Case Report

Primary Hepatic Diffuse Large B-Cell Lymphoma: A Diagnostic Challenge Mimicking Cholangiocarcinoma: Diagnostic Pitfalls and Role of Timely Biopsy

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Abstract

Primary hepatic diffuse large B-cell lymphoma (DLBCL) is a rare malignancy that is often misdiagnosed as hepatocellular carcinoma or cholangiocarcinoma due to nonspecific radiological findings, highlighting diagnostic challenges and underscoring the critical role of systematic biopsy. A 67-year-old Malay woman presented with progressive jaundice, abdominal distension and weight loss. Cross-sectional imaging revealed an infiltrative hepatic mass with vascular involvement, initially suggestive of cholangiocarcinoma. Two percutaneous core biopsies were nondiagnostic, with definitive DLBCL diagnosis (germinal center B-cell subtype) achieved through subsequent laparoscopic wedge biopsy. The patient commenced rituximab, cyclophosphamide, doxorubicin, vincristine, prednisolone (R-CHOP) chemotherapy with good tolerance. Primary hepatic lymphoma should be considered in atypical liver masses, particularly with inconclusive initial biopsies. A structured approach beginning with image-guided coaxial biopsy and escalating to surgical biopsy when necessary is essential to avoid diagnostic delays. Modern coaxial techniques minimise tumour seeding risk and should not deter adequate tissue sampling.

Keywords: Cholangiocarcinoma mimic; diagnostic challenge; diffuse large B-cell lymphoma; liver biopsy; primary hepatic lymphoma

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Introduction

Diffuse large B-cell lymphoma (DLBCL) is the most common subtype of non-Hodgkin lymphoma. However, primary hepatic involvement is exceptionally rare, accounting for less than 0.1% of all extranodal lymphomas (1). The clinical and radiological presentation of primary hepatic DLBCL is nonspecific, often mimicking more common hepatic malignancies such as hepatocellular carcinoma or cholangiocarcinoma. This frequently leads to diagnostic delays. As the curative treatment for lymphoma (systemic immunochemotherapy) is entirely different from that for primary liver cancers, obtaining a timely and accurate histological diagnosis is paramount (2,3). This case report illustrates these diagnostic pitfalls and demonstrates the successful application of a stepwise biopsy strategy to achieve a definitive diagnosis.

Case report

A 67-year-old Malay woman presented with a three-month history of progressive abdominal distension, jaundice, generalised pruritus and an unintentional weight loss of 7 kg. Her past medical history included type 2 diabetes mellitus, hypertension and stage I left breast carcinoma treated with mastectomy and adjuvant chemotherapy in 2008, with no evidence of recurrence.

Physical examination revealed cachexia, scleral icterus and a firm, nodular mass palpable in the epigastrium. No peripheral lymphadenopathy was detected. Initial

laboratory investigations showed a cholestatic pattern of liver enzyme elevation. Serological tests for viral hepatitis B surface antigen and anti-hepatitis C virus antibody were negative. Tumour markers were largely unremarkable, except for a mildly elevated carcinoembryonic antigen (CEA) level of 41 U/mL.

An abdominal ultrasound demonstrated multiple bilobar hypoechoic liver lesions. Contrast-enhanced computed tomography (CT) of the abdomen revealed an infiltrative mass in the left hepatic lobe with associated vascular encasement and mild intrahepatic biliary dilatation (Fig. 1). Incidental findings included a hypodense splenic lesion and a wedge-shaped renal infarct. The initial radiological impression favoured cholangiocarcinoma. However, several features were atypical for cholangiocarcinoma, including the absence of arterial phase hyperenhancement or delayed centripetal enhancement (Fig. 2), vascular encasement without luminal obstruction, normal alpha-fetoprotein (AFP) and carbohydrate antigen 19-9 (CA19-9) levels, and the presence of marked constitutional symptoms. These discordant findings prompted further evaluation for an alternative infiltrative malignancy, including lymphoma. Subsequent positron emission tomography-computed tomography demonstrated intense diffuse fluorodeoxyglucose uptake within the hepatic mass and spleen, a metabolic pattern that, while not specific, was more characteristic of lymphoproliferative disease than cholangiocarcinoma and further increased suspicion for lymphoma.

A diagnostic biopsy was pursued. An initial ultrasound-guided percutaneous core biopsy using an 18-gauge Temno needle yielded only benign inflammatory tissue, likely reflecting sampling limitations in a diffusely infiltrative lesion. A second ultrasound-guided percutaneous biopsy using an 18-gauge coaxial semi-automatic core biopsy system was performed to improve tissue yield; however, this also remained nondiagnostic, reinforcing concern for an infiltrative process with architectural distortion (4,5). Due to the high clinical suspicion for lymphoma and the nondiagnostic percutaneous biopsies, the patient underwent a diagnostic laparoscopy. Intraoperative findings included a nodular liver surface and minimal ascites. A wedge biopsy of liver segment III was performed.

Histopathological examination of the surgical specimen revealed a diffuse infiltrate of large, atypical lymphoid cells replacing the normal liver architecture (Fig. 3). On immunohistochemistry, the cells were positive for CD20 (Fig. 4), CD79a, and BCL-6, and negative for CD3, CD5, CD10, MUM1, c-MYC, and BCL-2 (in <50% of cells). The Ki-67 proliferation index was approximately 80% (Fig. 5). These findings confirmed the diagnosis of diffuse large B-cell lymphoma, germinal centre B-cell (GCB) subtype.

Staging work-up, including bone marrow trephine biopsy and cerebrospinal fluid cytology, showed no evidence of extrahepatic involvement, confirming the

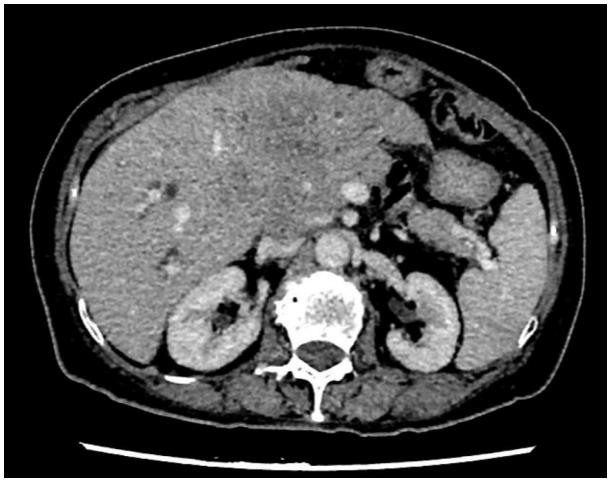

FIGURE 1: Axial contrast-enhanced computed tomography image of the abdomen showing an ill-defined, hypoenhancing infiltrative mass involving both hepatic lobes (white arrows), occupying segment II, III, IVa, IVb, V and VIII. The lesion demonstrated vascular encasement with mild intrahepatic ductal dilatation

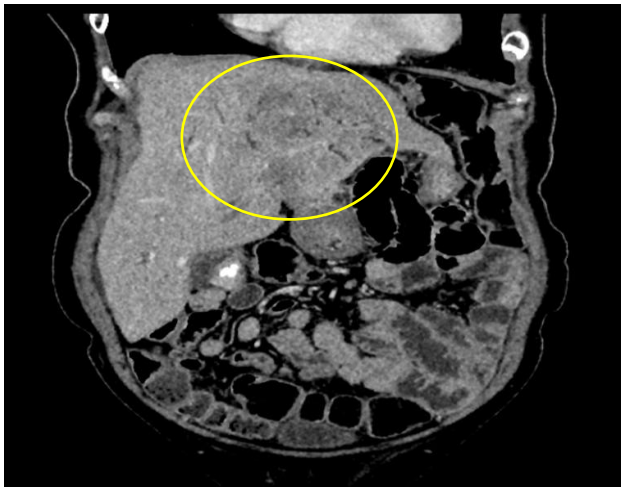

FIGURE 2: Coronal view contrast-enhanced computed tomography image demonstrating no arterial enhancing component within this mass (yellow circle). No gradual centripetal enhancement. This mass remained isodense to liver in delayed phase.

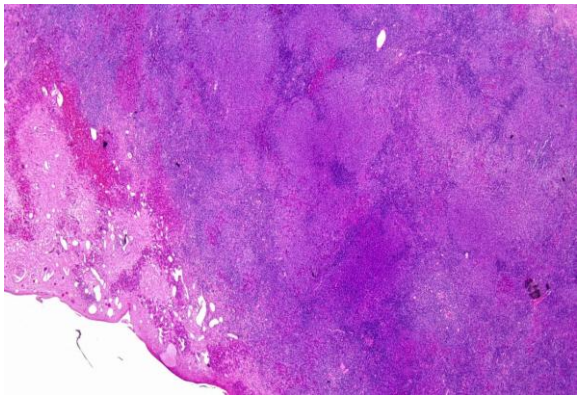

FIGURE 3: Malignant lymphoid cells arranged in sheets. Low-power photomicrograph (H&E stain) showing diffuse sheets of atypical lymphoid cells replacing the normal architecture

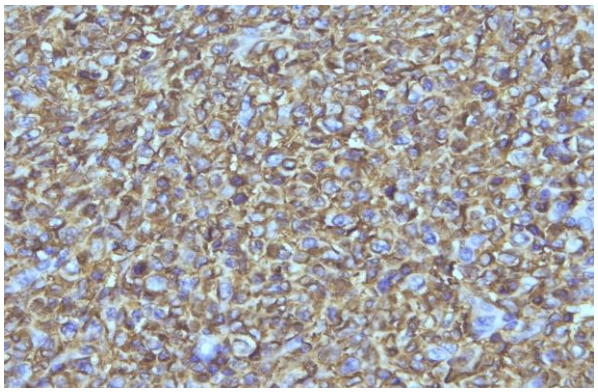

FIGURE 4: Immunohistochemical stain for CD20 highlighting a monomorphic population of B-lymphocytes. (Original magnification, 200X).

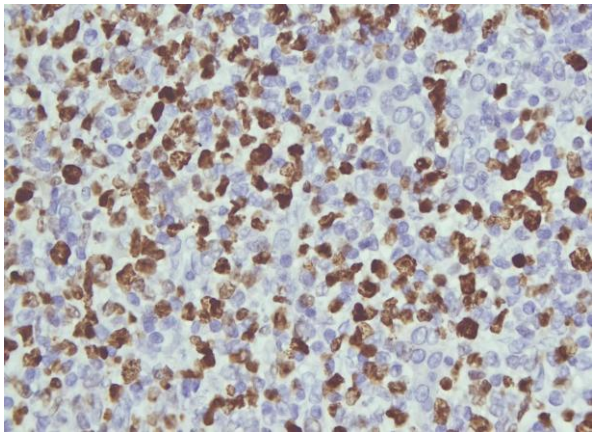

FIGURE 5: Photomicrograph of a tissue section stained with an anti-Ki-67 antibody (brown nuclear staining) demonstrating a high proliferative index of approximately 80%. This indicated a high proportion of tumour cells were actively dividing

diagnosis of primary hepatic DLBCL, Ann Arbor stage IE. The patient was commenced on rituximab, cyclophosphamide, doxorubicin, vincristine, prednisolone (R-CHOP) immunochemotherapy in line with standard guidelines (3) and had tolerated the first four cycles well without major complications. Contrast-enhanced computed tomography (CECT) neck, thorax, abdomen and pelvis on 12th of November 2025 showed treatment response as evidenced by smaller liver lesion.

Discussion

This case underscores several key challenges in diagnosing primary hepatic lymphoma. First, its rarity and nonspecific presentation often lead to an initial misdiagnosis of carcinoma, a pitfall particularly common in regions like Southeast Asia, where the prevalence of viral hepatitis and hepatocellular carcinoma is high (1). In our patient, the initial radiological diagnosis was cholangiocarcinoma, which delayed the correct diagnosis.

Percutaneous image-guided core biopsy remains the recommended first-line diagnostic modality for suspected primary hepatic lymphoma due to its minimally invasive nature and favourable safety profile (3,4). However, in diffusely infiltrative disease, sampling error is well recognised. In this case, two adequately performed percutaneous core biopsies including the use of a coaxial system-diagnostic tissue could not be obtained. Given the persistently high clinical suspicion and progressive disease, escalation to laparoscopic wedge biopsy was necessary to obtain sufficient tissue architecture for definitive histopathological and immunohistochemical analysis.

Second, the case highlights the critical importance of an adequate tissue sample. While current guidelines endorse percutaneous image-guided core biopsy as the safe and effective first-line diagnostic modality (3,4), it can be nondiagnostic in infiltrative lesions due to sampling error or extensive fibrosis (5). The use of a coaxial system, as in our patient's second biopsy, minimises the risk of needle-tract seeding and allows for multiple samples, but it does not guarantee diagnostic success in all cases (6,7). Our experience confirms that when clinical suspicion remains high despite nondiagnostic percutaneous biopsies, laparoscopic or open biopsy is a necessary and definitive next step to obtain sufficient tissue for architectural assessment and ancillary studies (8).

The timely and accurate diagnosis achieved through this stepwise approach directly impacted patient management. It allowed for the prompt initiation of R-

CHOP chemotherapy, the standard first-line regimen for DLBCL (3). The patient's good tolerance of initial therapy is an encouraging prognostic indicator. While primary hepatic DLBCL has a variable prognosis, modern immunochemotherapy has significantly improved outcomes, with reported 5-year survival rates now exceeding 50% in some series (1,8).

Compared with percutaneous core biopsy, laparoscopic biopsy allows acquisition of a larger tissue specimen, preservation of architectural features, and performance of comprehensive immunophenotyping and proliferation index assessment, all of which are critical for the accurate diagnosis of lymphoma.

This report adds to the sparse literature on this entity, particularly from the Malaysian context. It serves to increase awareness among hepatologists, surgeons and oncologists, promoting the consideration of lymphoma in the differential diagnosis of atypical liver masses.

Conclusion

Primary hepatic diffuse large B-cell lymphoma can closely mimic cholangiocarcinoma, leading to diagnostic delay if lymphoma is not actively considered. In patients with atypical imaging features and incongruent tumour markers, early pursuit of adequate tissue diagnosis is critical. When percutaneous biopsies are nondiagnostic, timely escalation to surgical biopsy should not be delayed. Prompt histological confirmation allows appropriate initiation of immunochemotherapy and can significantly alter prognosis in this otherwise treatable malignancy

Learning Points

(i) Consider lymphoma in atypical liver masses. Primary hepatic DLBCL is rare but should be considered in patients with liver masses demonstrating non-specific or discordant imaging findings and incongruent tumour marker profiles (1,2).
(ii) Adopt a stepwise biopsy strategy. Percutaneous image-guided core biopsy with a coaxial system is the recommended first step (3,4). If nondiagnostic, surgical (laparoscopic or open) biopsy should be pursued promptly without undue concern for tumour seeding (6,7).
(iii) Timely diagnosis directly influences outcomes. A definitive histopathological diagnosis is a prerequisite for initiating potentially curative immunochemotherapy and avoiding delays that can compromise patient prognosis (3).

Conflict of interest: The authors declare no conflicts of interest.

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Ethics statement: Written informed consent was obtained from the patient for publication of this case report and any accompanying images. The authors confirm compliance with institutional ethical standards and the principles of the Declaration of Helsinki.

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