Hepatic lymphoma presenting as liver abscess causing diagnostic dilemma: A case series

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SUMMARY

Hepatic lymphoma, including both primary and secondary involvement, can mimic liver abscesses due to overlapping clinical and radiological features. This case series presents four patients initially treated for liver abscesses based on symptoms of fever, abdominal pain, elevated inflammatory markers, and imaging showing hypodense liver lesions with rim enhancement. However, poor response to antibiotics prompted further evaluation. Biopsy and immunohistochemistry ultimately confirmed secondary hepatic lymphoma. These cases highlight the need to consider hepatic lymphoma in atypical or unresponsive liver abscess presentations. Early biopsy and histopathological analysis are essential for accurate diagnosis and timely initiation of appropriate lymphoma-directed therapy.

INTRODUCTION

Hepatic lymphoma is an uncommon cancer; it can be difficult to diagnose because of its vague symptoms. It can manifest as secondary hepatic lymphoma, in which the liver is impacted as a component of systemic lymphoma, or as primary hepatic lymphoma (PHL), which is limited to the liver with minimal nodal involvement.[1] Hepatic lymphoma is sometimes misinterpreted as more prevalent illnesses such as liver abscesses because of its rarity and overlapping clinical and radiological features with other hepatic lesions. Fever, pain in the right upper quadrant, and abnormal liver function tests are common presentations of liver abscesses, which are usually caused by bacteria, parasites, or fungi. Hypodense lesions with rim enhancement are frequently seen in imaging tests. Clinicians frequently start empirical antibiotic therapy and percutaneous drainage when confronted with such imaging findings. Alternative diagnoses should be considered if the clinical response is suboptimal. Radiological investigations play a crucial role in the initial evaluation of hepatic lesions. Abdominal ultrasonography (USG) often demonstrates hypoechoic lesions in the liver; however, these findings are nonspecific and may be observed in a broad spectrum of hepatic pathologies. Such lesions may reflect either benign or malignant hepatic conditions, including hepatic lymphoma, metastatic disease, pyogenic or amoebic abscesses, focal fatty changes, and hepatocellular carcinoma. In such cases, contrast-enhanced computed tomography (CECT) typically shows hypodense lesions with variable enhancement, often resembling liver abscesses. Magnetic resonance imaging (MRI) with the diffusion-weighted imaging (DWI) and hepatobiliary contrast agents can provide additional clues, with lymphoma often showing restricted diffusion and homogenous enhancement in later phases. Fluorodeoxyglucose positron emission tomography (FDG-PET/CT) is particularly useful in identifying systemic involvement, aiding in differentiation from isolated infections.[2]

This case series describes four patients who were initially diagnosed and treated as liver abscesses but were later found to have hepatic lymphoma. By presenting these cases, we aim to highlight the importance of maintaining a high index of suspicion in patients with atypical presentations or poor response to standard treatment, to avoid delays in appropriate management. A summary of the cases is presented in Table I.

CASE PRESENTATION

Case 1:

A 40-year-old male with newly diagnosed HIV infection presented with fever and epigastric pain for 3 months, associated with abdominal distension and jaundice. Laboratory tests showed leukocytosis with predominant neutrophils, elevated total bilirubin at 101.9 µmol/L (reference range: 3.4-20.5 µmol/L), ALT 87 U/L (0-55 U/L), and low inflammatory markers. Ultrasound (USG) revealed multiple hypoechoic lesions in the liver and splenic, with mild biliary dilatation, suggestive of metastatic disease. Contrast-enhanced CT (CECT) showed multiple hepatic and splenic masses; differentials included opportunistic infection in this immunocompromised patient. The patient was initially started on broad-spectrum antibiotics and antifungal. However, there was minimal clinical and laboratory improvement. A liver biopsy subsequently showed diffuse infiltration by large atypical lymphoid cells with high mitotic activity. Immunohistochemistry demonstrated diffuse CD20 and CD79a positivity, with CD10 and focal BCL6

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expression, consistent with diffuse large B-cell lymphoma (DLBCL), germinal center B-cell phenotype. Staging PET/CT demonstrated hepatomegaly with multiple hypermetabolic lesions in the liver and spleen (Figure 1).

Case 2:
A 21-year-old male with a history of immune thrombocytopenia in remission presented with lethargy, intermittent fever, loss of appetite and a 20 kg weight loss over 4 months. Full blood count was normal. However, total bilirubin was elevated at 49 µmol/L (3.4-20.5 µmol/L), ESR was 93 ml/hr (<15 mm/hr), C-reactive protein (CRP) 33.28 mg/dL (<0.3 mg/dL) and procalcitonin 0.39 ng/mL (<0.05 ng/mL). Abdominal ultrasound revealed multiple liver and splenic abscesses with several intra-abdominal lymph nodes; the largest lesion measured 2.3 x 4.0 cm in the spleen and 1.2 x 1.3 cm in the liver. CT abdomen and pelvis showed hepatosplenomegaly with multiple ill-defined lesions. He was initially treated with antibiotics, followed by empirical therapy for extrapulmonary tuberculosis. However, due to persistent fever and similar findings on post-treatment CT imaging, a liver biopsy was performed. Histology revealed granulomatous nodules containing scattered neoplastic cells with features of Reed-Sternberg and Hodgkin cells. The background revealed a mixed inflammatory infiltrate rich in eosinophils, reactive T lymphocytes, and histiocytes. Immunohistochemistry showed the neoplastic cells were positive for CD30 and PAX5, and negative for CD15, CD20, CD3, SMA, and CD34. These findings are consistent with classical Hodgkin lymphoma, likely of the mixed cellularity subtype.

Case 3:
A 65-year-old female with past medical history of type II diabetes mellitus, hypertension, and ischemic heart disease presented with prolonged fever, loss of appetite, and weight loss for 2 months. Initial blood test showed normal leukocyte count and liver enzyme level but elevated CRP at 20.8 mg/dL (<0.3 mg/dL). Blood culture on admission was positive for Salmonella non-typhi. In view of persistent fever during hospitalization, a CT scan was performed, revealing multiple ill-defined hypodense liver lesions (largest measuring 3cm x 3cm), likely representing liver abscess, along with intra-abdominal lymphadenopathy. Intravenous antibiotics were continued until a follow-up ultrasound revealed multiple ill-defined, partially liquefied hypoechoic liver collections at segment II, III, VI, and VII. Attempted pigtail drainage of the liver abscess yielded only approximately 3cc of cloudy fluid. A subsequent ultrasound performed three weeks after treatment showed no significant change in the liver lesions, with increasing size of segment III lesion and the appearance of new splenic lesions. Due to persistent fever and unresolved liver collections, a liver biopsy was performed. The liver biopsy showed diffuse infiltration by malignant lymphoid cells with enlarged pleomorphic nuclei, prominent nucleoli, occasional mitoses, and extensive necrosis, with no residual liver tissue. Immunohistochemistry was positive for CD20, BCL6, MUM1, and BCL2, negative for CD3, CD10, and CKAE1/AE3, with a high Ki-67 index of 80–90%, consistent with diffuse large B-cell lymphoma, activated B-cell subtype. Staging PET/CT revealed multiple hypermetabolic liver lesions (SUVmax: 21.2) along with hypermetabolic cervical, supraclavicular, axillary, and abdominopelvic lymph nodes (Figure 2).

Case 4:
A 38-year-old female with underlying paroxysmal supraventricular tachycardia was admitted for recurrent right parapneumonic effusion over the course of one month. Her full blood count and liver function test were normal, but CRP was elevated at 12 mg/dL (< 0.3 mg/dL). Pleural fluid drainage revealed an exudative picture, and pleuroscopy findings were unremarkable. Baseline abdominal ultrasound performed to investigate persistent fever showed hepatosplenomegaly with partially liquefied liver and splenic abscesses. Contrast-enhanced CT of the abdomen confirmed abscesses in segment V of the liver and the spleen, with surrounding inflammatory changes. She was treated empirically for disseminated tuberculosis but opted for early discharge. Approximately one month later, she re-presented with respiratory distress and required intubation. Repeated ultrasound showed unchanged liver and splenic lesion. Thus, a biopsy was performed and reported as diffuse large B-cell lymphoma, activated B-cell subtype. Unfortunately, the patient succumbed to secondary bacterial infection prior to the initiation of chemotherapy.

Table I: Typical Imaging Features of Liver Abscess and Hepatic Lymphoma Across Different Modalities

Imaging technique	Liver Abscess	Hepatic Lymphoma
CT	Typically appears hypodense with rim enhancement due to necrosis and inflammatory exudates. Gas bubbles may be present, especially in pyogenic abscesses caused by Klebsiella pneumoniae. Perilesional oedema and surrounding inflammatory changes are common.	Appears as a hypodense lesion, which may be solitary or multiple. They are often well-defined but lacks the classical rim-enhancement seen in abscesses. Necrosis, cavitation, and perilesional oedema are generally absent.
MRI	Demonstrates central necrosis, restricted diffusion on diffusion-weighted imaging (DWI), and perilesional oedema.	Lesions typically show homogeneous signal intensity, mild restricted diffusion, and absence of necrosis. The lack of perilesional inflammatory changes helps distinguish them from abscesses.
PET/CT	May exhibit mild-to-moderate FDG uptake	Shows intense FDG avidity due to the high metabolic activity of lymphoma.

Table II: Patient Demographic, Laboratory Findings, and Imaging Results

Clinical Data	Patient No.				Ref Range
	1	2	3	4	
Age, year	40	21	65	37	N/A
Sex	Male	Male	Female	Female	N/A
Comorbidities	RVD	ITP	DM/HPT//IHD	Paroxysmal SVT	N/A
Presentations Symptoms:					
Fever	+	+	+	+	N/A
Night sweats	-	+	+	+	N/A
LOA/LOW	+	+	+	+	N/A
Laboratory Findings:					
TWBC ($\times 10^9$/L)	14.3	4	9.3	10.5	4-10
LDH (U/L)	872	163	437	436	< 220
CRP (mg/dL)	1.05	33.28	20.81	7.93	< 0.3
PCT (ng/mL)	NA	0.39	0.21	0.26	< 0.05
CT Imaging Findings:	Multiple hypoechoic liver and splenic lesions	Multiple ill-defined non-enhancing hypodensities in liver. Multiple ill-defined non-enhancing hypodensities seen scattered throughout the spleen (largest 2.0 × 1.6 × 2.0 cm at inferior pole)	Multiple ill-defined hypodense liver lesion (largest 3cm x 3cm) suggestive of liver abscess with intraabdominal lymphadenopathy	Segment V liver and splenic abscesses with surrounding inflammatory changes	N/A
PET/CT	Hepatomegaly with multiple hypermetabolic liver and splenic lesions.	Not done	Multiple hypermetabolic liver lesion (SUVmax: 21.2) with multiple hypermetabolic cervical, supraclavicular, axillary, and abdominopelvic nodes	Not done	N/A
Initial diagnosis	Liver abscess	TB liver/spleen	Liver abscess	Disseminated TB	N/A
Definitive diagnosis	DLBCL, GCB subtype	Hodgkin Lymphoma, mixed cellularity subtype	DLBCL, ABC subtype	DLBCL, ABC subtype	N/A
Duration to diagnosis	10 days	30 days	39 days	32 days	N/A
Ann-Arbor Stage	IV	IV	IV	IV	N/A
Management	R-CHOP	ABVD	R-CHOP	NA	N/A
Outcome	CR	CR	CR	Deceased	N/A

Legend:
RVD: Retroviral Disease; ITP: Immune Thrombocytopenic Purpura; DM: Diabetes Mellitus; HPT: Hypertension; IHD: ischemic heart disease; SVT: Supraventricular Tachycardia; LOA: loss of appetite; LOW: loss of weight; TWBC: total white blood cells; LDH: Lactate Dehydrogenase; CRP: C-reactive protein; PCT: Procalcitonin; PET/CT: Positron Emission Tomography/Computed Tomography; TB: Tuberculosis; DLBCL: Diffuse Large B-cell Lymphoma; R-CHOP: Rituximab, Cyclophosphamide, Doxorubicin, Vincristine, and Prednisone; ABVD: Adriamycin (doxorubicin), Bleomycin, Vinblastine, and Dacarbazine; CR: complete remission; N/A: not available
GCB: germinal centre B-cell
ABC: activated B-cell

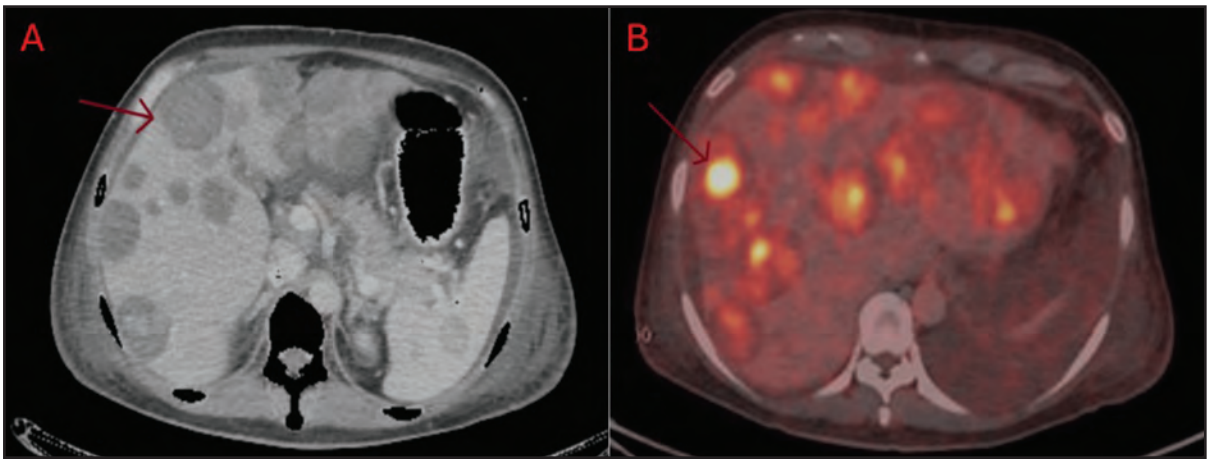

Fig. 1: Imaging Finding for Case 1: (A) Transaxial CT image showing multiple hypodense lesions in the liver (red arrow); (B) Corresponding PET/CT fusion image demonstrating diffusely increased FDG uptake in the liver (red arrow)

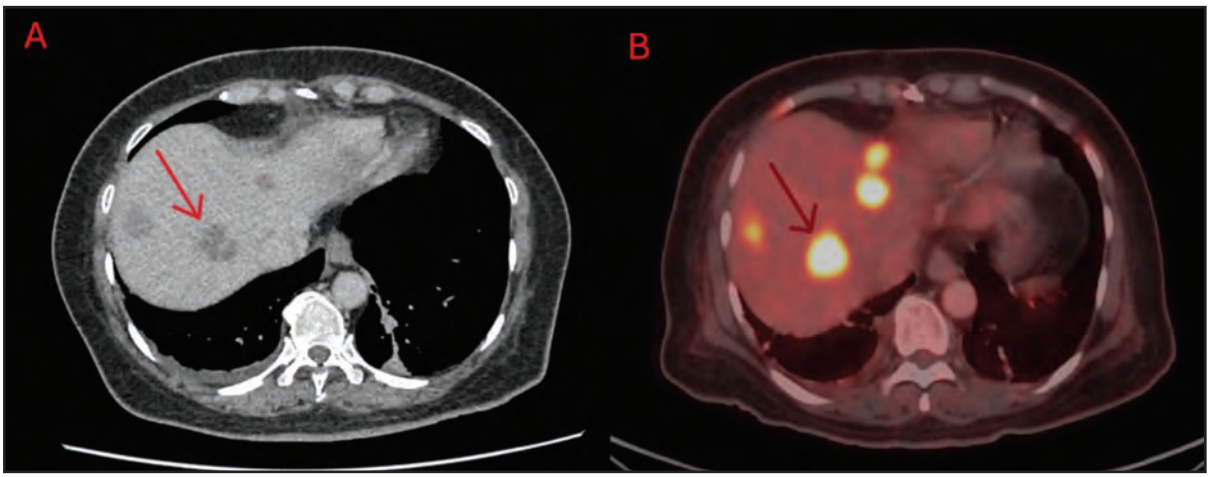

Fig. 2: Imaging Finding for Case 3: (A) Transaxial CT image showing multiple hypodense lesions in the liver (red arrow); (B) Corresponding PET/CT fusion image demonstrating diffusely increased FDG uptake in the liver (red arrow)

DISCUSSION

Hepatic lymphoma has been diagnosed in individuals aged 8 to 78 years (mean age: 48 years) and predominantly affects males.[1] This case series underscores the diagnostic dilemmas, radiological pitfalls, and critical role of histopathological confirmation in distinguishing hepatic lymphoma from infectious and inflammatory hepatic lesions. The clinical manifestations of hepatic lymphoma include right upper abdomen pain (43%), weight loss (35%), and fever (22%), and it has been associated with hepatitis B, hepatitis C, and human immunodeficiency virus.[3] In contrast, liver abscesses typically present with high fever, leukocytosis, right upper quadrant tenderness, and elevated inflammatory markers (CRP, ESR, procalcitonin).[4] These overlapping systemic inflammatory responses make symptom-based differentiation unreliable.

Xin Wei Yang et al. from China reported nine patients who were initially misdiagnosed with α-fetoprotein-negative hepatocellular carcinoma prior to pathological evaluation. The average delay from symptom onset to final diagnosis was 26.8 days (range: 14-47 days).[5] In our case series, all four patients were initially suspected of having liver abscesses based on presenting symptoms and imaging findings. They were empirically treated with broad-spectrum antibiotics or anti-tuberculosis medications, according to the working diagnosis. However, persistent symptoms despite adequate antibiotic therapy raised suspicion of an alternative aetiology. This underscores the importance of considering hepatic lymphoma in cases of liver abscess with poor clinical and radiological response.

Primary hepatic lymphoma (PHL) is extremely uncommon, as a healthy liver typically possesses a minimal interstitial component, with lymphocytes confined primarily to the portal region. As a result, liver lesions classified as lymphoma are more frequently observed as secondary extranodal infiltrations, as shown in the cases reported here. PHL was documented in only 6 cases (0.41%) in a study of 1,467 extranodal lymphoma cases conducted by Freeman et al.[6] Laboratory abnormalities associated with hepatic lymphoma include anaemia, neutropenia, hypercalcaemia and variably elevated levels of lactate dehydrogenase (LDH), serum alkaline phosphatase, β-microglobulin and aminotransferase activities.

Radiological examination is essential in the diagnosis of hepatic lesions. Secondary hepatic lymphoma is typically associated with nodal disease. Conversely, diagnosing primary hepatic lymphoma can be challenging, as it frequently mimics hepatocellular carcinoma or liver metastases from adenocarcinoma.[2] Imaging characteristics of hepatic lymphoma include a low-density mass on non-contrast CT, a slightly or internally enhanced mass on contrast-enhanced CT, and a homogeneously low-echo mass on ultrasonography. MRI can be particularly helpful in supporting the diagnosis of a lymphoma, when no morphological features of cirrhosis are evident in the surrounding liver parenchyma, when the tumour markers are negative, and when the hepatic lesion demonstrates iso-intensity with spleen parenchyma in both T1- and T2-weighted images.[2] FDG-PET may exhibit markedly diffuse hepatic tracer uptake, which can serve as the initial indicator of significant hepatic involvement.[7] In Cases 1 and 3, PET/CT revealed hypermetabolic hepatic and nodal involvement, prompting a diagnostic revision from infection to lymphoma. This underscores the diagnostic utility of PET/CT in cases where conventional imaging proves inconclusive. A study by Jia Chen et al. concluded that PET/CT demonstrates moderate sensitivity but low specificity for diagnosing lymphoma in patients with fever of unknown origin and lymphadenopathy.[8] However, due to limited resources, PET/CT imaging is not widely available at government hospitals. A summary of the radiological findings is presented in Table II.

Extended courses of antibiotic treatment should be avoided. Given the diagnostic ambiguity of hepatic lesions with overlapping imaging features, liver biopsy remains the gold standard for diagnosis. In our cases, image-guided core needle biopsies (CT- or US-guided) confirmed hepatic lymphoma through histopathology and immunohistochemistry (IHC). Once the diagnosis of lymphoma is established, the management strategy shifts significantly from treating infectious diseases to administering systemic chemotherapy. Diffuse large B-cell lymphoma is treated with the R-CHOP regimen, which includes rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone. ABVD (adriamycin, bleomycin, vinblastine, and dacarbazine) or more intensive regimens are used for patients with Hodgkin's lymphoma, depending on risk stratification.[9]

In all four cases, there were therapeutic delays prior to the accurate diagnosis of lymphoma. A liver biopsy should be considered in cases not responding to standard treatment. Delayed biopsy may lead to prolonged hospitalization, unnecessary procedures, and potential adverse outcomes. A multidisciplinary approach is essential; collaboration among radiologists, infectious disease physicians, and haematologists is critical for timely diagnosis and prevention of mismanagement.

CONCLUSION

Hepatic lymphoma masquerading as a liver abscess is an uncommon yet clinically significant presentation that poses both diagnostic and therapeutic challenges. This case series underscores the importance of maintaining a high index of suspicion for lymphoma in patients with atypical liver abscesses, particularly those unresponsive to standard antimicrobial therapy. Early integration of advanced imaging and histopathological evaluation is essential for accurate diagnosis and timely initiation of appropriate treatment. Further studies are warranted to better characterize this rare entity and to optimize management strategies aimed at improving patient outcomes.

DECLARATION

It is hereby acknowledged that consent for publication has been obtained from the patients or their caregiver.

CONFLICTS OF INTEREST

None.

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