and efficacy compared to R-CHOP [10]. In this case, bridging steroid therapy with dexamethasone was started while awaiting confirmatory FISH results, a standard approach in aggressive lymphomas. This early intervention can provide [11].

Prognosis in hepatic lymphomas is multifactorial. Key determinants include the patient's performance status, serum lactate dehydrogenase (LDH) concentration, International Prognostic Index (IPI) score, and the presence of genetic rearrangements such as MYC or BCL2. Early initiation of appropriate chemotherapy is crucial and has been associated with improved survival in patients with high-grade lymphomas. Ongoing follow-up, incorporating PET-CT imaging and routine liver function tests, is necessary to monitor therapeutic response and detect potential relapse at the earliest possible stage [12,13].

Conclusion

High-grade B-cell lymphomas should remain a consideration when evaluating patients with hepatic lesions, particularly if systemic symptoms are present and serological tests are non-diagnostic. Accurate diagnosis and effective management depend on a multidisciplinary team, with gastroenterology, oncology, pathology, and radiology all playing crucial roles. Ultimately, when hepatic pathology is ambiguous, liver biopsy remains an essential diagnostic tool.

Declarations
1. Funding
No specific funding was received for this study.
2. Conflicts of Interest / Competing Interests
The authors declare that they have no competing interests.
3. Ethics Approval
Not applicable.
4. Consent to Participate
Not applicable.
5. Written Consent for Publication
Written informed consent was obtained from the patient for publication of this case report and any accompanying images.
6. Availability of Data and Material (Data Transparency)
All data generated or analyzed during this study are included in this published article. No additional datasets were generated or analyzed beyond those presented in the manuscript.
7. Code Availability
Not applicable.
8. Authors' Contributions

- Nasim Salimiaghdam, MD: Conceptualized the case report, led data collection and clinical interpretation, drafted the manuscript, and coordinated revisions.
- Ummi Khan, MD: Contributed to clinical evaluation, provided internal medicine expertise, and critically revised the manuscript for important intellectual content.
- Ruchit Shah, MD: Contributed to diagnostic evaluation and interpretation, provided gastroenterology expertise, and critically reviewed the manuscript.

All authors read and approved the final manuscript and agree to be accountable for all aspects of the work.

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