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CASE REPORT | LIVER

# Challenges in Diagnosis: Primary Hepatic Lymphoma Presenting as a Space-Occupying Liver Lesion

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## ABSTRACT

Non-Hodgkin lymphoma is a heterogeneous group of lymphoid neoplasms, the incidence of which has increased over the past 3 decades. Primary non-Hodgkin lymphoma of the liver is a very rare malignancy. We outline a case describing primary hepatic lymphoma in an 85-year-old woman with a history of breast cancer who presented with generalized weakness and nonspecific symptoms. The patient had normal liver function, serum alpha fetoprotein level, and hemoglobin. A computed tomography scan of the chest, abdomen, and pelvis showed numerous low-attenuation lesions scattered throughout the liver. This case underscores the importance of including primary hepatic lymphoma as a differential diagnosis for space-occupying liver lesions, especially in the setting of normal alpha fetoprotein level.

**KEYWORDS:** lymphoma; liver; cancer

## INTRODUCTION

Primary hepatic lymphoma (PHL) is a lymphoma limited to the liver or having major liver involvement without evidence of extrahepatic involvement (eg, no spleen, lymph nodes, bone marrow, peripheral blood, or other lymphoid structures) for at least 6

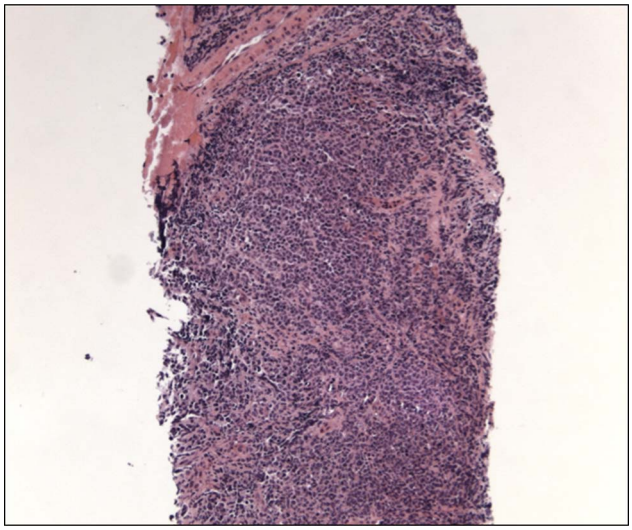

**Figure 1.** Pathology specimen with hematoxylin and eosin (H&E) stain at 100× magnification. The H&E stain reveals characteristic features suggestive of B-cell lymphoma with germinal center subtype.

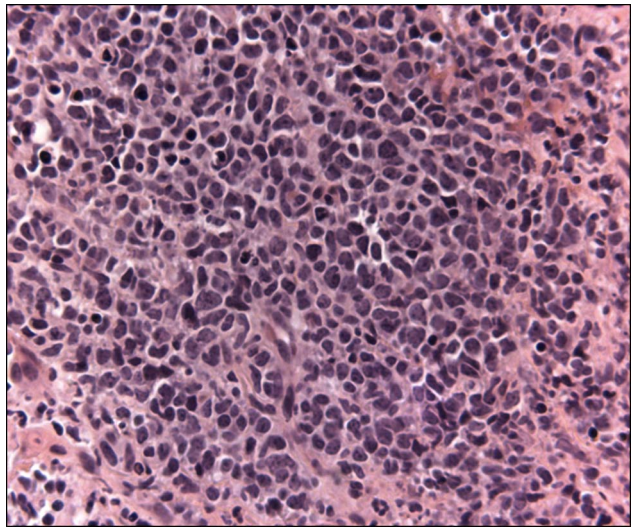

**Figure 2.** Pathology specimen with hematoxylin and eosin (H&E) stain at 400× magnification. The H&E stain reveals characteristic features suggestive of B-cell lymphoma with germinal center subtype.

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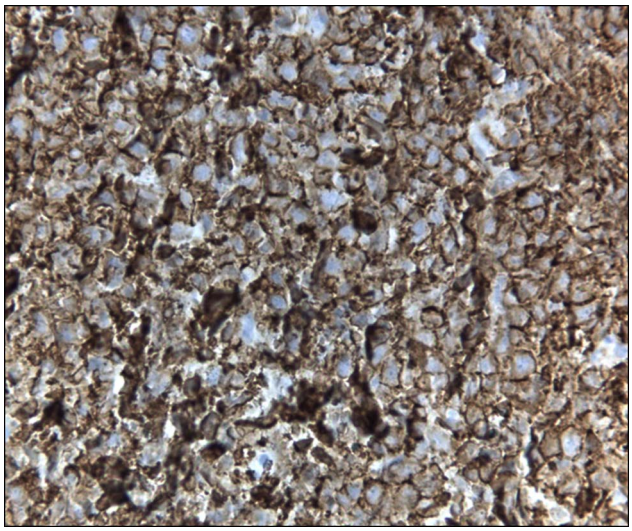

**Figure 3.** CD20 immunostain, which labels B cells. The brown staining indicates the presence of CD-20-positive B cells within the liver tissue.

months.[1] PHL is rare and represents 0.4% of extranodal non-Hodgkin lymphomas and 0.016% of all non-Hodgkin lymphomas and is most commonly a sequelae of chronic hepatitis C infection.[1,2] Based on liver infiltration, PHL can be subdivided into uninodular (39%–42%), multinodular (50%–55%), and diffuse (6%–8%) types.[3,4] We present a case of multinodular PHL in a patient with a history of breast cancer in remission.

## CASE REPORT

An 85-year-old female nonsmoker with a medical history of hypertension, chronic kidney disease stage III B, localized breast cancer s/p lumpectomy, and hormonal therapy presented to the hospital with 2 days duration of generalized weakness, myalgia, abdominal discomfort, nausea and vomiting, and reduced oral intake. On presentation, she was hypotensive, tachypneic, and afebrile. Liver function tests and bilirubin were unremarkable. Complete blood count showed normal hemoglobin, platelets, and white blood cell levels. Computed tomography scan of the chest, abdomen, and pelvis revealed bilateral ground glass nodules in the lower lobes of lungs and numerous low-attenuation lesions scattered throughout the liver which was suspicious for metastatic disease in the setting of a remote history of breast cancer which was originally treated with lumpectomy and anastrozole which was completed 10 years before presentation.

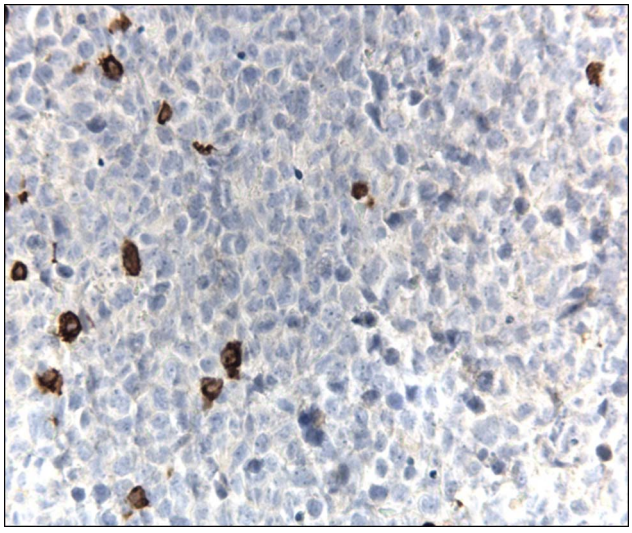

**Figure 4.** CD3 immunostain, which labels T cells. The very minimal staining indicates the low presence of T cells within the liver tissue.

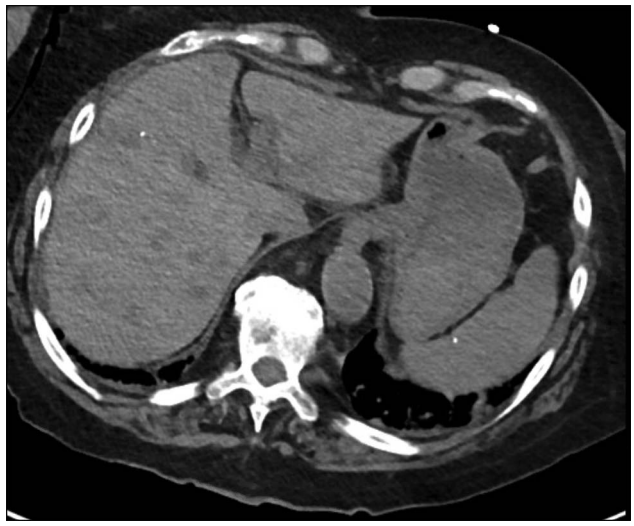

**Figure 5.** Computed tomography scan of the chest, abdomen, and pelvis showing numerous low-attenuation lesions scattered throughout the liver.

Patient subsequently underwent a bone scan and magnetic resonance imaging of the brain which were negative for bone and intracranial metastasis. Tumor markers including alpha fetoprotein level were noted to be negative. Lactate dehydrogenase was elevated at 478 U/L. The patient further underwent a computed tomography-guided liver biopsy, and histopathology revealed an aggressive diffuse large B-Cell lymphoma (DLBCL), germinal center subphenotype. Immunohistochemical stains were positive for CD-10, CD-20, and BCL-6 and negative for BCL-2, MUM-1, CD5, and cyclin D1. Fluorescence in situ hybridization was negative for BCL-2, BCL-6, and MYC rearrangements (Figures 1–5). The patient refused a bone marrow biopsy. She was subsequently seen by medical oncology who recommended treatment with mini R-CHOP (rituximab, cyclophosphamide, hydroxydaunorubicin, oncovin, prednisolone). Unfortunately, the patient declined treatment due to concerns about side effects and opted for hospice. She subsequently died.

## DISCUSSION

PHL was initially described as a disease entity in the 1960s. Subsequently, in 1986, Caccamo et al provided a more detailed definition, specifying it as a lymphoma primarily localized to

the liver with no extrahepatic spread.[5] PHL is rare, and DLBCL is the most common subtype. The etiology of primary hepatic DLBCL is unknown. However, immunocompromised patients are considered to be more vulnerable. Certain viral infections including Epstein-Barr virus, chronic hepatitis B, chronic hepatitis C, human immunodeficiency virus, chronic liver disease, and autoimmune conditions may promote development of this rare cancer.[6–8] Although our patient did not have a viral infection or an autoimmune diagnosis, we hypothesize that having a diagnosis of prior malignancy and undergoing chemotherapy and/or hormonal therapy renders patients susceptible to development of secondary malignancies including PHL, given the possibility of genetic mutations, hereditary cancer syndromes, or side effects of prior therapy.

The differential diagnosis for multiple liver lesions must remain broad and should always include, in addition to lymphoma, other infiltrative processes of the liver including hepatocellular carcinoma, metastatic malignancy, sarcoidosis, tuberculosis, and hemochromatosis.[8] Given the nonspecific symptoms, a high level of suspicion is required for the diagnosis of PHL. Tumor markers including alpha fetoprotein level and continuing education unit are usually normal. A liver biopsy is considered the gold standard for the diagnosis of PHL, which is confirmed by histology and immunohistochemistry.[9] Treatment options usually include either chemotherapy alone or rarely surgical resection or radiation in addition to chemotherapy.[1] PHL is generally considered a chemosensitive tumor with a complete response of 85% with chemotherapy and an event-free survival of 70%.[10] In older patients, mini R-CHOP regimen, where attenuated doses of cyclophosphamide, doxorubicin, and vincristine are used, is shown to have good responses with tolerable side effects.[11]

Since DLBCL presents with nonspecific symptoms and indeterminate radiographic findings, a high index of clinical suspicion and low threshold to obtain a biopsy is important to confirm the diagnosis of primary hepatic DLBCL. Our case highlights the importance of performing a biopsy of any concerning new lesion on imaging, not only to help with diagnosis but to see if tolerable treatments with good efficacy can be administered. Prior history of chemotherapy should always alert clinicians toward a diagnosis of secondary malignancies including lymphomas, and the differential should be broad.

## DISCLOSURES

Author contributions: R. Vasireddy: study idea, information acquisition, data interpretation and manuscript writing/initial review. M.M. Bilalaga: review and editing. J. Iding: pathology review. A. Sankineni is the article guarantor.

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Informed consent was obtained for this case report.

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## REFERENCES

1. Noronha V, Shafi NQ, Obando JA, Kummar S. Primary non-Hodgkin's lymphoma of the liver. *Crit Rev Oncol Hematol.* 2005;53(3):199–207.
2. Santos ES, Raez LE, Salvatierra J, Morgensztern D, Shanmugan N, Neff GW. Primary hepatic non-Hodgkin's lymphomas: Case report and review of the literature. *Am J Gastroenterol.* 2003;98(12):2789–93.
3. Page RD, Romaguera JE, Osborne B, et al. Primary hepatic lymphoma: Favorable outcome after combination chemotherapy. *Cancer.* 2001;92(8):2023–9.
4. Bronowicki JP, Bineau C, Feugier P, et al. Primary lymphoma of the liver: Clinical-pathological features and relationship with HCV infection in French patients. *Hepatology.* 2003;37(4):781–7.
5. Caccamo D, Pervez NK, Marchevsky A. Primary lymphoma of the liver in the acquired immunodeficiency syndrome. *Arch Pathol Lab Med.* 1986;110(6):553–5.
6. Swadley MJ, Deliu M, Mosunjac MB, Gunthel CJ, Nguyen ML, Hanley KZ. Primary and secondary hepatic lymphomas diagnosed by image-guided fine-needle aspiration: A retrospective study of clinical and cytomorphologic findings. *Am J Clin Pathol.* 2014;141(1):119–27.
7. Emile JF, Azoulay D, Gornet JM, et al. Primary non-Hodgkin's lymphomas of the liver with nodular and diffuse infiltration patterns have different prognoses. *Ann Oncol.* 2001;12(7):1005–10.
8. Dhingra R, Winter MW, Yilmaz OH, Jaiswal S, Sterling M. An unusual presentation of primary hepatic diffuse large B-cell lymphoma of the liver. *Cureus.* 2018;10(2):e2242.
9. Masood A, Kairouz S, Hudhud KH, Hegazi AZ, Banu A, Gupta NC. Primary non-Hodgkin lymphoma of liver. *Curr Oncol.* 2009;16(4):74–7.
10. Liu Y, Jiang J, Wu Q, et al. A case of primary hepatic lymphoma and related literature review. *Case Rep Hepatol.* 2016;2016:6764121.
11. Peyrade F, Jardin F, Thieblemont C, et al. Attenuated immunochemotherapy regimen (R-miniCHOP) in elderly patients older than 80 years with diffuse large B-cell lymphoma: A multicentre, single-arm, phase 2 trial. *Lancet Oncol.* 2011;12(5):460–8.

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